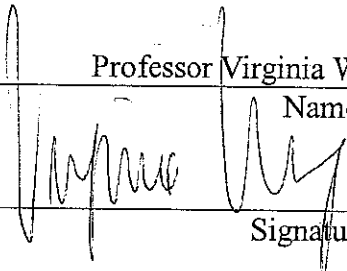
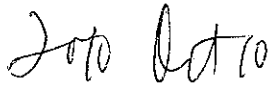




HKU/HA HKW IRB
STANDARD OPERATING PROCEDURES

In Accordance with
The Declaration of Helsinki
and
The ICH GCP (E6) Guideline
and
Local Regulations

APPROVED BY :

	Professor Virginia Wong, Chairman, IRB
	Name/Title
	
	Signature / Date

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1. GOALS OF HKU/HA HKW IRB

1.1 Primary Goal of HKU/HA HKW IRB

The primary goal of the HKU/HA HKW IRB is to ensure that, in research involving human subjects undertaken by full-time staff at the Faculty of Medicine The University of Hong Kong (HKU) and Hong Kong West Cluster Hospitals, Hospital Authority (HKW, HA), the rights and welfare of human subjects are adequately protected. To achieve this goal the HKU/HA HKW IRB will, assist investigators in designing their research projects in a manner to minimise potential harm to human subjects, review all planned research involving human subjects prior to initiation of the research, subsequently approve research that meets established criteria for protection of human subjects, and monitor approved research to ascertain that human subjects are indeed protected.

1.2 Secondary Goals of HKU/HA HKW IRB

Secondary goals of the HKU/HA HKW IRB are, to inform and assist HKU and HKW, HA and its researchers on ethical and procedural issues relating to the use of human subjects in research, to facilitate compliance with relevant regulations including the Personal Data (Privacy) Ordinance of the Hong Kong Special Administrative Region (SAR) Government, and to provide a framework suitable for continued support by Government agencies, private foundations and the industry for research involving human subjects at HKU and HKW, HA.

2. ROLE OF HKU/HA HKW IRB

1. The HKU/HA HKW IRB reports directly to the Dean of the Faculty of Medicine, and to the Cluster Chief Executive (CCE) of HKW, HA, Hong Kong SAR.
2. To conform to the Principles of the ICH GCP guideline E6 and the Declaration of Helsinki (version 1996) and to implement the regulatory procedures mandated by the Hong Kong SAR Government and guidance issued by the FDA and the Office of Human Research Protection (OHRP) under U.S. Department of Health and Human Services (HHS, FDA).

2.1 Region of Supervision of HKU/HA HKW IRB

In this document, the abbreviation "HKU/HA HKW IRB" indicates the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster.

The Hong Kong West Kong West Cluster hospitals of the Hospital Authority, include:

- Queen Mary Hospital
- Tsan Yuk Hospital
- Fung Yiu King Hospital
- Tung Wah Hospital
- Grantham Hospital
- Duchess of Kent Children's Hospital
- MacLehose Medical Rehabilitation Centre

The following categories of research involving human subjects may only be initiated after review and approval by the HKU/HA HKW IRB:

1. Research that is to take place on the premises of Hong Kong West Cluster Hospitals.
2. Research that is to take place elsewhere, and involves a full-time employee of HKU or the Hong Kong West Cluster hospitals.

At its discretion, the HKU/HA HKW IRB may accept for review and approve research projects that are to take place elsewhere in Hong Kong, off the premises of HKU and any Hong Kong West Cluster Hospitals. This includes multicentre clinical trials at any other HA hospital included in any of the following HA hospital clusters:

Hong Kong East Cluster

Cheshire Home, Chung Hom Kok
Pamela Youde Nethersole Eastern Hospital
Ruttonjee Hospital
St. John Hospital
Tang Shiu Kin Hospital
Tung Wah Eastern Hospital
Wong Chuk Hang Hospital

Hong Kong West Cluster

Duchess of Kent Children's Hospital at Sandy Bay
Grantham Hospital
MacLehose Medical Rehabilitation Centre
Queen Mary Hospital
Tsan Yuk Hospital
Tung Wah Group of Hospitals - Fung Yiu King Hospital
Tung Wah Hospital

Kowloon Central Cluster

HK Red Cross Blood Transfusion Service
Hong Kong Buddhist Hospital
Hong Kong Eye Hospital
Kowloon Hospital
Queen Elizabeth Hospital
Rehabaid Centre

Kowloon East Cluster

Haven of Hope Hospital
Tseung Kwan O Hospital
United Christian Hospital

Kowloon West Cluster

Caritas Medical Centre
Kwai Chung Hospital
Kwong Wah Hospital
Our Lady of Maryknoll Hospital
Princess Margaret Hospital
TWGHs Wong Tai Sin Hospital
Yan Chai Hospital

New Territories

Alice Ho Miu Ling Nethersole Hospital
Bradbury Hospice
Cheshire Home, Shatin
North District Hospital
Prince of Wales Hospital
Shatin Hospital

New Territories West Cluster

Tai Po Hospital
Castle Peak Hospital
Pok Oi Hospital
Siu Lam Hospital
Tuen Mun Hospital

2.2 Authority of HKU/HA HKW IRB in Overseeing Research Involving Human Subjects

HKU/HA HKW IRB is mandated to review and monitor any and all types of research, in which human subjects are involved. No research involving human subjects at HKW hospitals will be given exemption from HKU/HA HKW IRB review.

The authority conveyed to the HKU/HA HKW IRB includes the following:

1. To review all research projects involving human subjects.

2. To require from Investigators revisions in research protocols and informed consent documents, as a condition for initial or continuation approval.
3. To approve new research projects and continuation of previously approved projects.
4. To disapprove the initiation of a new research project.
5. To monitor the activities in approved projects, in any way deemed necessary, including regularly scheduled continuing review at least every twelve months, and verification of compliance with approved research protocols and informed consent procedures.
6. Initiating audits on approved projects periodically, as and when indicated.
7. To ensure prompt reporting to the HKU/HA HKW IRB of any planned changes in approved projects, and to ensure that no material changes occur without prior approval of the HKU/HA HKW IRB.
8. To ensure prompt reporting to the HKU/HA HKW IRB of any adverse events occurring in approved projects, or in other projects related in context to the approved projects.
9. To suspend or terminate a previously approved project.
10. To review and monitor the use of test articles (investigational drugs, biologicals and devices) for the purpose of treatment of serious or life-threatening illnesses.

The HKU/HA HKW IRB will employ a review process that conforms to the Principles of the ICH GCP guideline E6 and the Declaration of Helsinki (version 1996) and to implement the regulatory procedures mandated by the Hong Kong SAR Government and guidance issued by the FDA and the Office of Human Research Protection (OHRP) under U.S. Department of Health and Human Services (HHS, USA).

The review process will be the same for all research involving human subjects, supported or otherwise, regulated by the Dean of the Faculty of Medicine, The University of Hong Kong and the CCE of HKW, HA, Hong Kong SAR if applicable to the Hospital Chief Executive at an affiliated hospital.

The HKU/HA HKW IRB will notify the investigator of the proposed project, the Dean and the CCE (HKW, HA), of its decisions to approve, disapprove, suspend or terminate research projects. In the case of disapproval, suspension or termination, the notification statement will include clearly defined reasons for the decision.

The Dean and the CCE (HKW, HA) and if applicable the Hospital Chief Executive at an affiliated hospital will have the authority to review the decisions. In the case of an approval decision, should the Dean and the CCE (HKW, HA) conclude that a project does not fully comply with policies or obligations of HKW Cluster hospitals the project may be disapproved, suspended or terminated on behalf of the institution. However, in the case of a decision by the HKU/HA HKW IRB to disapprove, suspend or terminate a project, the investigator can apply to have the case reviewed by the Hospital Authority's own Research Ethics Committee (HAREC) - refer to HKU/HA HKW IRB Document HA RE001.

3. HKU/HA HKW IRB MEMBERSHIP

HKU/HA HKW IRB will conduct its business with the participation of the following persons: ex-officio members, regular members that comprise of clinical scientists and lay members.

All members will each be appointed for a two-year term.

A member can be re-nominated for a second, consecutive two-year period, as long as he/she continues to possess the required qualifications.

Lay members will be invited to join for a two-year term, renewable for successive two-year terms without limit, as long as a member continues to possess the required qualifications.

In the case of selection and appointment of a clinical scientist as a regular member, the Dean and the CCE (HKW, HA) will solicit nominations from Chiefs of Service / Heads of Department of HKW, HA and Faculty of Medicine, HKU.

Conditions of membership of the HKU/HA HKW IRB assume that a member will:

- a) be willing to publicise his/her full name, profession and affiliation;
- b) sign a confidentiality agreement regarding meeting deliberations, applications, information on research participants, and related matters.

Payment to IRB Members

HA policy does not preclude IRB members from being compensated for services rendered or expenses incurred from participating in the review process. Payment, however, must not be related to or dependent upon a favourable decision.

3.1 Ex-officio Members

HKU/HA HKW IRB has the following 3 ex-officio members:

- (I) Dean, Faculty of Medicine, HKU, or his/her representative
- (II) CCE (HKW, HA), or his/her representatives
- (III) Immediate Past IRB Chairperson

3.2 Regular Members

As mandated by the ICH-GCP E6 guideline, the HKU/HA HKW IRB will have at least five members, including the Chairperson. At least one HKU/HA HKW IRB member will be a person whose primary area of interest is in a non-scientific area* and at least one member who is independent of the institution/trial site and who is not part of the immediate family of a person who is affiliated with the institution.

* Can be a professional person such as a lawyer and may also represent the member of the IRB who is independent of the institution/trial site. However, such persons will not be permitted to serve on the IRB if they are employees of the Hospital Authority or the institution/trial site.

Clinical Scientist members of the HKU/HA HKW IRB will have had experience in research involving human subjects, and will be nominated at the request from the Dean and the CCE (HKW, HA) by their Chiefs of Service / Heads of Department. Lay member will have had expertise in human rights issues and / or ethical or legal issues considered to be relevant to human subject research, and will be invited by the Dean and the CCE (HKW, HA). The HKU/HA HKW IRB will ascertain that its membership possesses the professional competence necessary to review human subjects research in all categories encountered at the hospital, and can judge the acceptability of the research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

The Dean and the CCE (HKW, HA) will formally appoint the clinical scientist members and the laypersons. The Chairperson and several Deputy Chairpersons will be appointed from the Clinical Scientist members by the Dean and the CCE (HKW, HA).

To be effective and efficient in its operations and to be responsive to the needs of the research community it serves, in its discretion, the HKU/HA HKW IRB may increase, above the mandated minimum, the number of its members. With the exception of the Chairperson and the laypersons the IRB members should be equally, or close to equally, selected from the three medical areas listed below and every non-discriminatory effort to ensure that the IRB does not consist entirely of men or entirely of women should be undertaken. Selections must not, however, be made based on gender.

In its discretion, the HKU/HA HKW IRB may also reduce its membership, as long as the membership conforms to the mandated minimum and composition. The HKU/HA HKW IRB membership will determine the scope of expertise of its members to assure appropriate review of the types of applications it receives.

Medical Sciences	Surgical Sciences	Health Sciences
Medicine	Surgery	Obstetrics and Gynaecology
Radiology	Pathology	Paediatrics and Adolescent Medicine
	Orthopaedic Surgery	Psychiatry
	Clinical Oncology	Nursing Studies
	Anaesthesiology	Microbiology
		Community Medicine
		Allied Health

In addition to the Chairperson, a layperson should also be present at each meeting and at least three or more of the remaining meeting members should be selected from each of the three areas listed above.

In addition to the Chairperson, there will be several Deputy Chairpersons, who will take turns in chairing the IRB meetings.

Conflicts of Interest

Member who has a conflicting interest to a proposal must not participate in its review.

A list of current IRB members should be submitted to the HAREC and kept with the IRB records. The list should identify members by name; earned degrees, representative capacity, and indications of experience sufficient to describe a member's chief anticipated contributions to IRB deliberations, and any employment or other relationship between a member and the

institution (e.g., employee, unpaid consultant, or board member). Any changes in IRB membership must be updated accordingly.

3.3 Co-opted Reviewers

The HKU/HA HKW IRB, at its discretion, may invite scientists or non-scientists from within or outside HKW, HA who are not members of the HKU/HA HKW IRB, and have special expertise to function as co-opted reviewers of a project application, to assist the HKU/HA HKW IRB in its review process. These co-opted reviewers will have access to all documents submitted to the HKU/HA HKW IRB relevant to the specific project under review, may participate at the deliberations and make recommendation on the project, but may not vote with the HKU/HA HKW IRB.

3.4 HKU/HA HKW IRB Chairperson

When the HKU/HA HKW Chairperson is not available, one of the Deputy IRB Chairpersons or one of the three ex-officio members will assume the responsibilities of the Chairperson during the period of his / her absence.

4. HKU/HA HKW IRB MEETINGS

HKU/HA HKW IRB members will convene about twice a month to fulfil their mandate to oversee research involving human subjects undertaken by staff at HKU or HKW, HA.

4.1 HKU/HA HKW IRB Meeting Agenda

The HKU/HA HKW IRB will have an agenda for each of its meetings. The agenda will include listing and identifiers for all research project applications awaiting action by the HKU/HA HKW IRB. At least seven days in advance of the scheduled meeting date, the agenda will be made available by email or post for review by members of the HKU/HA HKW IRB. All documents relating to a study submitted by an investigator will be distributed as hard copies and sent to the panel members of the IRB scheduled to conduct the full review. Only the document entitled 'Clinical Research Ethics Review Application Form' and the Informed Consent Documentation (English and Chinese versions) will be sent to the remaining members of the IRB, who can request if they require, a hard copy of any of the documents.

4.2 HKU/HA HKW IRB Meeting Procedures

The HKU/HA HKW IRB will meet about twice a month, whenever practicable, to review the research project applications submitted for approval. With the exception of applications eligible for expedited review (Section 9), the HKU/HA HKW IRB will determine the outcome of its review of research project applications at meetings, where a quorum has been established. A quorum requires the presence of a minimum of five regular members at each meeting and a vote of at least one lay member. The Chairperson, the deputy Chairperson or, in their absence, another ex-officio member of the HKU/HA HKW IRB will chair the meetings.

Whenever a research project application is being reviewed, in which a member of the HKU/HA HKW IRB may have a conflict of interest, that member will leave the site of the

HKU/HA HKW IRB meeting for the duration of the review of that application, will not participate in the discussion in any way, and will not vote on the application.

4.3 HKU/HA HKW IRB Meeting Minutes

The Secretary of HKU/HA HKW IRB will prepare minutes of each meeting of the HKU/HA HKW IRB, during which research projects are being reviewed.

The minutes will be in sufficient detail, and will include the followings:

1. Date and venue of the meeting.
2. Attendance and absence.
3. Decisions reached on each research project application reviewed.
4. Distribution of membership votes on the decisions, documenting the number of votes for, against and abstaining.
5. Reasons for requiring changes in a project, or disapproving, suspending or terminating a project.
6. If vulnerable groups of subjects were included in the research, the justification for their inclusion, and adequacy of special precautions taken to minimise risks.
7. Summary of the discussion of disputed issues and their resolution.
8. Date of next scheduled continuing review of a project, and the perceived level of risk on which the time of next review was based.

The minutes will be made available for review by email and posted to the HKU/HA HKW IRB members and the CCE (HKW, HA).

4.4 HKU/HA HKW IRB Notification of Meeting Decisions

Upon completion of the review of a research project application, the Secretary of HKU/HA HKW IRB will prepare a notification document, to inform the applicant or principal investigator of the outcome of the review. Such notification should be signed by the Chairperson or his/her delegate and should include the following information:

1. The outcome of the review by the HKU/HA HKW IRB, and the date the decision was reached for approved projects, the date of next scheduled continuation review (one year from the date of approval), and the reporting requirements for the principal investigator.
2. For disapproved, suspended or terminated projects, the reasons for these decisions, and the rights of the investigators for rebuttal of the decision.
3. The membership roster of the HKU/HA HKW IRB.

The notification documents will be made available by email for review by the HKU/HA HKW IRB members and CCE (HKW, HA).

5. HUMAN SUBJECTS OF RESEARCH

The focus of activities of the HKU/HA HKW IRB will be human subjects, who are involved in research.

5.1 Definition of Human Subjects of Research

Human subject of research means a living individual, about whom a professional or student investigator conducting research obtains data through intervention or interaction with the individual, or collects identifiable private information.

Interventions in human subjects include physical procedures by which data are gathered, and manipulations of the subject or the subject's environment for research purposes.

Interactions with human subjects include communications or interpersonal contacts conducted for research purposes.

Private information includes information collected under circumstances the subject can reasonably expect that no observation or recording is taking place, and information the subject can reasonably expect will not be made public in a manner exposing the identity of the subject.

5.2 Vulnerable Populations

Vulnerable subjects should not be included in research unless the research is necessary to promote the health of the study population represented and the research cannot instead be performed on other, less vulnerable subjects.

The HKU/HA HKW IRB will consider certain groups of human subjects to be particularly vulnerable to coercion or undue influence in a research setting, to include:

- Children - also indirectly an infant, if a mother nursing an infant is a subject of research
- Foetuses and human in vitro fertilisation
- Pregnant and lactating women
- Mentally ill
- Intellectually disabled
- Cognitively impaired persons
- Prisoners and economically or educationally disadvantaged persons
- Minorities

The particular needs of the economically and medically disadvantaged must also be recognised. This could be subtle. If subjects are given payment, the amount and method of payment should not cause undue influence on the subjects.

In reviewing research projects, the HKU/HA HKW IRB will scrutinise those involving these vulnerable groups, to ascertain that their use is adequately justified, and additional safeguards are implemented to minimise risks unique to each group.

If the Chairperson considers that the research involves sensitive issues he/she should consult with a member of the IRB, in order to seek a second opinion before making a decision.

The HKU/HA HKW IRB will consider for approval of research projects involving vulnerable populations, if one of the following conditions is met:

1. The research does not involve more than minimal risk to the subject. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.
2. The research is likely to benefit the subject directly, even if the risks are considered to be more than minimal.
3. Requests for approval of any research that exposes vulnerable populations to risks significantly greater than minimal, without providing obvious direct benefit to the subject, will have been sent all members of the HKU/HA HKW IRB for review and approval.
4. The HKU/HA HKW IRB will not review or approve any research involving prisoners, unless it has already been approved by another IRB that acts in accordance with ICH-GCP guidelines who has a prisoner member.

5.3 Students and Employees as Healthy Subjects of Research

Whenever students or employees at HKU, or Hong Kong West Cluster Hospitals are to be used as "healthy subject pools" in research, the HKU/HA HKW IRB will scrutinise the recruitment process, to ascertain that consent for participation is sought only under circumstances that minimise the possibility of coercion or undue influence, and that public advertisement is employed to facilitate participation of equivalent healthy subjects not susceptible to coercion or undue influence.

6. INFORMED CONSENT OF HUMAN SUBJECTS OF RESEARCH

Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them; the informed consent process is the instrument to provide this opportunity. The HKU/HA HKW IRB will ascertain that the investigators of a research project will obtain from human subjects or their legally authorised representatives a legally valid informed consent. In obtaining informed consent, the investigators shall:

1. Give the subject (or representative) sufficient information about the study and how the study may affect the subject.
2. Deliver the information in a comprehensible manner, using a language readily understandable by the subject.
3. Assure voluntary capacity of the participant, by providing sufficient opportunity to consider whether or not to participate, and minimising the possibility of coercion, undue influence, or harassment.

The process of obtaining informed consent has two components:

1. Providing the person, who is being recruited to become a subject of research, or that person's legally authorised representative, with the information necessary to give

informed consent by means of a Patient/Subject Information Sheet, and obtaining the consent to participate in the research as a subject.

2. Documenting that informed consent has been obtained by means of a Patient/Subject Consent Form.

The basic rule of human subject research is that both components of the informed consent process shall be completed. However, in accordance with ICH GCP Guideline (E6) and local regulatory requirements, under certain circumstances, the HKU/HA HKW IRB has the authority to waive the requirement for obtaining informed consent (Section 6.1), or for documenting that the consent has been obtained (Section 6.5).

6.1 Projects Eligible for Waiver of the Written Informed Consent Process

The HKU/HA HKW IRB will consider waiving the requirement of obtaining written informed consent from a subject of research, if the nature of the research meets one of the following definitions:

1. Is not violative and not invasive, and
2. Does not involve risks to the subjects that are more than minimal.

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the 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, that is to say the nature of the research meets one of the following definitions:

1. Research involving collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, in which the investigator records the information in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects, or if the sources of the information are publicly available.
2. Research involving normal educational practices.
3. Research involving use of educational tests, survey procedures, interview procedures or observation of public behaviour without revealing subjects' identity, placing them at risk of criminal or civil liability, or damaging their financial standing, employability or reputation.
4. Research Involving sensitive information which may include but is not limited to:
 - a) Information relating to sexual attitudes, preferences, or practices.
 - b) Information relating to the use of addictive products.
 - c) Information pertaining to illegal conduct.
 - d) Information that if released could reasonably be damaging to an individual's financial standing, employability, or reputation within the community.
 - e) Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatisation or discrimination.
 - f) Information pertaining to an individual's psychological well-being or mental health.

5. Research that anticipates but lacks definite plans for involvement of human subjects, such as institutional-type centre or training grants; any study involving human subjects under the umbrella of such grants will have to be reviewed subsequently by the HKU/HA HKW IRB, prior to its initiation.
6. Research that cannot practicably be carried out, if informed consent were to be obtained in advance, provided that the rights and welfare of the subjects will not be adversely affected; in this instance, arrangements shall be made to provide pertinent information to the subjects after their participation.

6.2 Elements of Informed Consent

According to the ICH GCP Guideline (E6), the Patient/Subject Information Sheet and the Patient/Subject Consent Form should include twenty different aspects of the study (see the ICH GCP (E6) Guideline or the HKU/HA HKW IRB Patient/Subject Information Sheet template).

6.3 Patient/Subject Information Sheet

The HKU/HA HKW IRB requires that the information necessary to give informed consent by the person being recruited as a research subject be given to that person or the person's legally authorised representative in writing.

1. The written document - Patient/Subject Information Sheet - shall include the title of the study, the names of the investigators, and how the investigators can be reached.
2. The content shall include at least the basic elements of the Patient/Subject Information Sheet; the use of the template prepared by the HKU/HA HKW IRB is strongly recommended. In most instances, a single document shall be employed, encompassing all aspects of the research; the information shall not be fragmented.
3. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the persons legally authorised representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.
4. The content shall be easily understandable by a layperson with modest education and written in a language comprehensible to the study subject.
5. The investigator shall present the written document to the subject or the subject's legally authorised representative, and provide adequate opportunity for them to study the document.
6. At the time of obtaining the consent, the investigator shall provide additional verbal information, as needed, so that the nature and anticipated consequences of the study are sufficiently clear.

In most instances, in addition to the information given to the subject or the subject's legally authorised representative, the written document shall contain a section to document that informed consent has been obtained, as described in Section 6.4. In rare instances, the

documentation section may be deleted from the written informational document, if the HKU/HA HKW IRB has waived that requirement, as described in Section 6.5.

Before the study may start, the informed consent document shall be submitted for approval to the HKU/HA HKW IRB, together with the application for initiation of a new project, or continuation of a previously approved project. The consent document will gain validity only after the approval of its text by the HKU/HA HKW IRB. Each copy of the document to be presented to the subject of research shall contain a "Date of Approval" and a "Date of Expiration", respectively corresponding to the date of the initial approval of the project by the HKU/HA HKW IRB, and the date the next continuation review has been scheduled by the HKU/HA HKW IRB.

6.4 Documentation for Obtaining Informed Consent

In most instances, the act of obtaining consent shall be validated on the written document that contains the information needed to give informed consent, i.e. the Patient/Subject Consent Form. The validation shall be implemented by the signature of the subject or the subject's legally authorised representative, and by the investigator obtaining the consent.

Subjects who are illiterate or physically unable to write may have the consent explained to them verbally and indicate approval or disapproval by other means. In such circumstances, it is essential to document the method of communication, the explanation given (and by whom), and the means by which the subject indicated his/her wish. An impartial third party must witness the entire consent process and sign the consent document. Video taping the consent process is recommended.

In the case of a child being recruited as a subject of research, an assenting signature of the subject of an age (7 or above) sufficient to comprehend the nature, risks and benefits of the study, shall be obtained on the Patient/Subject Consent Form, in addition to the signature of the legally authorised representative. The documentation shall be executed on three copies of the written consent document carrying the subject's legal name, the hospital case identification number, and the date of execution. One copy of the executed document shall be given to the subject or subject's legal guardian, one copy shall be incorporated into the research documents kept by the investigators, and one copy shall be placed in the subject's hospital record. The Patient / Subject Consent Form shall be dated by the person or persons whose signature is required to be obtained.

Clinical investigators should be cautious when enrolling subjects who may not truly understand what they have agreed to do.

6.5 Projects Eligible for Waiver of the Requirement for Documentation of the Informed Consent

The HKU/HA HKW IRB may waive the requirement for documentation of the informed consent (a signed Patient/Subject Consent Form), but not that of obtaining informed consent, under one of the following circumstances:

1. The principal research risk is potential harm resulting from a breach of confidentiality, and the only record linking the subject and the research is the consent document.

2. The research presents no more than minimal risk of harm to subjects, and does not include any procedure, for which written consent would be required, if it were to be performed for clinical management.

In cases where the HKU/HA HKW IRB will waive the requirement for documentation of informed consent, the investigators shall still provide the subject with the written Patient/Subject Information Sheet described in Sections 6.2 and 6.3, the text of which shall be reviewed and approved by the HKU/HA HKW IRB. Based on this information, the investigator shall obtain oral consent to participate, but the granting of the consent will not be documented in writing.

6.6 Legally Authorised Representative

Under the current state of the law, the consent to participate in a research project given by a third party (relative or otherwise) on behalf of a mentally incapacitated adult is not legally effective. Therefore, 'legally authorised representative' used in this Section 6 has no application to mentally incapacitated adults.

7. INITIAL REVIEW BY HKU/HA HKW IRB OF HUMAN SUBJECT RESEARCH

An Investigator, who intends to initiate a research project involving human subjects, shall be responsible for submitting to the HKU/HA HKW IRB an application for review and approval of the project, before the project begins. No aspect of use of human subjects in research may begin, until HKU/HA HKW IRB has granted the approval.

7.1 Documents Required for Initial Review

To apply for initial review and approval of a new project, the principal investigator shall complete a Clinical Research Ethics Review Application Form, the template of which can be found on the HKU/HA HKW IRB homepage. All other relevant documents can be found here in an electronic template format. One original copy shall accompany each application and all other documents necessary for an orderly review of the project particularly those aspects involving human subjects. In addition, the application shall be accompanied by one copy each of:

Clinical Research Ethics Review Application Form (both hard and soft copy).

Study Protocol

Investigator's Brochure including number and version, (if applicable)

HKU/HA HKW IRB 001F4 - Investigator's Conflict of Interest Declaration Form

Investigator's short CV

Patient/Subject Information Sheet – English - including a software copy

Patient/Subject Information Sheet – Chinese (Traditional) - including a software copy

Patient/Subject Consent Form – English - including a software copy

Patient/Subject Consent Form – Chinese (Traditional) - including a software copy

Texts of advertisements for subject recruitment English (where appropriate)
Texts of advertisements for subject recruitment Chinese (Traditional) (where appropriate)

Questionnaires/Interviews – English (where appropriate)
Questionnaires/Interviews – Chinese (where appropriate)

HKU/HA HKW IRB T1 Submission Letter

Insurance Policy (if applicable)

Indemnity Agreement

Application fee *

* Required only for phase I, II and III sponsored drug trials.

For all trials of New Investigational Drugs, including traditional medicine compounds, diagnostic test appliances and devices for which a product licence does not exist and for some other studies like new indications for already approved products as requested by the HKU/HA HKW IRB, each application shall be accompanied by one copy each of;

- i. Insurance policy document
- ii. Study Protocol
- iii. HKU/HA HKW IRB 001F4 - Investigator's Conflict of Interest Declaration Form
- iv. Investigator's Brochure
- v. Any other supporting document that would facilitate a meaningful review

7.2 HKU/HA HKW IRB Criteria for approval of Initial Review

In consideration of approval of a new research project involving human subjects, the HKU/HA HKW IRB will review the application to determine if all of the following criteria are met:

General Considerations

- a) Study has potential in enhancing health or advancing knowledge.
- b) Methodology (design, sample size, etc.) is adequate to answer the questions posed.
- c) Has a favourable risk-benefit ratio basing on an adequate assessment.
- d) Adequate measures to minimize risk and detect adverse events timely.
- e) If the nature of the research requires repeated assessment of the balance between risks and benefits, there are adequate provisions for such monitoring.

- f) The nature of the research justifies the proposed subject population. Vulnerable subjects are involved only if it is not suitable to conduct the study with other, less vulnerable subjects.
- g) Subject selection and treatment allocation procedure are fair.
- h) Recruitment process assures voluntary participation and protects subjects from being unduly influenced.
- i) Subjects will be well informed in the consent process.
- j) Is any problem (e.g. withdrawal of an effective treatment) likely to occur after study?
- k) Insurance cover and/or indemnity agreement is adequately addressed.
- l) Subject's privacy and data confidentiality are adequately protected.
- m) Rights and interests of vulnerable subject, wherever applicable, are adequately protected.
- n) Payment (amount or method) does not cause undue influence to subjects.
- o) Source of funding is disclosed.
- p) Potential conflicts of interest of investigators are addressed.

Consent Form

- a) Use languages suitable to the intended subjects.
- b) Explain purpose of study and indicate which aspect of study is experimental.
- c) Explain study details such as nature of intervention, possible use of a placebo, method of assignment, probability of being assigned to different study arms, invasive procedures involved, duration of involvement, sample size, likelihood of premature termination.
- d) Describe reasonably foreseeable risks or discomforts to subject and foetus/nursing infant if applicable.
- e) Describe reasonably expected benefits to subject or to others.
- f) Subject will be updated timely of new information that may be relevant to his/her willingness to continue participation in study.
- g) Describe how data will be handled to protect subject's privacy and mention potential audit needs.
- h) Explain alternatives if subject refuse to participate.

- i) Assure voluntary participation and right to refuse, withdraw at any time without reprisal.
- j) Explain possible reasons under which the subject's participation in study may be terminated.
- k) Explain anticipated expenses by or payment to subject, when applicable.
- l) Explain commitment of sponsor(s), study institute(s) and investigators, where appropriate.
- m) Explain compensation and treatment available for study-related injury.
- n) Provide information of research institution and investigators.
- o) Provide contact for queries & adverse event reporting.

7.3 HKU/HA HKW IRB Process of Initial Review

Initial Review

Upon receipt of the documents for an initial review, the Secretary of the HKU/HA HKW IRB will notify all regular members. Regular members (those assigned to a scheduled meeting) would receive a copy of the full protocol, while the remaining regular members would receive the 'Clinical Research Ethics Review Application Form' and 'Informed Consent Documentation' by email. A complete set of submitted protocol, in hardcopy, will be available to the latter group of regular members on request.

The HKU/HA HKW IRB office should endeavour to distribute the application documents and a form for declaration of conflicts of interest to reviewers at least 7 days prior to the meeting.

To facilitate the review, the co-opted reviewers will be provided with all application documents and a work sheet, to ensure that inadvertent omissions do not occur in considering the conformity of the application to all criteria for approval of research, and that a proposed continuation date and special monitoring requirements are identified. The work sheet will itemise the criteria outlined in Section 7.2 of this SOP and include additional items on the following:

- Proposed interval until next continuation review, based on the estimated extent of risks (longest interval one year)
- Whether or not the written informed consent document is sufficiently informative and includes all elements of informed consent, and whether and what kind of revisions in the protocol or consent document have been or need to be obtained for the application to be approved.

Prior to the HKU/HA HKW IRB meeting to discuss the project, all HKU/HA HKW IRB members will have the authority to request from the applicant Investigator, via the Secretary of HKU/HA HKW IRB, revisions or additional information or documents. Upon completing his / her review, members could present his / her comments to the HKU/HA HKW IRB via

the Secretary. After sufficient discussion, the members attending the IRB meeting will vote on the application, to approve it, disapprove it, or defer a decision until revisions are implemented, additional information is provided, or further expert review is obtained (including invitation of co-opted reviewers; Section 3.4). In order for the research to be approved, it shall receive the consensus of those members present at the meeting.

Investigators may be invited to attend the meeting to describe their proposed study and to answer any additional questions posed by members of the IRB.

Under certain circumstances, if minor revisions to the submitted documents are required or a missing document of minor importance is to be obtained, the HKU/HA HKW IRB may delegate the Chairperson or the primary reviewer to subsequently approve the project on behalf of the HKU/HA HKW IRB, upon completion of these tasks. "Conditional" approvals will not be granted.

The outcome of any review conducted by the HKU/HA HKW IRB will be sent directly to the appropriate Investigator concerned. The content of the reply letter that is sent to the Investigator will be presented according to the format shown in the example of the IRB Approval Form (HKU/HA HKW IRB 001F6a) or the HKU/HA HKW IRB Clarify/Disapprove Form (HKU/HA HKW IRB 001F6b) or IRB Disapprove Form (HKU/HA001F6c).

In case of disagreement between the HKU/HA HKW IRB and the investigators of a project under review with regards to requested revisions or a decision to disapprove the project, the HKU/HA HKW IRB will provide the opportunity of rebuttal for the investigators, either in writing, or by appearing at a meeting of the HKU/HA HKW IRB, to defend their cases.

Under no circumstances will subjects be admitted to a trial before the IRB issues its written approval/favourable opinion of the trial.

8. HKU/HA HKW IRB MONITORING OF HUMAN SUBJECT RESEARCH IN PROGRESS

The HKU/HA HKW IRB will monitor all active research projects involving human subjects, to ascertain that the subjects are being protected adequately from research risks and from any other breaches of human rights.

Regular monitoring of all previously approved projects will be in the form of continuing reviews scheduled at the time of most recent HKU/HA HKW IRB approval of the project. The frequency of the scheduled continuation reviews will be appropriate to the degree of risk, but not less than once per year, and the schedule of the continuing review will be decided upon approval. In addition, the HKU/HA HKW IRB will ensure that the investigators of active research projects carry out the following, as needed, as a condition of approval of their projects:

1. Report to the HKU/HA HKW IRB any planned change in the study, and do not implement any change without receiving prior approval, except to eliminate immediate hazard.
2. Report to the HKU/HA HKW IRB any unanticipated problems involving risks to subjects.

3. Report to the HKU/HA HKW IRB any new information on the project that adversely influences the risk/benefit ratio.

The investigators will be informed and reminded of these conditions of approval, using several methods of communication:

1. Messages included in letters of notification of approval of the project.
2. Periodic electronic mail to be sent to principal investigators of all projects.
3. Notices placed in various newsletters that are routinely sent to researchers.

8.1 Regular, Scheduled Continuing Review

At the time of initial review or the most recent scheduled continuing review, the HKU/HA HKW IRB will establish the interval until the next continuation review (one year from the date of approval), by taking into consideration the presumed degree of research risks; the higher the risk, the sooner will the continuing review be scheduled.

The principal investigator of an active research project shall be responsible for submitting to the HKU/HA HKW IRB office an application for continuing review and approval of the project. To these investigators, the HKU/HA HKW IRB will send a reminder notice, two months in advance of the expiration of the approval period.

If approval for continuation has not been issued by the HKU/HA HKW IRB, the investigator is obligated to suspend all subject recruitment activity in the project, until the HKU/HA HKW IRB has issued approval for continuation.

To apply for continuing review and approval, the investigator shall complete a 'Research Progress Reporting Form - HKU/HA HKW IRB 001F9a', which can be found on the HKU Faculty of Medicine Internet website, HA HKW intranet website and the QMH intranet website.

The information to be provided by the investigator in the application form shall include the following:

1. Number of subjects accrued since last approval.
2. Number of subjects expected to be recruited in the future.
3. Description of,
 - a) Any adverse events or unanticipated problems involving risks to subjects or others.
 - b) Any withdrawal of subjects from the research and the particular reasons (voluntary or otherwise).
 - c) Complaints about the research.
4. Summary of any recent literature and/or findings obtained thus far.

5. Latest information relating to the risk/benefit ratio.
6. Summary of any amendments or modifications to the research since last review.
7. Summary of any reports on multi-centre trials and any other relevant information, especially information about risks associated with the research.
8. Text of the latest version of informed consent document, and any revisions in the text to accommodate any protocol amendments or adverse events encountered.
9. Any changes in study site personnel since last approval.
10. Renewed Certificate of Insurance, if the existing one is expired.

The review process for application for continuation approval of a research project will be similar to that for initial approval of a new research project (Section 7.3).

8.2 Amendment Requests Prior to Scheduled Continuing Review

Investigators of a previously approved project must request approval from the HKU/HA HKW IRB approval to make amendments to various aspects of the project, before the project's next regularly scheduled continuing review. No amendment may be implemented without the approval of the Chairperson of the HKU/HA HKW IRB, except to eliminate immediate hazard. The date of approval of an amendment does not change the date by which the regularly scheduled continuing review of the project is to be completed.

An amendment may be in the content or the form of documentation. Types of amendments include the following:

1. Amendment to the study protocol.
2. Amendment to the investigator's brochure describing a test article.
3. Amendment to the informed consent document.
4. Amendment to the Investigatorship.

Different types of amendments may be requested individually or in combination. Particularly, a change in the study protocol or investigator's brochure may require a change in the informed consent document. The HKU/HA HKW IRB will scrutinise the amended documents to determine the degree to which risks to human subjects may have changed, if there is any need to revise the consent document, and if changes to the consent document are adequate. A copy of the current or revised informed consent document shall accompany the amendment application.

8.3 Serious Adverse Event (SAE), and Research-Related Incident Reports Prior to Scheduled Continuing Review

Investigators of a previously approved project are obligated to report to the HKU/HA HKW IRB, without waiting for the next regularly, scheduled continuing review and within the timeframes specified below, the following types of events using the 'Serious Adverse Event Report Form - HKU/HA HKW IRB 001F8'

1. SAE

A SAE is defined as:

Any untoward medical occurrence (unexpected or expected) that at any dose: results in death; is life threatening requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect.

Note:

All SAEs occurring at other study sites in a multi-centre study as well as those that involve the use of an investigational or approved drug, biologic or device, observed in a previously approved project, or in other research settings similar to that of the approved project must also be reported to the HKU/HA HKW IRB.

2. Research-Related Incidents

- a) A procedural error involving a human subject enrolled in the study.
- b) Physical or emotional harm to the subject during the execution of the experimental protocol.
- c) A breach of confidentiality or privacy.

Timeframes for Reporting Events

Serious Adverse Events	Reporting Time Frame*
1. All local unexpected and expected drug related, or not drug related, SAEs, irrespective of the treatment, involving human subjects of research.	≤ 15 days from the date that the Investigator receives a formal written report of the event(s).
2. All overseas reports of unexpected SAE(s), and unexpected Serious Adverse Drug Reactions involving human subjects of research.	≤ 30 days from the date that the Investigator receives a formal written report of the event(s)

Note:

These are the minimum reporting requirements. There may be other requirements in a sponsored trial that may have to be followed and the IRB reserves the right to request a more stringent requirement.

Research-Related Incidents	Reporting Time Frame
1. A procedural error involving a human subject enrolled in the study	≤ 15 days from the date that the investigator became aware of the event.
2. Physical or emotional harm to the subject during the	

<p>execution of the experimental protocol</p> <p>3. A breach of confidentiality or privacy</p>	
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The Chairperson of the HKU/HA HKW IRB will scrutinise the adverse event and/or other event documents to determine the degree to which risks to human subjects may have changed, if there is any need to revise the consent document, and if changes in the consent document are adequate. A copy of the current or revised informed consent document shall accompany the adverse event and/or other event report.

8.4 Additional Measures of HKU/HA HKW IRB to Monitor Active Research Projects

Additional monitoring of approved projects may occur at the discretion of the HKU/HA HKW IRB, in the form of targeted or random

1. Requests for progress reports from investigators.
2. Examinations of research records.
3. Dispatch of observers to the sites, where research involving the human subjects is being conducted.
4. Verification from sources other than investigators that no material changes in the study have occurred. In targeting research projects to be subjected to these additional monitoring activities, the HKU/HA HKW IRB will consider the level of risks of harm, the frequency and nature of adverse events, the vulnerability of the subjects of research, and any complaints received from the subjects.
5. Identify published human research from the HKW or its affiliated hospitals and ask the principle author to provide the HKU/HA HKW IRB with the IRB approval number related to the published results.

If the information gained during its monitoring process indicates that human subjects of a research project are exposed to unexpected serious harm, or the requirements of the HKU/HA HKW IRB are not being met, the HKU/HA HKW IRB will suspend or terminate the research. In such instances, the HKU/HA HKW IRB will provide the opportunity of rebuttal for the investigators, either in writing, or by appearing at a meeting of the HKU/HA HKW IRB to defend their cases.

9. HUMAN SUBJECT RESEARCH ELIGIBLE FOR EXPEDITED REVIEW

Certain types of research project applications submitted to the HKU/HA HKW IRB for initial or scheduled continuing review, requests for amendments, or adverse event reports will be eligible for "expedited review". The basic element determining the eligibility for expedited review is the magnitude of the risks to which the human subjects of the research will be exposed.

Only projects involving no more than minimal risk (Refer to Section 6.1 for a definition of minimal risk) will be considered for expedited review.

Expedited review is permitted for research that satisfies ALL the following conditions:

1. Does not incur an additional clinical intervention (drug or invasive procedure) or involves no more than minimal risk to study subjects, and
2. Does not include vulnerable subjects*, and
3. Does not raise sensitive privacy concerns.

The HKU/HA HKW IRB Chairperson shall decide which applications are qualified for an expedited review.

An expedited review may be performed by the HKU/HA HKW IRB Chairperson or by the Deputy Chairpersons. The reviewer(s) may exercise all the authorities of the HKU/HA HKW IRB, except disapproval, which should be made by a Review Panel.

The HKU/HA HKW IRB office should adopt a method of keeping members advised of research studies that have been approved by expedited review.

Examples suitable for expedited review include:

- a) Review of previously approved research for changes without risk implication.
- b) Surveys by interview or questionnaire on non-sensitive issues.
- c) Research of data, records and specimens obtained in the usual course of patient management or existing prior to research proposal.
- d) Collection of blood samples by venipuncture, in amounts not exceeding 450ml in an eight week period and no more often than two times per week from subjects who are 18 years of age and who are not anaemic, in good health and not pregnant.
- e) Collection of excreta, external secretions (e.g. urine, sweat, uncannulated saliva), placenta at delivery, amniotic fluid at the time of rupture of membrane, etc.

Sensitive information includes, but is not limited to:

- a) Information relating to sexual attitudes, preferences, or practices;
- b) Information relating to the use of addictive products;
- c) Information pertaining to illegal conduct;
- d) Information that if released could reasonably be damaging to an individual's financial standing, employability, or reputation within the community;
- e) Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatisation or discrimination;
- f) Information pertaining to an individual's psychological well being or mental health.

*If the subjects of the research include vulnerable populations as defined under section 5.2 the project will not be eligible for expedited review, regardless of the risk. Exceptions are for studies conducted on vulnerable subjects that involve research requiring non-sensitive information and /or ordinary clinical management. For such studies, the Chairman of the IRB should consult with another IRB member who is an expert in the field to decide if an expedited review is appropriate or not.

9.1 HKU/HA HKW IRB Process for Expedited Review

Expedited review of a new project or previously approved project may be requested by the principal investigator at the time of submission of the application, by indicating the applicable criterion for expedited review. Alternatively, the Chairperson or Deputy Chairperson may choose to process an application by expedited review.

Expedited review will be carried out by the IRB Chairperson or by one or more Deputy Chairpersons of the HKU/HA HKW IRB designated by the Chairperson. The reviewer(s) may exercise all of the authorities of the IRB, except disapproval. If the reviewer(s) believe that there is reason for disapproval, or the nature of the project is not suitable for expedited review, the reviewer(s) will defer any decision, and submit the project to a full review by the HKU/HA HKW IRB (refer to Section 7 for initial, and Section 8 for continuing reviews).

For research studies based on expedited review, the Chairperson of the HKU/HA HKW IRB is required to adopt a method of keeping all members advised of research studies that have been approved by expedited review. In addition such information and any observations made by members should also be recorded in the minutes of a meeting.

9.2 Research Considered by HKU/HA HKW IRB as Suitable for Expedited Review

The following types of research, considered to have no more than minimal risk, and not involving children, foetuses, pregnant women, prisoners, mentally ill or cognitive impaired or intellectually disabled persons have been explicitly identified as eligible for expedited review:

1. Collection of hair and nail clippings in a non-disfiguring manner; deciduous teeth, and permanent teeth if patient care indicates a need for extraction.
2. Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane prior to or during labour.
3. Recording of data from subjects, using non-invasive procedures routinely employed in clinical practice (including use of physical sensors applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or invasion of the subject's privacy; procedures such as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echocardiography, and electroretinography, not including exposure to electromagnetic radiation outside the visible range, such as x-rays and microwaves).
4. Collection of blood samples by venipuncture, in an amount not exceeding 450 millilitres in an eight-week period and no more than two times per week, from subjects, who are in good health and not pregnant.
5. Collection of supra-gingival and sub-gingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth, and is accomplished in accordance with accepted prophylactic techniques.

6. Voice recordings made for research purposes, such as investigations of speech defects.
7. Moderate exercise by healthy volunteers.
8. Study of existing data, documents, records, pathological specimens, or diagnostic specimens.
9. Research on individual or group behaviour or characteristics of individuals, such as perception, cognition, game theory, or test development, where the investigator does not manipulate subjects' behaviour and the research will not involve stress to subjects.
10. Research on drugs or devices for which an investigational new drug exemption or investigational device exemption is not required.

The decision to conduct an expedited review may only be made by the Chairperson of the IRB. If the Chairperson considers that the research involves sensitive issues and cannot be reviewed in an expedited manner, the Chairperson should consult with a member of the IRB, in order to seek a second opinion before making a decision.

If yes, then the Chairperson should consult with another member to seek a second opinion.

9.3 Research Considered Eligible for Exemption from Review, but Subject to Expedited Review by HKU/HA HKW IRB

Overseas regulatory agencies recognise certain types of research as having no or negligible risk to the subjects, and considered them to be eligible for exemption from review by institutional review boards. The HKU/HA HKW IRB will not grant exemption from review for such research, but will consider processing them by expedited review.

9.4 Institutional-Type Applications Considered by HKU/HA HKW IRB as Eligible for Expedited Review

Applications and proposals lacking definite plans for involvement of human subjects, such as institutional-type centre or training grants, will be eligible for expedited review. Any study involving human subjects under the umbrella of such grants will have to be reviewed subsequently by the HKU/HA HKW IRB, prior to its initiation.

9.5 Previously Approved Research Eligible for Expedited Review

Research approved previously by expedited review will be considered eligible for expedited review at the time of its regular continuing review, if during the course of the study, the risks of the study have not increased.

Prior to the scheduled date of regular continuing review, changes may have to be implemented in an approved project. Amendments to a previously approved research protocol of administrative or logistical nature, revisions in the text of an informed consent document, or corrections in text of documents, all of which are minor in nature and do not increase the risks involved, will be considered eligible for expedited review.

10. USE OF TEST ARTICLES BEYOND THE CONTEXT OF RESEARCH

Overseas regulatory authorities recognised circumstances, where a test article (an investigational drug, biologic or device) may be made available for use in patients with life threatening or other serious diseases, for which no satisfactory alternative treatments exist.

10.1 Emergency Use of a Test Article

Under certain circumstances, a test article may have to be administered to a human subject in a life-threatening situation, when there is no standard acceptable treatment available, or the standard treatments have failed and the subject is not enrolled, or is not eligible to enrol in a research protocol involving the test article.

The following criteria apply:

1. To be used in a single subject by a physician licensed to practise medicine in Hong Kong.
2. The subject is facing a life-threatening condition, for which there is no conventional treatment, or conventional treatments have failed.
3. The physician has legitimate access to a test article, and believes that there is a reasonable likelihood that it may be helpful in the life-threatening condition.
4. The subject to receive the test article will not be enrolled in a research study involving the test article employed.
5. If subsequent use of the test article is contemplated in the same subject or in others, a new project application to the HKU/HA HKW IRB is required in advance of that use.

If these criteria are met, a physician may use the test article on a subject, without prior approval of the HKU/HA HKW IRB. In this instance, the physician is required to do the followings:

1. Obtain written informed consent from the subject or subject's legal representative.
2. Use the test article on the subject.
3. Enter a description of the procedure in the patients' medical record and attach a copy of the informed consent document.
4. Within five days of using the test article, submit to the HKU/HA HKW IRB the following information in writing:
 - a) Identity and address of the responsible physician.
 - b) Name and hospital case number of the subject.
 - c) Name and source of the test article; investigational new drug/device (IND) number.
 - d) How much, by what route and on what date the test article was administered.
 - e) Information about any adverse effects observed.
 - f) Copy of the informed consent document used.

The HKU/HA HKW IRB will process such notifications as an expedited review (Section 9), and issue an acknowledgement letter. Any subsequent use of the test article will be subject to prior full review and approval by the HKU/HA HKW IRB.

10.2 Treatment Investigational New Drug or Device Exemption (Treatment INDs)

The purpose of the Treatment IND exemption is to facilitate the availability of promising test articles to seriously ill patients, as early in the development process as possible, and to obtain additional data on the test article's safety and effectiveness. The Treatment IND protocol is added to an existing IND application, and allows the use of a test article in a group of subjects, who are not enrolled in a clinical study testing the safety and efficacy of the test article.

For use in seriously ill patients, there must be sufficient evidence that the test article is safe and effective; usually, such evidence becomes available during Phase III investigations or after all clinical trials have been completed.

For use in patients, whose life is in immediate danger, information available must be sufficient to conclude that the test article may be effective for the intended use, and would not expose the patient to an unreasonable risk; usually, this information becomes available early in Phase III, or sometimes in Phase II clinical trials.

The physician intending to initiate a Treatment IND protocol shall be the investigator of a study involving the test article, which has been reviewed and approved previously by the HKU/HA HKW IRB. The investigator shall have received permission of the holder of the IND exemption (sponsor of the research) to use the test article for treatment purposes. The physician shall submit an application to the HKU/HA HKW IRB prior to the initiation of the protocol, following the procedures described in Section 7 for initial review. Procedures described in Section 8 will be applicable for continuing review. The accompanying informed consent document shall be particularly explicit with regards to the use of a test article in a health care setting, and the assessment of the risk/benefit relationships.

10.3 Single Patient Use of a Test

A test article may be used in a single patient with a serious or life-threatening illness, for which all customary treatments have failed, or there is no recognised treatment available. There must be a reasonable likelihood on theoretical grounds, or based on anecdotes of success, that the test article may be helpful. The physician intending to use the test article will obtain it from its source, and either secure an extension of the source's IND exemption or submit a treatment IND exemption request with the help of the sponsoring company to the appropriate (usually overseas) regulatory authority, requesting authorisation to use a test article for the purpose of treatment for medical reasons. An application shall be submitted to the HKU/HA HKW IRB prior to the initiation of the protocol, according to the procedures described in Section 7 for initial review, and in Section 8 for continuing review. The accompanying informed consent document shall be particularly explicit with regards to the use of an investigational drug in a health care setting, and the assessment of the risk/benefit relationships.

10.4 Parallel Track Use of a Test Article in Treatment of HIV-Infected Persons

Persons with acquired immunodeficiency syndrome (AIDS) or diseases related to the human immunodeficiency virus (HIV) will be provided access to promising test articles, if they are unable to take standard therapy, or for whom standard therapy is no longer effective, and who are not able to participate in ongoing controlled clinical trials. These patients may be enrolled in studies, which do not have concurrent control groups, if they are being conducted in parallel with controlled clinical trials. Parallel track protocols are similar to Treatment IND protocols, except that the evidence for efficacy of the test article is sought less stringently, and it may be based on information available from late Phase I or Phase II clinical trials.

The HKU/HA HKW IRB will process applications for Parallel Track protocols in the same manner as applications for treatment IND protocols (Section 10.2).

11. REQUIREMENT FOR APPROVAL OF CERTAIN TYPES OF HUMAN SUBJECT RESEARCH BY ADDITIONAL AGENCIES OF HKU AND HKW CLUSTER HOSPITALS

Certain types of research involving human subjects will have to be reviewed and certified by additional agencies of HKW, and HA or its cluster hospitals as required by Hong Kong SAR government regulatory agencies, sponsors, or the Hospital Authority itself. Depending upon the type of research, one or more certifications will be a requirement for approval by the HKU/HA HKW IRB. To prevent delays in the total review process, at its discretion, the HKU/HA HKW IRB may accept concurrent review by the HKU/HA HKW IRB and the other agency, but defer the final decision until a notice of certification has been received.

1. The HKU/HA HKW cluster hospitals may be responsible for safekeeping, dispensing and monitoring of investigational drugs administered to human subjects within the confines of the institution. The same regulations will apply to studies involving marketed drugs and a placebo, being dispensed in a blinded or masked manner. For such drug studies, the HKU/HA HKW IRB will require prior certification by the appropriate hospital pharmacy as a condition for approval.
2. The protocol of research studies involving the administration of radioactive substances to human subjects will be reviewed and approved by an appropriate committee. When applicable, the HKU/HA HKW IRB will require prior certification as a condition for approval.
3. Research involving tissues from human foetuses will be reviewed and approved by an appropriate committee. For these projects, the HKU/HA HKW IRB will require prior certification as a condition for approval.
4. Research projects involving transfer of genetic materials to human subjects will be reviewed and approved by an appropriate committee. The HKU/HA HKW IRB will require prior certification as a condition for approval.
5. All devices, regardless of whether they are investigational or marketed devices will be reviewed and approved by an appropriate committee. For studies involving devices to be used on or in human subjects, the HKU/HA HKW IRB will require prior certification as a condition for approval.

12. EDUCATIONAL ACTIVITIES OF HKU/HA HKW IRB

The HKU/HA HKW IRB will provide services to inform the research community on issues related to use of human subjects in research and ethics in research, and to make researchers aware of applicable local and international regulations.

12.1 HKU/HA HKW IRB Educational Activities Aimed at Research Community at Large

The HKU/HA HKW IRB will disseminate new information on ethical and safety issues involving human subject research. Speakers, who are experts in the subject matter, maybe invited from other institutions as well, to take part in these activities.

12.2.1 HKU/HA HKW IRB Educational Activities Aimed at Investigators of Projects Involving Human Subjects

Intermittently, using the electronic mail system of HKW, HA the HKU/HA HKW IRB will broadcast to researchers who have active research projects involving human subjects, reviews of the rationale for selected regulatory policies, and reminders on periodic actions expected by the HKU/HA HKW IRB from the researchers.

The HKU/HA HKW IRB will maintain on the hospital intranet system an electronic "page", containing documents published by local and international regulatory agencies, as well as those prepared by the HKU/HA HKW IRB, as listed in Section 13.5.

12.3 HKU/HA HKW IRB Educational Activities Aimed at Members of HKU/HA HKW IRB

At the time of induction of a new member, the Chairperson or Deputy Chairperson of the HKU/HA HKW IRB will review with the member all procedures of the HKU/HA HKW IRB.

The hospital will provide the opportunity to each new member of the HKU/HA HKW IRB to attend a workshop on human subject issues in research. The same opportunity will be provided also to existing members of the HKU/HA HKW IRB. Participation in such courses must be documented for each member of the IRB.

13. HKU/HA HKW IRB RECORDS

13.1 Archiving of HKU/HA HKW IRB Documentation

All documentation and communications of the HKU/HA HKW IRB shall be dated, filed and archived. Documents will be filed and archived for a minimum period of 3 years following the completion of a study and will include, but not be limited to the following;

1. The constitution, written standard operating procedures of the HKU/HA HKW IRB, and regular (annual) reports.
2. Member records of the HKU/HA HKW IRB.

3. Published guidelines for submission established by the HKU/HA HKW IRB.
4. Agendas of the HKU/HA HKW IRB meetings.
5. Minutes of the HKU/HA HKW IRB meetings.
6. Reports of internal audits of the HKU/HA HKW IRB.
7. One copy of all materials submitted by an applicant.
8. Correspondence by the HKU/HA HKW IRB members, with applicants or concerned parties regarding application, decision and follow-up.
9. A copy of the decision and any advice or requirements sent to an applicant.
10. All written documentation received during the follow-up.
11. Notification of the completion, premature suspension, or premature termination of a study.
12. Research Final Report - HKU/HA HKW IRB 001F9b.

13.2 HKU/HA HKW IRB Research Projects

The HKU/HA HKW IRB will maintain an archive of files for all research projects approved by the HKU/HA HKW IRB. Such files will be retained for at least three years after completion of the research. Each project folder will include the following types of documents, as conventional hard copies:

1. Clinical Research Ethics Review Application Form - HKU/HA HKW IRB 001F3.
2. Study Protocol.
3. Investigator's Brochure.
4. Patient/Subject Information Sheet – English.
Patient/Subject Information Sheet – Chinese (Traditional)
5. Patient/Subject Consent Form – English.
Patient/Subject Consent Form – Chinese (Traditional)
6. Texts of advertisements for subject recruitment - English (where appropriate).
Texts of advertisements for subject recruitment – Chinese (Traditional) (where appropriate).
7. Questionnaires/Interview Guides – English (where appropriate).
Questionnaires/Interview Guides – Chinese (Traditional) (where appropriate).
8. Investigator's short CV.

9. Insurance policy document.
10. Investigator's Conflict of Interest Form - HKU/HA HKW IRB 001F4.
11. Certification documents from other agencies, as mandated by federal regulatory agencies or by HKW, HA to review and approve a project of a specific type.
12. IRB Approval Form - HKU/HA HKW IRB 001F6a.
13. Research Progress Report Form - HKU/HA HKW IRB 001F9a.
14. Research Final Report Form - HKU/HA HKW IRB 001F9b.
15. Protocol Amendment Application Form - HKU/HA HKW IRB 001F7
16. Statements on significant new findings.
17. Correspondence between HKU/HA HKW IRB and investigators of the project.

13.3 HKU/HA HKW IRB Relational Database

To facilitate tracking of the steps involved in accepting, reviewing and monitoring research projects involving human subjects and evaluation of its activities statistically, the HKU/HA HKW IRB will maintain a computerised relational database on all research projects submitted for review. It will be maintained indefinitely.

13.4 HKU/HA HKW IRB Meeting Records

Agendas and minutes of the HKU/HA HKW IRB meetings will be stored in digitised-electronic form on the computer fileserver of the HKU/HA HKW IRB. They will be maintained indefinitely.

13.5 HKU/HA HKW IRB Member Records

HKU/HA HKW IRB member records should include the term and status of each member, Curriculum Vitae, appointment document, declaration of confidentiality, and information about training received. Such information should be maintained and updated as necessary (refer to Section 3) and should be retained for at least 3 years after completion of the service of active members of the HKU/HA HKW IRB.

13.6 Informational Documents

The HKU/HA HKW IRB will make available to the entire research community of HKW, HA or it's affiliated hospitals, electronic copies of various informational documents relevant to human subject research, by storing them in digitised-electronic form on the HKU and HA Internet websites. In addition, hard copies of such documentation will be circulated to the following personnel:

1. All members of the HKU/HA HKW IRB.
2. HKU/HA HKW IRB Administrative staff.
3. Heads of Departments within the Faculty of Medicine.

4. Directors of Research Centres and Institutes of the Faculty of Medicine.
5. The Dean and Associate Deans.
6. Pro-Vice Chancellor of Research.
7. Chiefs of Service of Clinical Departments (if different from heads of Departments).

13.7 Review of HKU/HA HKW IRB Documents

The Chairperson of the IRB must review all HKU/HA HKW IRB documents annually or whenever there is a change of IRB Chairperson, whichever occurs the soonest. The documents that are to be reviewed and signed, where appropriate, by the Chairperson include the those listed in under section 13.7

13.8 HKU/HA HKW IRB Documents

Standard Forms for Investigators

HKU/HA HKW IRB 001F3	Clinical Research Ethics Review Application Form
HKU/HA HKW IRB 001F3a	Clinical Research Ethics Review Application Form for Expedited Review for Multi-center Trial approved by another Cluster REC
HKU/HA HKW IRB 001F4	Investigator's Conflict of Interest Declaration Form
HKU/HA HKW IRB 001F7	Protocol Amendment Application Form
HKU/HA HKW IRB 001F8	Serious Adverse Event Reporting Form
HKU/HA HKW IRB 001F9a	Research Progress Report Form
HKU/HA HKW IRB 001F9b	Research Final Report Form
HKU/HA HKW IRB D1	Declaration of Support from other Departments/Services of QMH / TYH / TWH / GH / DKCH / FYKH / MMRC

Standard Templates for Investigators

HKU/HA HKW IRB T1	Submission Cover Letter
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Supporting Documents for Investigators

HKU/HA HKW IRB 001F10	Guidance Notes for Preparation of Study Protocol
HKU/HA HKW IRB 001F11	Guidance Notes for Preparation of Informed Consent Documents
HKU/HA HKW IRB 001F12	Guidance Notes for Preparation of Curriculum Vitae
HKU/HA HKW IRB 001F13	Declaration of Helsinki - 1996 Version

Information for Investigators and IRB Members

HKU/HA HKW IRB M1	General Research Ethics Information and Definitions for Investigators and IRB Members
HKU/HA HKW IRB 000F0	Standard Operating Procedures (SOPs)
HA RE001	Hospital Authority Guide for Cluster REC (or IRB)
HA RE002	Clinical Research Study Site Guide
HA RE003	Investigator's Code of Practice in Undertaking Clinical Research

Documents for IRB Members

HKU/HA HKW IRB 001F1	Declaration of Confidentiality
HKU/HA HKW IRB 001F2	Reviewers Conflict of Interest Declaration Form
HKU/HA HKW IRB 001F5	IRB Review Checklist

Documents issued by IRB to Investigators

HKU/HA HKW IRB 001F6a	IRB Approval Form
HKU/HA HKW IRB 001F6b	IRB Clarification Form
HKU/HA HKW IRB 001F6c	IRB Disapproval Form

