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Consortium on Harmonization of Institutional Requirements for Clinical Research (CHAIR)

Standard Operating Procedure of the Joint Scientific Committee for Phase 1 Clinical Trials

Document Particulars	
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Approval

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(a) A Standard Operating Procedure (SOP) is an official document outlining the necessary procedures for executing a specified task, which shall be approved by the authorized representative(s) of the organization(s) and complied with by the relevant operating unit(s) and personnel.

(b) A Guideline is a guidance document for elaborating and facilitating compliance with the relevant SOP(s) or requirement(s), which could be approved by the authorized quality assurance specialist(s) and/or the authorized representative(s) of the organization(s).

(c) A Working Manual is a document providing more details about execution of the required procedures under the relevant SOP(s), which could be approved by the authorized representative(s) of the operating unit(s) responsible for the task concerned and followed by the relevant operational personnel.

Version and Review History

Version No.	Review Date (DD/MM/YY)	Issue Date (DD/MM/YY)	Effective Date (DD/MM/YY)	Highlights for the Issue
1	N/A	01/04/14	01/04/14	New SOP for the newly established Joint Scientific Committee for Phase 1 Clinical Trials
2	08/06/18	09/07/18	16/07/18	(1) Clarifying the definition of phase 1 clinical trials; (2) Updating the requirement for lead scientific reviewers; (3) Clarifying the concept of conflicts of interest; (4) Correction of typo errors.
3	07/07/21	16/07/21	16/07/21	(1) Updating the list of ICH regulatory members; (2) Updating the name of the China drug regulatory authority; (3) Clarifying the considerations for sharing of SRP evaluations and recommendations between IRB/RECs; (4) Correction of typo errors.
4	03/10/24	25/10/24	01/11/24	(1) Adjusting the role of the JSC to a consultation body providing expert scientific opinions/recommendations to the relevant IRB/RECs; (2) Removing the restriction of appointing JSC members who are non-employees of the Governing Institutions; (3) Clarifying the SRP's 14-day response timeline as a target rather than a mandatory requirement; (4) Replacing all references to "subject(s)" by "participant(s)" in line with the latest research ethics practice.

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1. Establishment and Mission

1.1 Establishment

1.1.1 The Joint Scientific Committee for Phase 1 Clinical Trials ("**JSC**") was established jointly by The University of Hong Kong ("**HKU**"), The Chinese University of Hong Kong ("**CUHK**") and the Hospital Authority ("**HA**") for supporting their institutional review boards/research ethics committees ("**IRB/RECs**") in performing scientific evaluation of phase 1 clinical trials on new drugs undertaken by and/or conducted in the premises owned, managed and/or controlled by HKU, CUHK and/or HA.

1.2 Mission

1.2.1 The mission of the JSC is protecting the safety of trial participants and ensuring the scientific validity of phase 1 clinical trials under HKU, CUHK and HA through rigorous scientific evaluation of the properties of IMPs, trial designs, pre-clinical data and initial human data (where applicable).

2. Governance

2.1 Consortium on Harmonization of Institutional Requirements

2.1.1 The JSC is governed jointly by HKU, CUHK and HA (jointly the "**Governing Institutions**") through the Consortium on Harmonization of Institutional Requirements for Clinical Research ("**CHAIR**").

2.1.2 The establishment, governance, composition and terms of reference of CHAIR are attached under Appendix 2.

2.1.3 The organizational relationship among CHAIR, the JSC and the relevant IRB/RECs is illustrated in Appendix 3.

3. Scope of Responsibilities

3.1 Clinical Trials Covered

3.1.1 Upon request by a relevant IRB/REC, the JSC shall, via a Scientific Review Panel ("**SRP**") specifically formed, assist in the performance of scientific evaluation of a phase 1 clinical trial on novel chemical or biological drugs not registered in Hong Kong – hereinafter referred to as investigational medicinal products ("**IMPs**") – undertaken by and/or conducted in the premises owned, managed and/or controlled by

HKU, CUHK and/or HA.

3.1.2 For the purpose of this standard operating procedure ("**SOP**"), a phase 1 clinical trial means a clinical trial on an IMP and fulfills any of the following criteria:

(a) A clinical trial which is designated a phase 1 clinical trial on its protocol;
(b) A clinical trial on an IMP which is tested in humans for the first time;
(c) A clinical trial with only human pharmacology (such as pharmacokinetics ("**PK**") and pharmacodynamics ("**PD**")), toxicity and/or safety (but not efficacy) of the IMP as its primary objective(s);
(d) A clinical trial which is reasonably deemed by the relevant IRB/REC a phase 1 clinical trial or equivalent to a phase 1 clinical trial from the perspective of clinical risk.

3.1.3 For the avoidance of doubt,

(a) any PK, PD, bioavailability ("**BA**") or bioequivalence ("**BE**") trial on a chemical drug (i) with its active chemical entity registered in Hong Kong or any country/place in the "ICH Region"; and (ii) with the same route of administration of the corresponding chemical drug registered in Hong Kong or any country/place in the "ICH Region"; shall not be regarded as a phase 1 trial under this SOP; and
(b) any clinical trial on a biosimilar that is not registered in Hong Kong and fulfills the criteria under Section 3.1.2 shall be regarded as a phase 1 trial under this SOP;

where the "**ICH Region**" refers to the corresponding countries/regions of the ICH's founding regulatory members, standing regulatory members and regulatory members.

3.2 Responsibilities and Rights

3.2.1 Upon request by a relevant IRB/REC, a trial-specific SRP should be formed (in accordance with Section 7.1.3) to:

(a) assist in the performance of scientific evaluation of a phase 1 clinical trial; and
(b) give expert scientific opinions and recommendations to the requesting IRB/REC for approval or disapproval of the phase 1 trial and give other opinions with respect to the scientific aspects of the trial evaluated.

3.2.2 The SRP has the rights to:

(a) request for, collect and review information, documents and materials necessary for

performance of its responsibilities; and

(b) recommend modifications to study designs and arrangements on sound scientific basis and in line with the JSC's mission.

4. Membership

4.1 Composition and Qualification of Members

4.1.1 The JSC shall have a minimum of six (6) members, and shall possess relevant scientific expertise such as clinical sciences, pharmacology/clinical pharmacology, pharmacy and medical statistics.

4.1.2 The members of JSC will not be limited to the employees of the Governing Institutions..

4.2 Appointment of Members and Membership Term

4.2.1 JSC members shall be nominated by the Governing Institutions and appointed by CHAIR.

4.2.2 Each term of membership shall be up to three (3) years. There is no restriction for reappointment as long as a member continues to fulfill the relevant requirements.

4.3 Termination of Membership

4.3.1 Membership of any JSC member may be terminated:

(a) by CHAIR anytime in writing if the member no longer fulfills the relevant requirements or is deemed by CHAIR unsuitable to continue to be a JSC member; or

(b) by a JSC member on 30-day prior written notice to CHAIR.

4.4 Conflicts of Interest

4.4.1 Conflicts of interest and potential conflicts of interest may lead to bias in evaluation and should be avoided.

4.4.2 Each JSC member participating in a scientific evaluation shall make a declaration of interest by completing a Declaration of Interest Form prior to his/her participation in an evaluation. Any member having a conflict of interest or potential conflict of interest that may affect his/her unbiased evaluation of the study shall not participate in the scientific evaluation.

4.5 Confidentiality Obligations

4.5.1 All the information submitted for scientific evaluation shall be deemed confidential and shall not be disclosed by the JSC to any third party, save and except for CHAIR and the Governing Institutions.

4.5.2 Upon acceptance of an appointment as a JSC member, the member shall be required to sign a Statement of Confidentiality to confirm his/her agreement to the confidentiality obligations in the JSC.

4.6 Payment to Members

4.6.1 CHAIR may, as it deems appropriate and at its discretion, formulate its policy and mechanism for paying the JSC members for their contributions in the JSC.

5. Administration

5.1 General Administration

5.1.1 The HA shall provide general administrative support to CHAIR and the JSC, including (but not limited to):

(a) maintenance of the records of CHAIR (e.g. meeting agendas and minutes);
(b) maintenance of the latest and all previous versions of this SOP; and
(c) administrative assistance with respect to membership to CHAIR and the JSC (e.g. processing of appointment of JSC members and maintenance of the updated membership lists of CHAIR and JSC).

5.2 Trial-specific Administration

5.2.1 The IRB/REC requesting for a scientific evaluation shall be responsible for the trial-specific administration, including (but not limited to):

(a) inviting JSC members as the scientific reviewers for the trial concerned;
(b) collecting and submitting the necessary information, documents and materials to the scientific reviewers;
(c) communicating with scientific reviewers with respect to the scientific evaluation arrangements;
(d) collecting recommendations and/or opinions from scientific reviewers; and
(e) documenting the process and relevant information with respect to the scientific evaluation.

5.3 Management for Trial-specific Records

5.3.1 All the records relating to a scientific evaluation shall be maintained and retained by the requesting IRB/REC together with the other IRB/REC records of the same trial in accordance with the IRB/REC's SOP.

6. Quality Assurance

6.1 Maintenance of Standard Operating Procedure

6.1.1 This SOP is jointly endorsed by the three Governing Institutions and is signed in triplicates. One originally signed copy shall be kept by each Governing Institution.

6.1.2 This SOP shall be reviewed by CHAIR about every three (3) years. Additional reviews may be performed as deemed required by CHAIR.

6.1.3 The reviewer(s) shall give recommendations (e.g. making modifications or keeping the SOP unchanged) to CHAIR after completing the review. Such recommendations shall be duly considered by CHAIR. No matter the SOP is modified or not after a review,

(a) the version and review history at the front part of this SOP shall be updated;
(b) the SOP shall be endorsed and signed in triplicates by the authorized representatives of the Governing Institutions; and
(c) one originally signed copy shall be kept by each Governing Institution.

6.2 Review by IRB/RECs

6.2.1 The relevant IRB/RECs will have the right to review the JSC's operations as needed and to provide feedback to CHAIR as appropriate.

6.3 Regulatory Inspections

6.3.1 Regulatory inspections of the JSC's operations and relevant records by local regulatory authorities (e.g. Hong Kong Department of Health) and other competent regulatory authorities (e.g. National Medical Products Administration of China) shall be allowed on legitimate requests.

7. Scientific Evaluation Process

7.1 Initiation of Scientific Evaluations

7.1.1 A request for scientific evaluation of a clinical trial shall be initiated by the IRB/REC responsible for overseeing the trial. No request for scientific evaluation shall be accepted directly from principal investigators or other study personnel.

7.1.2 An IRB/REC shall review a clinical trial application and determine if a scientific evaluation by the JSC is required according to its SOP. If a scientific evaluation by the JSC is deemed required, the IRB/REC shall:

(a) form a SRP in accordance with Section 7.1.3 to perform scientific evaluation of the trial; or
(b) in case the trial has already been evaluated by a SRP formed by another IRB/REC in accordance with this SOP and that SRP's evaluation/recommendation is still deemed valid considering the documents/information evaluated, request for that SRP's written recommendations from another IRB/REC (instead of forming another SRP as required under Section 7.1.2(a)), subject to completion of a separate Declaration of Interest Form by each SRP member (as required under Section 4.4.2).

7.1.3 A SRP shall be composed of at least three (3) members. The requesting IRB/REC shall invite any one (1) member from the JSC to be the lead scientific reviewer. The requesting IRB/REC will then recommend to the lead scientific reviewer a minimum of two (2) other members from the JSC as scientific reviewers to form a SRP for the trial. In the event that the requesting IRB/REC is unable to identify sufficient number of suitable and available scientific reviewers from the JSC, it may recommend suitable candidate(s) to CHAIR for consideration for appointment as JSC member(s).

7.1.4 Any member having a conflict of interest or potential conflict of interest that may affect his/her unbiased evaluation of the study shall not participate in the scientific evaluation. Each invited JSC members shall determine if he/she has a conflict of interest or potential conflict of interest based on at least the following information provided by the requesting IRB/REC:

(a) Sponsor(s) or the coordinating organization(s) of the trial.
(b) Name or identifying code of the IMP.
(c) Name of the principal investigator(s) and the other key study team members.

7.1.5 Upon formation of a SRP, the requesting IRB/REC shall provide to each scientific reviewer a scientific evaluation package (by electronic mail or facsimile) including at least:

(a) a completed ethics review application form;
(b) a trial protocol;
(c) an investigator's brochure and/or other documents detailing the nature, properties, pre-clinical data and, if available, human data about the IMP;
(d) each principal investigator's curriculum vitae ; and
(e) a scientific reviewer's Declaration of Interest Form.

7.2 Performance of Scientific Evaluations

7.2.1 The JSC aims at protecting the safety of trial participants and ensuring the scientific validity of phase 1 clinical trials through rigorous scientific evaluations. Each scientific evaluation shall be performed by a SRP based on the core principle of participant protection and scientific validity.

7.2.2 In each scientific evaluation, the scientific reviewers will consider all the information that is relevant to participant protection and scientific validity, such as:

(a) the risk of the IMP;
(b) the scientific basis of participant selection;
(c) the formulation and route of administration of the IMP;
(d) the starting dose of the IMP (for first-in-human/first-in-patient trials);
(e) the dose escalation scheme (for ascending dose trials);
(f) the dosing schedule; and
(g) the stopping rules.

7.2.3 Scientific reviewers will consider the above aspects by referencing the relevant provisions in the Guideline on Ethics Oversight and Scientific Evaluation for Phase 1 Clinical Trials (CHAIR/GL/001) issued jointly by HKU, CUHK and HA.

7.2.4 The SRP has the right to request for addition information or clarification as it deems required for performing a scientific evaluation.

7.2.5 Scientific reviewers shall perform evaluation independently and may discuss through teleconferences, emails and/or face-to-face meetings as they deem appropriate.

7.2.6 If deemed required by the SRP or the requesting IRB/REC for facilitating a scientific evaluation, a meeting or teleconference between the SRP and the principal

investigator(s) (and/or the designee(s) of the principal investigator(s)) may be arranged by the requesting IRB/REC.

7.3 Recommendations by Scientific Review Panel

7.3.1 Each scientific reviewer shall sign and return the Declaration of Interest Form to the requesting IRB/REC before making any recommendation or expressing any opinion with respect to the trial concerned.

7.3.2 The lead scientific reviewer should, on behalf of the SRP, provide recommendations or otherwise make a request for additional information or clarification within fourteen (14) calendar days from the day of receipt of the scientific evaluation package from the requesting IRB/REC. The SRP should also use its endeavours to respond to the requesting IRB/REC within fourteen (14) days from the day of receipt of the requesting IRB/REC's further request or information.

7.3.3 The requesting IRB/REC shall consider the SRP's recommendations as well as its only ethics and scientific evaluation and make its judgment on approval, disapproval or otherwise with respect to each application for phase 1 clinical trial in accordance with its SOP.

Appendix 1:
List of Abbreviations

BA	Bioavailability
BE	Bioequivalence
CHAIR	Consortium on Harmonization of Institutional Requirements for Clinical Research
CUHK	The Chinese University of Hong Kong
HA	Hospital Authority
HKU	The University of Hong Kong
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
IMP	Investigational medicinal product
IRB/REC	Institutional review board/research ethics committee
JSC	Joint Scientific Committee for Phase 1 Clinical Trials
PD	Pharmacodynamics
PK	Pharmacokinetics
SOP	Standard operating procedure
SRP	Scientific Review Panel

Appendix 2:
Establishment, Governance, Composition and Terms of Reference of CHAIR

Establishment and Governance of CHAIR

The Consortium on Harmonization of Institutional Requirements for Clinical Research ("CHAIR") is a consortium jointly established and governed by The University of Hong Kong, The Chinese University of Hong Kong and the Hospital Authority (jointly the "Governing Institutions").

Composition of CHAIR

CHAIR is composed of nine (9) members, including three (3) members delegated by each of the Governing Institutions.

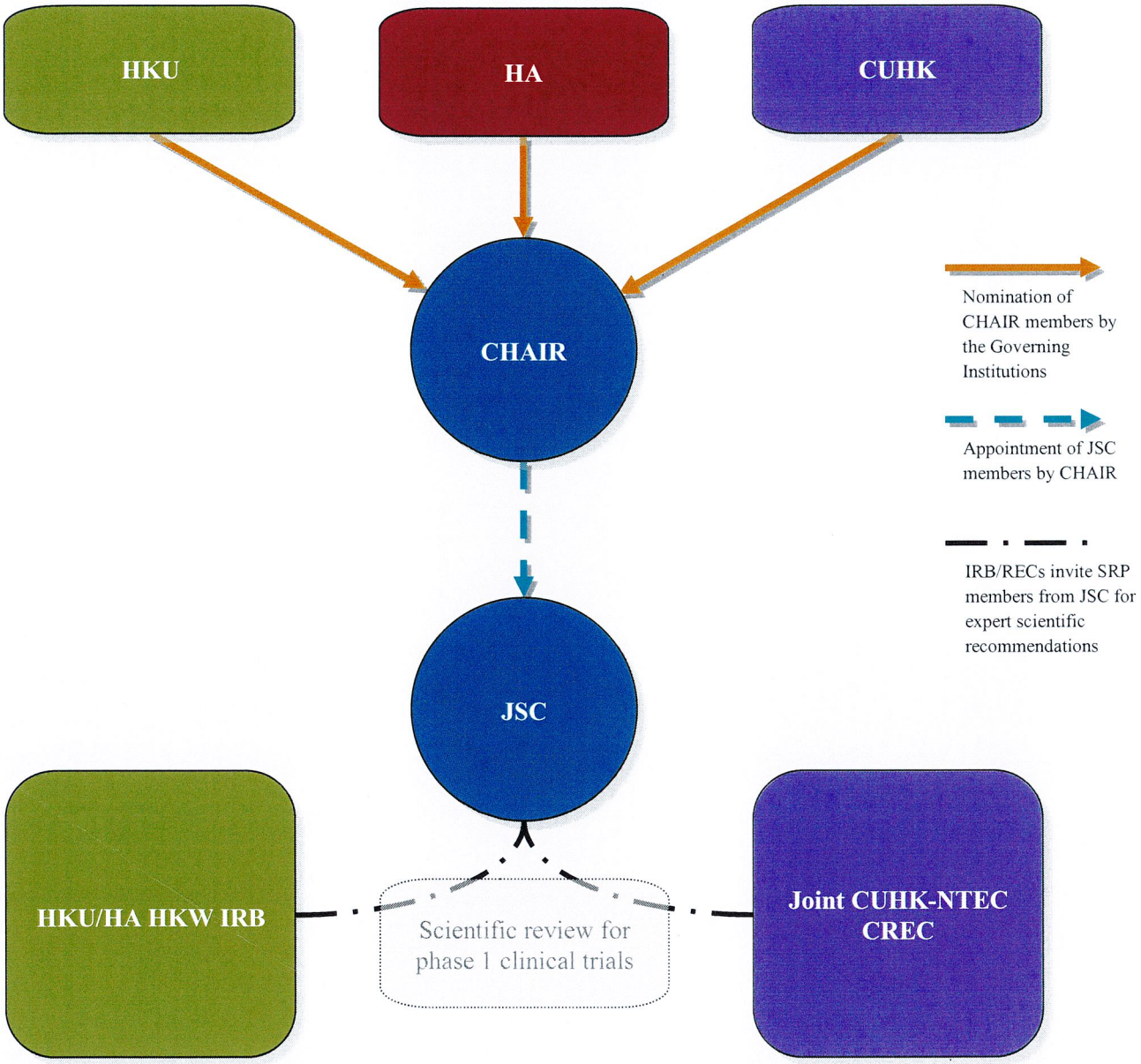
Terms of Reference of CHAIR

1. To align and harmonize the frameworks for scientific evaluation of phase 1 clinical trials with international standards.

2. To appoint and renew members of the Joint Scientific Committee for Phase 1 Clinical Trials ("JSC").

3. To develop and revise the standard operating procedure ("SOP") of the JSC and the relevant guidelines.

Appendix 3:
Organizational Relationship among CHAIR, JSC and IRB/RECs



CHAIR	Consortium on Harmonization of Institutional Requirements for Clinical Research
CUHK	The Chinese University of Hong Kong
HA	Hospital Authority
HKU	The University of Hong Kong
HKU/HA HKW IRB	The University of Hong Kong/Hospital Authority Hong Kong West Cluster Institutional Review Board
Joint CUHK-NTEC CREC	Joint The Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee
JSC	Joint Scientific Committee