

First Edition

Malaysian Guideline *for* Independent Ethics Committee Registration and Inspection



National Pharmaceutical Control Bureau
Ministry of Health Malaysia



Malaysian Guideline for Independent Ethics Committee Registration and Inspection

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This Guideline is adapted from:

1. World Health Organization (TDR/WHO) (2000): *Operational Guidelines for Ethics Committees That Review Biomedical Research*. WHO, Geneva.

(*Operational Guidelines for Ethics Committees That Review Biomedical Research*, 2000)
2. World Health Organization: *Surveying and evaluating ethical review practices*. Geneva. 2002.(*Surveying and evaluating ethical review practices*, 2002)
3. World Health Organization: *Standards and operational guidance for ethics review of health-related research with human participants*. Geneva. 2011.(*Standards and operational guidance for ethics review of health-related research with human participants*, 2011)
4. European Medicines Agency: *Procedure for reporting of GCP inspections requested by the Committee for Medicinal Products for Human Use (CHMP)*. London. 2013. EMA/INS/GCP/588734/2012

(*Procedure for reporting of GCP inspections requested by the Committee for Medicinal Products for Human Use (CHMP)*, 2013)
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7. United States Food and Drug Administration. Code of Federal Regulations, Title 21, Volume 1, Part 56 Institutional Review Boards. Revised April 1, 2014.
8. United States Food and Drug Administration. Code of Federal Regulations, Title 21, Volume 1, Part 50 Protection of Human Subjects. Revised April 1, 2014.

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FOREWORD

The Drug Control Authority (DCA)'s mission is to ensure the implementation of Good Clinical Practice (GCP), which is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Ethics committees play a crucial role in assessing the scientific and ethical aspects of a clinical trial to safeguard the rights, safety and well-being of clinical trial subjects. In recent years, National Pharmaceutical Control Bureau, in particular of Center for Investigational New Products has expanded its activities in ethical committee inspections.

The DCA is at the forefront to create an eco-system environment in clinical research platform to ensure all parties involved in clinical trials in Malaysia comply with the principles embossed in the GCP. Independent ethics committee inspection plays an important role in upholding the quality conduct of an ethic committee in line with international ethical practice and requirements.

This guideline, Malaysian Guideline for Independent Ethics Committee Registration and Inspection, 1st edition specifically narrates the registration process for a new ethical committee, conduct of ethical committee inspection and administrative maintenance of ethical committee with DCA. This guideline supersedes the appendix VI in the Guideline for Good Clinical Practice Inspection Programme.

I would like to express my deepest appreciation to the committee members and stakeholders whom inspired and shared their insight to develop this guideline. It is my pleasure that this guideline will contribute to catalyst the process of ethics committee registration and inspection.



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ABBREVIATION

| | |
|------|---|
| CAPA | Corrective Action and Preventive Action |
| CDCR | Control of Drugs and Cosmetics Regulation |
| CRO | Contract Research Organisation |
| CTIL | Clinical Trial Import Licence |
| CTX | Clinical Trial Exemption |
| CV | Curriculum Vitae |
| DCA | Drug Control Authority |
| EMA | European Medicines Agency |
| GCP | Good Clinical Practice |
| ICH | International Conference of Harmonisation |
| IEC | Independent Ethics Committee |
| NCCR | National Committee for Clinical Research |
| NPCB | National Pharmaceutical Control Bureau |
| PI | Principal Investigator |
| SAE | Serious Adverse Events |
| WHO | World Health Organisation |

1.0 INTRODUCTION

Independent Ethics Committee (IEC) is an independent body constituted of medical/scientific and non medical/scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a clinical trial. The principles, requirements and standards set out in this document apply to IEC reviewing drug related clinical trials that relates to areas of responsibility of NPCB. This guideline does not cover for non-drug related clinical trials.

2.0 REGULATORY FRAMEWORK AND SCOPE

2.1 Regulatory Framework

This guideline should be read in conjunction with Control of Drug and Cosmetic Regulation 1984, The Poison Regulations (Psychotropic Substances) 1989 and Sale of Drug Acts 1952. Under Regulation 29, Control of Drug and Cosmetic Regulation 1984, the Director of Pharmaceutical Services may issue written directives or guidelines to a group of persons as he thinks necessary for the better carrying out of the provisions of these Regulations and in particular relate to clinical trials. The Director of Pharmaceutical Services, Ministry of Health Malaysia issued directive KKM-55/203/001/04 Bhg4 (9) dated 12 June 2007 stating that all IEC approving drug related clinical trial must be registered with the Drug Control Authority (DCA). This guideline is intended to provide information regarding to the registration of IECs with the National Pharmaceutical Control Bureau (NPCB) which is the secretariat of DCA. This guideline also layout the inspection procedure involved. Under Regulation 30, CDCR 1984, any person who contravenes any directives or guidelines issued by the Director of Pharmaceutical Services commits an offence.

2.2 Scope

This guideline will address IECs that reviews all drug related clinical trials that is conducted in Malaysia as defined in Directive Ref KKM-55/203/001/04 Bhg (9) dated 12 June 2007.

This guideline will be divided into two main sections:

- IEC Application

It is the administrative procedures for an IEC that review clinical trials to register and provide updated information to NPCB according to section 6.

- IEC Inspection

IEC inspection delineates the procedures involved in inspections to the IEC conducted by NPCB. IECs that comply with the Malaysian Guideline for Good Clinical Practice and regulatory requirements will be listed into the "National Pharmaceutical Control Bureau Independent Ethics Committee Compliance Programme"

No CTIL/CTX and BE notification shall be issued by the DCA if the drug-related clinical trial is approved by an IEC which is not registered with the DCA.

3.0 DEFINITIONS

Clinical Trial/ Study

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s) and/or to identify any adverse reactions to an investigational product(s) and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

Clinical Trial Exemption (CTX)

An exemption issued under regulation 15 (5), Control of Drugs and Cosmetics Regulations 1984 by Director of Pharmaceutical Services which exempts a person who wishes to manufacture product(s) solely for the purpose of producing samples for clinical trials from the provisions of regulation 7 (1) or regulation 18A of Control of Drugs and Cosmetics Regulations 1984.

Clinical Trial Import Licence (CTIL)

A license in Form 4 in the Schedule of the Control of Drugs and Cosmetics Regulations 1984, issued by Director of Pharmaceutical Services under regulation 12(1)(c) of the same Regulations which authorises the licensee to import any product for purposes of clinical trials, notwithstanding that the product is not a registered product.

Clinical Trial/ Study Report

A written description of a trial/study of any therapeutic, prophylactic, diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report (see the ICH Guideline for Structure and Content of Clinical Study Reports).

Compliance

The state of conformity of a regulated party or a product with a legislative or regulatory requirement or a recognized standard or guideline.

Confidentiality

Prevention of disclosure, to other than authorised individuals, of a sponsor's proprietary information or of a subject's identity.

Contract

A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

Contract Research Organisation (CRO)

A person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Drug Control Authority (DCA)

An authority set up under the Control of Drugs and Cosmetics Regulations 1984 and as such its responsibility, role and mandate are defined by law.

Direct Access

Permission to examine, analyse, verify and reproduce any records and report that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor's monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information.

Drug

Includes any substance, product or article intended to be used or capable, or purported or claimed to be capable, of being used on humans or any animal, whether internally or externally, for medicinal purposes.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are protected.

Independent Ethics Committee (IEC)

An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical/scientific professionals and non-medical/non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favourable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The legal status, composition, function, operations and regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in Malaysian Guideline for GCP.

Informed Consent

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

Inspection

The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial that may be located at the site of the trial, at the sponsor's and/or contract research organisation's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

Inspector

Any person appointed to be an inspector under Section 3 of Dangerous Drugs Act 1952, Section 31 of Poisons Act 1952, Section 21 of Registration of Pharmacists Act 1951, Section 6A of Medicines (Advertisement and Sale) Act 1956, Section 3 (1) and Section 3 (2) of Sale of Drugs Act 1952.

Institution (medical)

Any public or private entity or agency or medical or dental facility where clinical trials are conducted.

Investigation

Specific response to known or suspected non-compliance. Investigations typically are undertaken when there are reasonable grounds to suspect that non-compliance has occurred and that enforcement measures may be necessary (e.g. product quality complaints, reports from other regulatory authorities, reports of adverse reactions or etc.).

Investigator

A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Investigator's Brochure

A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.

Medicinal Purpose

Any of the following purposes;

- a. Alleviating, treating, curing or preventing a disease or a pathological condition or symptoms of a disease;
- b. Diagnosing a disease or ascertaining the existence, degree or extent of a physiological or pathological condition;
- c. Contraception;
- d. Inducing anaesthesia;
- e. Maintaining, modifying, preventing, restoring or interfering with, the normal operation of a physiological function;
- f. Controlling body weight;
- g. General maintenance or promotion of health or well-being.

National Committee for Clinical Research (NCCR)

A committee established for the purpose of coordinating and promoting clinical research in Malaysia, chaired by the Director General of Health, Ministry of Health.

Observation

A deviation or deficiency noted by an Inspector during an inspection.

Opinion (in relation to Independent Ethics Committee)

The judgement and/or the advice provided by an Independent Ethics Committee (IEC).

Product

- a. A drug in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for a medicinal purpose; or
- b. A drug to be used as an ingredient for a preparation for a medicinal purpose.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the Malaysian Guideline for GCP the term protocol refers to protocol and protocol amendments.

Protocol Amendment

A written description of a change(s) to or formal clarification of a protocol.

Sponsor

An individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.

Trial Site

The location(s) where trial-related activities are actually conducted.

Unregistered Product

Any product which is not registered in Malaysia by the DCA.

4.0 APPLICATION PROCEDURES

An IEC not registered with DCA shall submit an application form for registration.

4.1 Approval from NCCR

The applicant shall seek approval from the NCCR prior to applying to the NPCB for inclusion in the NPCB IEC Compliance Program. The applicant shall submit the following (but not limited to) documents to NCCR:

- Letter of intent
- List of Members

The NCCR reserves the right to request for additional documents to be submitted. NCCR will meet twice a year and will determine if the IEC should proceed with the application process. A written response from NCCR will be sent to the applicant on the outcome of the meeting.

4.2 Application to the NPCB

The IEC is required to complete the application form as described in 4.2.4 and submit the application in hardcopy to NPCB. Links to the application form and instructions to complete it can be downloaded from the NPCB official website at <http://bpfk.moh.gov.my/>. The application shall be made and signed by the chairperson of the IEC.

4.2.1 Responsibility of the applicant

- The applicant is responsible for all the information supplied in support of his/ her application for registration of IEC. He/ She shall be responsible for updating any information relevant to the application.
- Any person who knowingly supplies any false or misleading information in connection with his/ her application commits an offence under the Regulation 13(4), CDCR 1984.

4.2.2 Administrative requirements

All IEC registration application including supporting documents should be submitted in a bound form. Binders with durable covers containing A4 size paper, which can be separated and recombined, are required. External dimensions of the white 2-ring binders should be 290 x 370 mm and 30-50 mm in thickness. Should more than one binder is necessary, please labelled clearly as number volume, as an example "volume 1 of 2", "volume 2 of 2" etc.

The documents should be arranged in the sequence outlined in **Annex I**, equipped with tab file divider.

Application form as well as supportive documents shall each be printed on double sided A4 sized paper with one page per sheet. NPCB reserves the right to request the IEC to submit copies of these documents in softcopy.

4.2.3 Language

The application form and all supportive documents must be legible. The application form must be completed in either English or *Bahasa Melayu*.

4.2.4 Application form

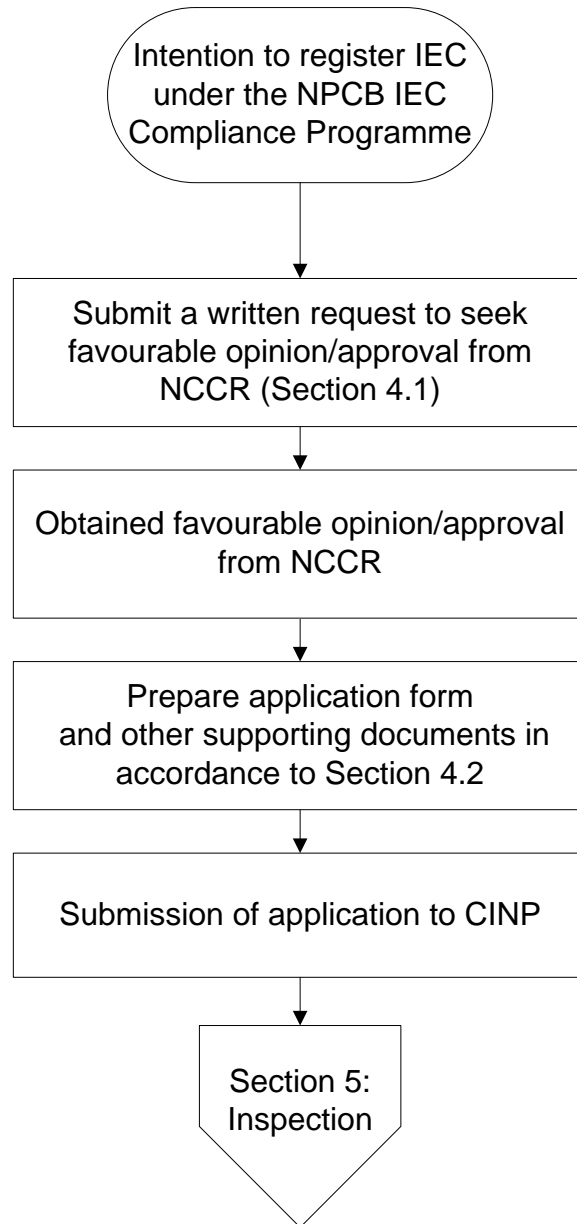
The applicant shall submit a completed application form *NPCB Independent Ethics Committee (IEC) Compliance Programme Application Form (PKPB/300/561)* which is available from the NPCB website at <http://bpfk.moh.gov.my/>. The application shall be signed and dated by the IEC chairperson. Each IEC is required to provide the following information in the application form:

1. Full legal name of the IEC,
2. Location of this IEC, including the mailing address, phone number, facsimile number, and electronic mail address
3. IEC chairperson's full name, phone number, and electronic mail address.
4. Members list to the IEC.
 - All members should be listed in the form. Note: Both voting and non-voting individuals who attend EC meetings shall be included.
 - "Gender" (e.g., male or female).
 - Highest "Earned Degree(s)" (e.g., Ph.D., M.D.).
 - Identify if the IEC member is a Scientist or Non-scientist.
 - Identify the IEC member's primary scientific or nonscientific specialty.
 - Information on IEC member's affiliation to institution(s)

4.2.5 Documents to be submitted in an application

| | |
|---|---|
| 1 | <p>Cover Letter</p> <p>The applicant shall submit a signed cover letter with the application. The cover letter shall be signed by the IEC chairperson.</p> |
| 2 | <p>Application form</p> <p>A completed <i>Application for Independent Ethics Committee Registration & Inspection Form NPCB Independent Ethics Committee (IEC) Compliance Programme Application Form (PKPB/300/561)</i> which can be downloaded from the NPCB official portal shall be submitted. The application shall be signed and dated by the IEC chairperson.</p> |
| 3 | <p>Approval letter / favourable opinion from NCCR</p> <p>A copy of the approval letter / favourable opinion from NCCR shall be submitted. NPCB will only accept approval letter / favourable opinion issued by the NCCR.</p> |
| 4 | <p>Documents referring to the establishment of the IEC</p> <p>A letter of authority under which the IEC was established/formed;</p> |
| 5 | <p>IEC memberships</p> <ul style="list-style-type: none"> a. List of members b. CV for all members c. List of independent consultants/experts (if any) d. CV for all independent consultants/experts (if any) |
| 6 | <p>Standard operating procedures (SOPs)</p> <ul style="list-style-type: none"> a. Master list of SOPs b. All written SOPs as listed in the master list. |

4.3 Flow Chart: IEC application process



5.0 INSPECTION OF IEC

5.1 Categories of IEC inspection

Description of the inspection categories are as follows:

5.1.1 Provisional Inspection

The purpose of this provisional inspection is to verify that the new IEC has established SOPs and other references in compliance with the Malaysia Guideline for Good Clinical Practice, Malaysian regulatory requirements and other established guidelines before the IEC approving any drug related clinical trial.

The liaison officer will contact the IEC for the provisional inspection within 30 working days upon receiving a complete application.

A provisional registration letter will be issued if the provisional inspection was found to be satisfactory and the IEC will be listed in the NPCB IEC Compliance Programme provisionally. The IEC can start reviewing drug related clinical trial once the provisional registration letter has been received. The provisional registration letter issued will stipulate the need for a full inspection to be conducted on the IEC within one year. Procedures for the conduct of a provisional inspection are detailed in Section 5.2.1.

5.1.2 Full inspection

The purpose of this inspection is to verify that the provisionally registered IEC complies to the Malaysian Guideline for Good Clinical Practice, Malaysian regulatory requirements and other established guidelines in order for the IEC to be officially listed in NPCB IEC Compliance Programme. The IEC would undergo a full inspection within **one year** from the date of provisional registration letter as stated under section 5.1.1. Procedures for the conduct of a full inspection are detailed in Section 5.2.2.

5.1.3 Surveillance inspection

Surveillance inspection is an inspection conducted on the IEC to ensure that the IEC functions is in accordance with the Malaysia Guideline for Good Clinical Practice, Malaysian regulatory requirements and other established guidelines. The IEC listed under the *NPCB IEC Compliance Programme* would undergo a surveillance inspection by NPCB within **one year** before the expiry of certificate's validity date. Procedures for the conduct of a Surveillance Inspection are detailed in Section 5.2.2.

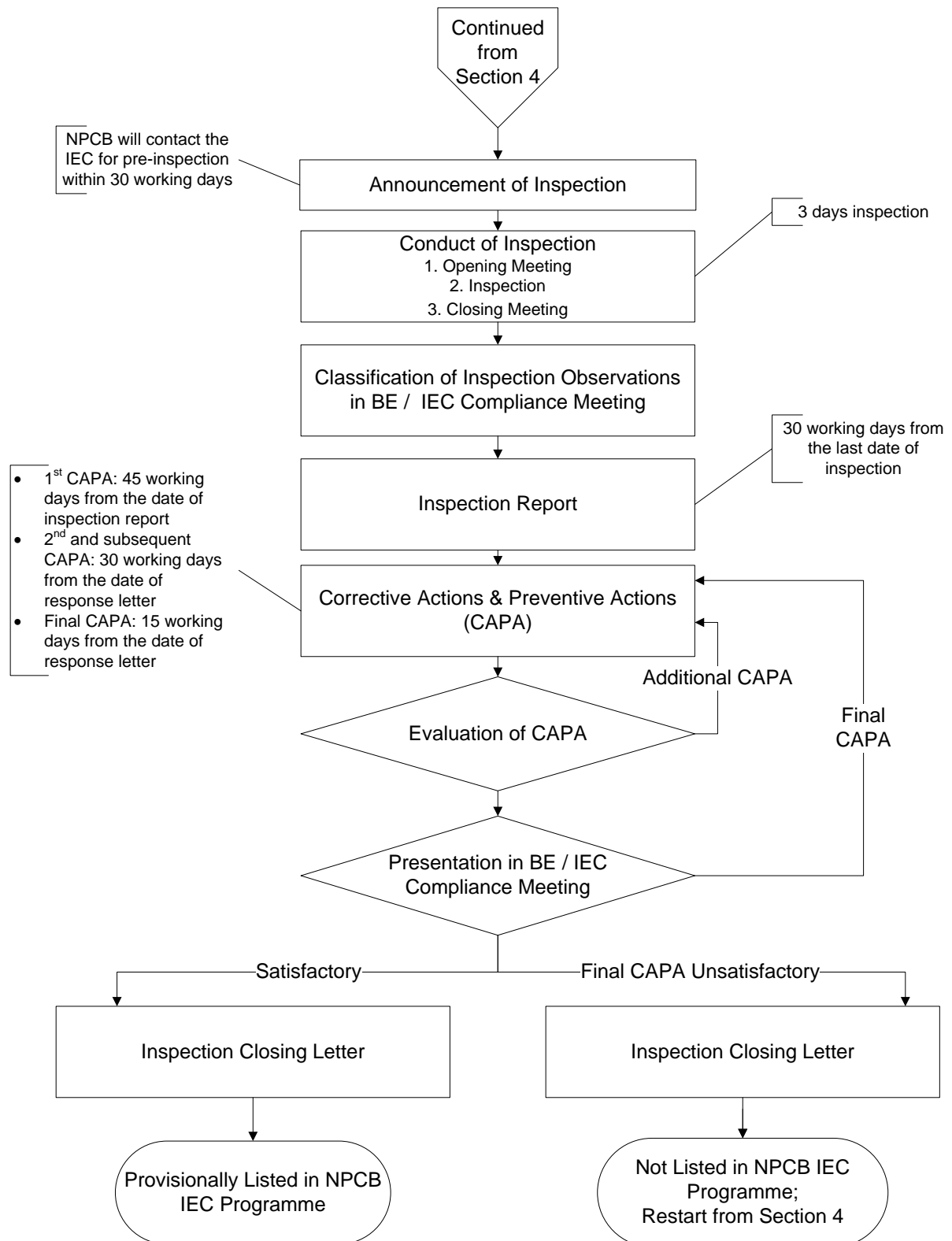
5.1.4 Extraordinary inspection

Extraordinary inspection is an inspection that is triggered due to specific concerns. This investigation may be conducted at any time after the IEC has been listed in *NPCB IEC Compliance Programme*. Specific concerns which may trigger an extraordinary inspection are:-

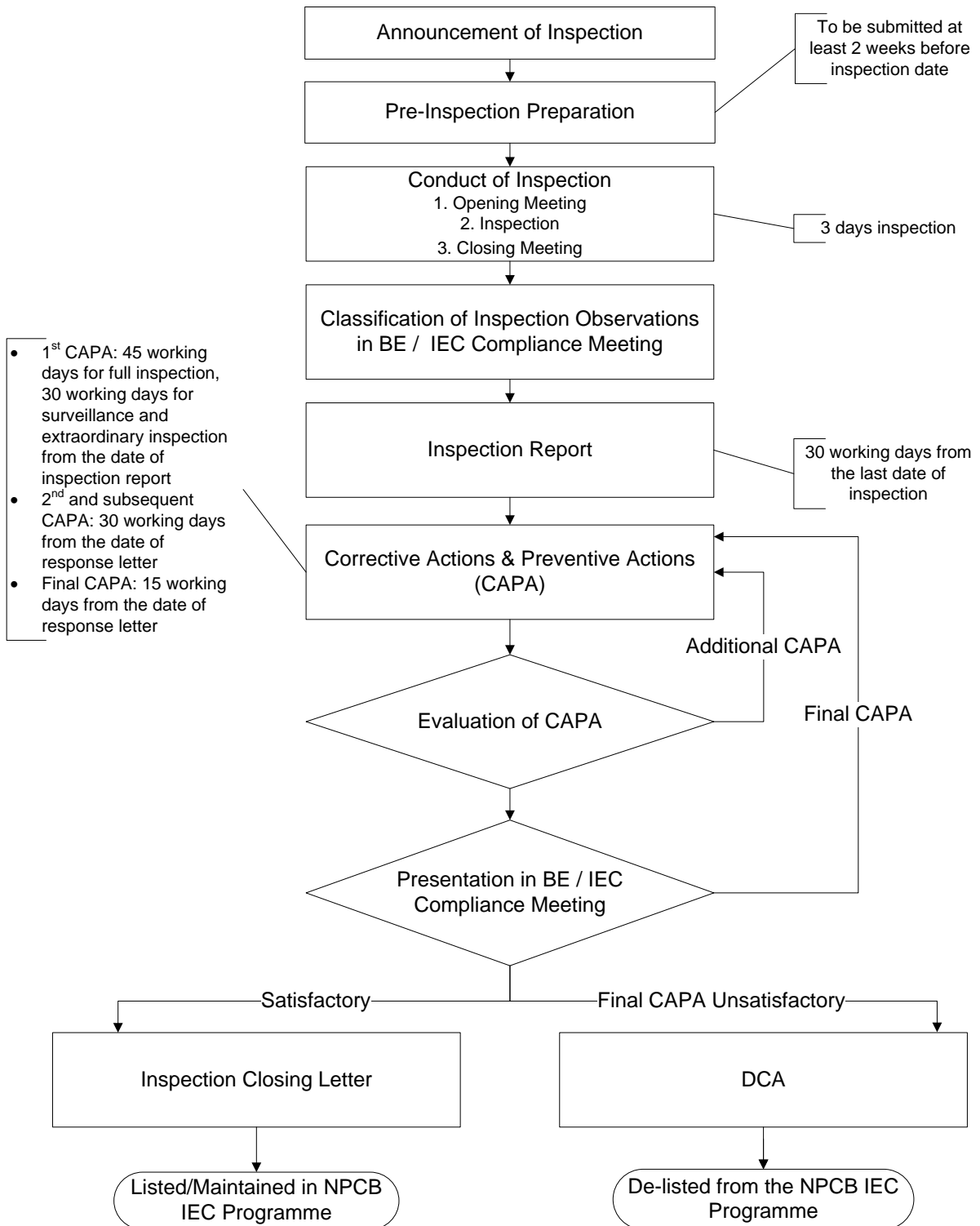
- Complaints received by the regulatory authority on the IEC.
- Reports received by the regulatory authority on clinical trials with possible ethical and safety issues.
- Non-adherence to legal requirements.
- Verification on the implementation of the corrective actions.
- Other issues deemed necessary by the regulatory authority.

5.2 Flow Chart: IEC Inspection

5.2.1 Provisional Inspection



5.2.2 Full Inspection / Surveillance Inspection / Extraordinary Inspection



5.3 Conduct of IEC inspection

An inspection shall be conducted based on an established inspection plan whenever possible. The plan shall be based on the type and scope of the inspection.

5.3.1 Announcement

An announcement letter containing the date of inspection, objectives of inspection, duration of inspection, name of inspectors, inspection schedule and pre-inspection documents to be submitted to NPCB shall be issued to the IEC for all types of inspections. Under normal circumstances, the IEC shall be required to submit the pre-inspection documents at least two weeks before the agreed inspection date.

5.3.2 Opening meeting

The inspection begins with an opening meeting between the inspectors and representative(s) of the IEC. This meeting shall be attended by the chairperson or other senior members of the IEC, the IEC secretariat and the inspectors.

The purpose of an opening meeting is to (but not limited to):

- Highlight the scope of the inspection
- Explain the regulatory framework for the conduct of the inspection
- Explain the methods and procedures to be used during the inspection
- Confirm that the resources, documents and facilities needed by the inspector(s) are made available
- Confirm the time and date for the closing meeting and interim meetings, if any.

This shall be followed by a presentation from the representative of the IEC on the current activities, workload and function of the IEC. An attendance will be kept by the inspectors.

5.3.3 Conduct of inspection

The inspection activities will be detailed in the inspection plan. During the inspection, the inspector(s) reserve the right to make adjustments to the plan to ensure all the inspection objectives are achieved. The secretary or at least one representative from the secretariat who is familiar with the functions of the IEC should be present throughout the conduct of the inspection.

Inspector(s) shall be granted direct access to all source data/documents, books, records and reports in hardcopy or softcopy that are relevant to the inspection. Direct access is defined as permission to examine, analyse, verify and reproduce any records and reports that are important to the inspection process.

During the inspection, documents as listed in **Annex I** (but not limited to) may be requested by the inspectors to be inspected. Inspectors will attempt to reconstruct the work process involved in the core activities of the IEC based on available SOP, documents and records.

IEC shall ensure that its management and other key personnel are available during the inspection in the event that their input is required by the inspectors. The IEC shall also make

available a room for document examination as well as assist in any other inspection related activities.

5.3.4 Closing meeting

The closing meeting should be participated by the IEC Chairperson or senior IEC member and the IEC secretariat. During this meeting, the inspectors shall present to the IEC representatives all observations made during the inspection verbally. At the end of the session, representatives from the IEC will be given the opportunity to clarify on the observations made by the inspectors. Attendance will be kept by the inspector and an acknowledgement will be obtained from the representatives of the IEC on the evidences collected during the inspection.

5.3.5 Inspection report and CAPA

All observations will be classified as per definitions in *Section 5.5* and presented as a written inspection report. The IEC shall receive a written inspection report detailing the observations within 30 working days from the last day of inspection. The IEC should provide a written Corrective And Preventive Actions (CAPA) in both hard copies and soft copies in response to the observations within 45 working days for full inspection and 30 working days for surveillance inspection from the date of the inspection report. If the assessed CAPA(s) is/are deemed unsatisfactory, second CAPA may be requested and shall be resubmitted to the inspector no later than 30 working days under normal circumstances.

A final CAPA may be requested by NPCB from the IEC. The IEC is given 15 working days to response to NPCB regarding to the final CAPA.

5.3.6 Final Approval of Inspection Results

5.3.6.1 In Compliance

An Inspection closing letter and a certificate will be issued to the IEC to indicate that it has been listed under the NPCB IEC Compliance Program. Under normal circumstances, the certificate is valid for 3 years. However, depending on the severity of observations in the last inspection, this validity period may be less than the maximum of 3 years. Once the certificate of the IEC is not valid, approval of new studies reviewed by the IEC issued during this period will not be accepted for CTIL/CTX and BE notification application.

For provisional registered IEC, a decision shall be made by DCA to list the IEC in the NPCB IEC Compliance Programme. A new certificate shall be issued to replace the registration letter and listed in NPCB IEC Compliance Programme.

For IEC already in the NPCB IEC Compliance Programme, a renew certificate shall be issued.

5.3.6.2 Not in compliance

For provisional registered IEC not in compliance, the IEC shall not be listed in the NPCB IEC Compliance Programme. For listed IEC which are not in compliance, DCA may decide to delist the IEC from the NPCB IEC Compliance Programme.

5.4 Power of Inspector

NPCB Inspector(s) have the right to enter any sites involved in the conduct of IEC to carry out inspections, take samples, require the production of books and documents, and to take copies of, or copies of entries in, such books and document which inspector(s) reasonably believes would furnish evidence of the inspection and observations without any redaction. Inspectors shall have full access to the facilities and relevant documentations to conduct any type of inspections; otherwise the IEC would not be included in the NPCB IEC Compliance Programme.

5.5 Classification of findings

The classification of the inspection findings is intended to help classify the severity of observations. Overall, the evaluation will commensurate with the nature and extent of the deviations (i.e. severity). The findings shall be classified as critical, major and minor as per the definitions in Sections 5.5.1, 5.5.2, and 5.5.3 respectively.

5.5.1 Critical

Conditions, practices or processes that adversely affect the rights, safety or well being of the subjects.

Critical observations are considered totally unacceptable.

5.5.2 Major

Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects.

Major observations are serious deficiencies and are direct violations of GCP principles and regulatory requirements.

5.5.3 Minor

Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well being of the subjects.

Observations classified as minor, indicate the need for improvement of conditions, practices and processes.

6.0 MAINTENANCE OF IEC REGISTRATION

6.1 IEC listed in NPCB IEC Compliance Programme

Once an IEC has been issued a closing letter and compliance certificate, its information will be made available to the public via the NPCB website. The IEC's name, address, chairperson's name, contact number and email address will be available at <http://bpfk.moh.gov.my/>.

6.2 Revision of Registration Information

The IEC is responsible for notifying the NPCB on any amendment(s)/updating any information pertaining to the IEC once it is registered under NPCB IEC Compliance Programme. The IEC is required to notify the NPCB within **30 working days** if any of the following information is changed:

- a. IEC's contact or chairperson information which includes IEC's name, address, chairperson's name, contact number and email address.
- b. Any change of membership, composition of the IEC.
- c. The IEC decision to discontinue reviewing of drug related clinical research.

The DCA may request for further supplementary information and/or documentation if deemed necessary.

6.3 Annual Report

The IEC shall submit annual reports to NPCB detailing the activities for the IEC throughout the year. Please refer to **Annex II** for the format of an annual report. The annual report shall be submitted in both softcopy and hardcopy to NPCB before the end of the first quarter (Q1) in the following calendar year.

Any person who knowingly supplies any false or misleading information in connection with the IEC commits an offence under the Regulation 13(4), CDCR 1984.

6.4 The IEC termination/suspension of approved Clinical Trials

The IEC should promptly notify the DCA with detailed written information if the IEC terminates/suspends a clinical trial that has been given an approval/favourable opinion.

6.5 Notification Administrative Requirement.

All the notifications from 6.1 to 6.4 shall be submitted by post in hard copy and/or soft copy in CD to NPCB.

7.0 ANNEX

7.1 Annex I : Review of Documentation

CONDUCT OF INSPECTION AT INDEPENDENT ETHICS COMMITTEE (IEC)/INSTITUTIONAL REVIEW BOARD (IRB)

The aim is to assess ethical review of research proposal is carried out according to the IEC's/IRB's own written standard operating procedures (SOP). It is also to assess IEC/IRB operates in conformity with the Declaration of Helsinki, the ICH/Malaysia GCP Guidelines, relevant laws / regulatory requirements

1.0 ESTABLISHMENT OF THE IEC/IRB

The main points to consider are the following:

- The authority under which the IEC/IRB was established
- A statement that the IEC/IRB operates in conformity with the Declaration of Helsinki, the ICH/Malaysia GCP Guidelines, relevant laws and regulatory requirements
- Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data

2.0 THE MEMBERSHIP OF THE IEC/IRB

The main points to consider are the following:

- The membership requirements, including the duties and responsibilities of member
- The terms for the appointment of members of the IEC/IRB (for example, duration, renewal procedure; disqualification, and resignation and replacement procedures)
- The conditions of appointment (for example, withdrawal from the decision-making process if there is a conflict of interest; willingness to publicise his/her full name, profession and gender; and the signing of confidentiality agreement)
- The procedure for making appointment including the individual or party that makes the appointment, selection of candidates (for example, by consensus, by majority vote, or by direct appointment)
- A listing of current and previous members of the IEC/IRB
- The curriculum vitae of the current and past members of the IEC/IRB
- A description of the requirements for the IEC/IRB offices (for example, chairperson, secretary)
- The quorum requirements, including the minimum and maximum numbers of IEC/IRB to be present
- If an IEC/IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with those subjects.

3.0 APPLICATIONS MADE TO THE IEC/IRB

The main points to consider are the following:

- The published guidelines for submission of application for the review by the IEC/IRB
- The required documentation to be included in the application, including:
 - Application form
 - The protocol

- A recent investigator's brochure or equivalent describing recent pharmacological and toxicological data if absent from the protocol
- Recent curriculum vitae (signed and dated) of the investigator (s),
- Recruitment of trial participants documentation including any advertisement material, all payment and compensations to the trial participations, informed consent forms in core and local language and indemnity agreements for liability
- The registration procedure for applications
- The maintenance of records for communications regarding the application
- The review procedure timelines

4.0 REVIEW PROCEDURES OF THE IEC/IRB

The main points to consider are the following:

- The meeting procedures
- The provisions and conditions for expedited IEC/IRB review and decision for-certain kinds of research involving no more than minimal risk, and for minor changes in approved research. A written procedure shall address who will have the responsibilities of making this determination, as well as the number of reviewers required for expedited review and how those reviewers will be selected.
- The elements of the review of the application
 - Scientific design and conduct of the study
 - Risks and potential benefits
 - Selection of study population and recruitment of research participants
 - Inducements, financial benefits and financial costs
 - Protection of research participants' privacy and confidentiality
 - Informed consent process
 - Community considerations
- The decision-making procedure
- The procedure for communicating a decision
- The follow-up review at intervals appropriate to the degree of risk, but no less than once per year.
- The documentation and archiving procedures; including an inventory of all documents archived and the length of storage of the documents
- Each IEC/IRB which uses an expedited review procedure shall adopt a method for notifying all members.
- When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects.

5.0 ACTIONS TAKEN BY THE IEC/IRB

The main points to consider are the following:

- The materials submitted by applicants (including protocols, informed consent materials, advertising materials, all payments for trial participants, and the curriculum vitae of investigators)
- The correspondence regarding applications, decisions, and follow-ups
- The record of incomes and expenses of the IEC/IRB
- The agenda of IEC/IRB meetings
- The minutes of IEC/IRB meetings with detail to show attendance at the meetings

- The decisions and advice provided to applicants
- Notifications of completion or premature study suspensions/terminations
- Final summaries or reports of studies regular (annual) reports of the IEC/IRB

6.0 RECORDS AND REPORTS

The main points to consider are the following:

- Maintain adequate documentation of IEC/IRB activities, including the following:
 - Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
 - Minutes of IEC/IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IEC/IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.
 - Records of continuing review activities.
 - Copies of all correspondence between the IEC/IRB and the investigators
 - A list of IEC/IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IEC/IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.
 - Written procedures/standard operation procedures (SOP)
- The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Regulatory Authority at reasonable times and in a reasonable manner.

7.2 Annex II : Annual Reports of IECs

An IEC's annual report shall include at least the following:

1. The IEC's name, secretary's name, mailing address, phone number, fax number and electronic mail address.
2. The IEC chairperson's name, mailing address, phone number, fax number and electronic mail address.
3. Organisation chart, details of the officers and staff of the IEC
4. Details of the membership of the IEC, voting and non-voting members, including their occupation, expert/ lay status, initial date of appointment and where applicable the date on which the term of membership expired or the member resigned.
5. The attendance record of each member during the year.
6. A list of full meetings held during the year, including their dates and the number of members attending
7. The list of training record for each member for the current year.
8. A list of the applications reviewed during the year, including the final decision reached on each application and the time taken to complete the review (or the current status of the review) according to pre-defined format.