GUIDELINES FOR GOOD CLINICAL PRACTICE (GCP) INSPECTION

National Pharmaceutical Control Bureau

Ministry of Health

Malaysia

First Edition (Version 1.0)

October 2010

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Adapted from the

1. INS-GCP-1 Procedure for coordinating GCP inspections requested by the EMEA
2. INS-GCP-2 Procedure for preparing GCP inspections requested by the EMEA
3. INS-GCP-3 Procedure for conducting GCP inspections requested by the EMEA
4. INS-GCP-3 Annex I to Procedure for conducting GCP inspections requested by the EMEA- Investigator Site
5. INS-GCP-3 Annex II to Procedure for conducting GCP inspection requested by the EMEA- Clinical Laboratories
6. INS-GCP-3 Annex III to Procedure for conducting GCP inspection requested by the EMEA- Computer Systems Rev. 1
7. INS-GCP-3 Annex IV to Procedure for conducting GCP inspections requested by the EMEA- Sponsor and CRO
8. INS-GCP-4 Procedure for reporting of GCP inspections requested by the EMEA
9. Classification of observations made in the conduct of inspections of clinical trials (GUIDE-0043) by Health Canada
10. Surveying and Evaluating Ethical Review Practices a Complementary Guideline to the Operational Guidelines for Ethics Committees That Review Biomedical Research by World Health Organization, Geneva, February 2002 (TDR/PRD/ETHICS/2002.4)

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THESE GUIDELINES ARE ISSUED BY THE DIRECTOR OF PHARMACEUTICAL SERVICES UNDER REGULATION 29, CONTROL OF DRUG AND COSMETICS REGULATION 1984. HE/SHE RESERVES THE RIGHT TO AMEND ANY PART OF THE GUIDELINE WHICHEVER IT DEEMS FIT

FOREWORD

Good Clinical Practice (GCP) inspection is necessary to ensure the protection of the rights, safety and well being of study subjects as well as to assure the integrity of scientific testing and study conduct. It helps to determine whether local trials are conducted in accordance with Malaysian Guidelines for GCP, ethical standards and other applicable regulatory requirements.

The formulation of this Guideline for GCP Inspection is indeed very timely and necessary as more drug-related clinical trials are conducted in Malaysia. This guideline is intended to provide comprehensive information on National Pharmaceutical Control Bureau (NPCB) inspection programme and covers inspections at the clinical trial sites, clinical laboratories, computer systems, sponsors and/or contract research organisations (CRO), bioequivalence studies and independent ethics committee/ institutional review boards.

This guideline is also intended to serve as a guide to the sponsors/CROs, local investigators and others on NPCB inspection procedures.

Apart from the above, the guideline also provides additional information on how observations/non-compliances recorded during the inspections of drug related clinical trials can be classified based on the severity of deviations noted. The examples listed in the guidelines however are not exhaustive and merely serve as illustrations. They should certainly be interpreted on case to case basis.

Finally, I wish to take this opportunity to congratulate and extend my deepest appreciation to the committee members on Guidelines for GCP Inspection for their hard work and contribution which have ensured the success of this first edition of the Guidelines for GCP Inspection.

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CONTENTS

Abbreviation

CIEP	Committee For Inspection And Evaluation Of Premises
CRF	Case Report Form
CRO	Contract Research Organisation
CTIL	Clinical Trial Import License
CTR	Clinical Trial Report
CTX	Clinical Trial Exemption
CV	Curriculum Vitae
DCA	Drug Control Authority
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
ICH	International Conference of Harmonisation
IEC/IRB	Independent Ethics Committee/ Institutional Review Board
IVRS	Interactive Voice Response System
NPCB	National Pharmaceutical Control Bureau
QA	Quality Assurance
QC	Quality Control
SOP	Standard Operating Procedure
SUSARs	Suspected Unexpected Serious Adverse Drug Reaction

1.0 INTRODUCTION

The National Pharmaceutical Control Bureau (NPCB) has the responsibility for the inspections and investigations in all clinical trials pertaining to medicinal products for human use.

Following the decision made by Ministry of Health on the National Medicines Policy, there should be an established requirement for compliance with Good Clinical Practice for all clinical studies pertaining to medicinal products for human use to determine whether the clinical studies were conducted in accordance with applicable regulatory requirements which include regulations, ethical standards, the Malaysian Guidelines for Good Clinical Practice and the Declaration of Helsinki.

The Drug Control Authority (DCA) had endorsed Guideline for Good Clinical Practice inspection in accordance to the regulation 29 under Control of Drugs and Cosmetics Regulation 1984 in the 221 meeting on the 29th October 2009. The Guidelines for Good Clinical Practice Inspection will integrate the principles of GCP as described in the Malaysian Guidelines for Good Clinical Practice, regulations and also to ensure that the clinical trials are carried out in accordance with the ethical principles that are reflected, for example, in the Declaration of Helsinki. This may include but may not be limited to conducting clinical trials in accordance with the approved protocol, that the data generated are accurate; that subjects enrolled in clinical trials are not subjected to undue risks and that the trial is conducted in accordance with the generally accepted principles of GCP.

Clinical trials may be inspected while the trial is still on-going, when subjects were currently enrolled in a trial or completed. An inspection may also be conducted when triggers by a complaint or there is a suspicion of serious non-compliance integrity issues and/or scientific/ethical misconduct.

The inspection of clinical trials usually will be initiated in close collaboration with the Center for Product Registration, National Pharmaceutical Control Bureau. These inspections may be routine or may be triggered by issues arising during the assessment of the dossier or by other information such as previous inspection experience. The inspections may be requested during the initial review of a product registration, but could arise post-registration (e.g. inspection of studies conducted or completed as part of the condition of a product registration or because of concerns arising about the studies previously submitted).

An inspection may be conducted at the qualified investigator (clinical trial site), facility of the sponsor, Independent Ethics Committee (IEC)/Institutional Review Board (IRB) and

Contract Research Organisation's (CRO) facilities and other establishment deemed appropriate by NPCB.

2.0 OBJECTIVEs

The objectives of a GCP Inspection are to:

- Ensure the rights, safety and well-being of study subjects have been protected
- Determine whether the trial was conducted in accordance with applicable regulatory requirements, ethical standards and Malaysian Guidelines for Good Clinical Practice
- Determine whether the data submitted in the dossier are credible and accurate
- Assure the integrity of scientific testing and study conduct
- Take corrective action to ensure compliance and enforcement actions when deemed necessary

3.0 TERMS AND DEFINITIONS

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

Drug Control Authority (DCA)
A regulatory authority established for the purpose of regulating the Control of Drugs and Cosmetics Regulations, 1984.

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 favorable 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, compositions, functions, 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 the Malaysian Guidelines for Good Clinical Practice.

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 Sale of Drugs Act 1952

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

Institutional Review Board (IRB)
An independent body constituted of medical, scientific, and non-scientific members whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving and providing continuing review of trial protocol and amendments of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

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).

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

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.
b. A drug to be used as an ingredient for a preparation for a medicinal purpose.

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

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

Triggered Inspection
This is an inspection requested because there is a concern due to either the actual issues observed or the potential impact of deviations from regulatory requirements/GCP on the conduct of the study as a whole or at a particular site. In addition, product(s) with a major impact factor could be considered to require special attention.

Routine Inspections
Routine inspections are inspections carried out as a routine surveillance of GCP compliance in the absence of specific trigger elements. These routine inspections should have a random element in that not all applications would necessarily give rise to a GCP inspection. However, the applications of clinical trials and sites should be selected based on a set of criteria to ensure that a range of different situations are covered (e.g. origin of pivotal data, target population, type of product etc).

4.0 CONDUCT OF GCP INSPECTION

During the preparation of the inspection, an inspection plan is established. For inspection requested by Centre for Product Registration, NPCB, the plan will depend on the scope of the inspection needed or requested. Then, the inspection will be conducted at the selected site.

4.1 Announcement Of The Inspection To The Applicant
NPCB shall notify the applicant not less than 2 weeks except for triggered inspection using a standard letter, that an inspection shall be conducted. In the announcement letter, the applicant is requested to confirm in writing that the sites have received the announcement to be inspected and will make all required documents available for direct access by the inspectors.

4.2 Opening Meeting
Before the start of the inspection an opening meeting must take place between the inspector(s) and the inspectee(s).

The purpose of an opening meeting is to:
- Introduce the inspector(s) to the inspectee(s)
- Explain the regulatory framework for the conduct of the inspection
- Be informed of any departmental or other practices which affect the implementation of quality systems or Good Clinical Practice compliance by the inspectee(s)
- Identify the distribution of duties and functions for the conduct of the trial among the inspectee(s)
- Review the scope and the objectives of the inspection
- Provide a short summary of the methods and procedures to be used to conduct the inspection
- Confirm that the resources, documents and facilities needed by the inspector(s) are available
- Confirm the time and date for the closing meeting and any interim meetings
- Clarify the inspection plan, if necessary

4.3 Conduct Of The Inspection/Collecting Information

The inspection activities should be detailed on the inspection plan. Nevertheless during the inspection, the inspector(s) may adjust the plan to ensure the inspection objectives are achieved.

Sufficient information to fulfill the inspection objective(s) should be collected through examination of relevant documents with direct access, interviews and observation of activities, equipment and conditions in the inspected areas.

If access to records or copying of documents is refused for any reason or there is any withholding of documents or denial of access to areas to which the inspector has legal access, these refusals should be documented and included in the inspection observations.

For each type of site to be inspected as well as for the archiving, an appendix gives detailed items that may be checked during the inspection.

- Appendix I: Conduct Of The Inspection At Investigator Site
- Appendix II: Conduct Of The Inspection At Clinical Laboratories
- Appendix III: Conduct Of The Computer Systems Inspection
- Appendix IV: Conduct Of The Inspection At Sponsor Site And/Or Contract Research Organisations
- Appendix V: Conduct Of Inspection Of Bioanalytical Part, Pharmacokinetic And Statistical Analyses Of Bioequivalence Trials
- Appendix VI: Conduct Of Inspection Of An IEC/IRB

For every item it should be checked, if applicable, how data was generated, collected, reported, analysed or modified.

4.4 Inspection Observations And Minute Of The Inspection

All inspection observations should be documented. If appropriate, copies should be made of records containing inconsistencies or illustrating non-compliance.

At the end of the inspection, the inspector(s) should review all observations to determine which observations are to be reported as non-compliance and/or quality system deficiencies. The inspector(s) should then ensure that these are documented in a clear, concise manner and are supported by objective evidence. All reported observations should be identified with reference to specific requirements of the standard(s) or other related documents against which the inspection has been conducted. The names and titles of persons interviewed or present during the inspection meetings and the details of the inspected organisation should be documented.

4.5 Closing Meeting with the Inspectee(s)

At the end of the inspection, the inspector(s) should hold a closing meeting with the inspectee(s). The main purpose of this meeting is to present inspection observations to the inspectee(s) and appropriate management board, if necessary, to ensure that the results of the inspection are clearly understood and that there is no misunderstanding by either the inspector(s) or the inspectee(s).

4.6 Reporting After the Inspection

The inspector should prepare a narrative inspection report detailing inspection observations, as soon as possible after the inspection. The inspection report should fully describe the nature and scope of the inspection. The report should explain the reason for the inspection, for example, was it routine or conducted for a special purpose? It should also describe the scope of the inspection, for example, was it limited to a narrow record review to address a specific concern or was it a comprehensive inspection of the study conduct? In describing the scope of the inspection, the report should state what records were covered and the number of files or case histories covered relative to the number of subjects on the study. The report should also include the name of the test drug, study sponsor, protocol title and number, date of the study and number of subjects. It should identify individuals who performed significant study functions as well as those providing information during the inspection.

The most important part of the report is the description of the inspection observations. The inspector should describe each of the observation in detail. This description should be specific and quantify what was observed in terms of the total number of record examined. Inspection observations should be objective and the report should include, as exhibits, copies of records taken to document objectionable observations. All exhibits should have all pages numbered and be specifically referenced in the report.

The report should include a discussion of the exit interview with the inspectee(s) at which inspection observations were discussed.

Issues to be followed up by the inspectee(s) should be addressed, including any additional documents that may need to be sent to the inspection team. The inspectee(s) is requested to response to all observations made with corrective actions for every observation. Within the requested time frame, the inspector should receive responses from the inspectee(s) and assess the corrective actions.

Should corrective actions be assessed as not satisfactory, additional actions are requested from the inspectee(s) until they are assessed as satisfactory.

An inspectee(s) must respond to all the inspection observations with corrective actions by the stated deadline. Then, the file is reviewed internally through the Committee for Inspection and Evaluation of Premises (CIEP). The final reports with the corrective action taken by the inspectee(s) and recommendation by the CIEP shall be tabled to DCA for decision.

5.0 CLASSIFICATION OF INSPECTION OBSERVATIONS

The classification of the observations is intended to help classify the severity of observations noted during inspections of clinical trials. Overall, the evaluation will commensurate with the nature and extent of the deviations (i.e. severity). The specific examples provided in this document would apply to specific inspected parties and should be interpreted case by case.

The appendices attached to this document provide examples of observations listed in decreasing level of severity. Please note that the list of observations in each appendix is **not exhaustive** and that additional observations may be added if/ and when appropriate.

Observations classified as major may be upgraded to critical when accompanied with an arrow up sign (↑), depending on the quantity and/ or nature of the deviations.

Critical

Conditions, practices or processes that adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data.

Critical observations are considered totally unacceptable.

Possible consequences: rejection of data and/or legal action and/or regulatory action required.

Remark: Observations classified as critical may include a pattern of deviations classified as major, bad quality of the data and/or absence of source documents. Fraud belongs to this group.

Appendix A - Examples of observations that are considered critical

Major

Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data.

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

Possible consequences: rejection of data and/or regulatory action required.

Remark: Observations classified as major may include a pattern of deviations and/or numerous minor observations.

Appendix B – Examples of observations that are considered Major

Minor

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

Possible consequences: Observation classified as minor indicate the need for improvement of conditions, practices and processes.

Remark: Many minor observations might indicate a bad quality and the sum might be equal to a major finding with its consequences.

Appendix C – Examples of observations that are considered Minor

6.0 DECISION BY DRUG CONTROL AUTHORITY (DCA)

Based on the inspection report, the response/corrective actions taken by the inspectee(s) and recommendation by the CIEP, DCA will make the final decision. Any decision made by DCA shall be final.

APPENDIX A

CRITICAL OBSERVATIONS

Prohibition
- Clinical Trial Import License and Clinical Trial Exemption is not obtained, as required and in accordance with Controls of Drugs and Cosmetics Regulation 1984 and Guidelines for Application of Clinical Trial Import License and Clinical Trial Exemption in Malaysia.

General
- Use of a prohibited substance(s) without having received prior authorisation.

Application for Authorisation
- Misrepresentation or falsification of data submitted to obtain authorisation to conduct clinical trials.

Authorisation
- Clinical trial ongoing after authorisation suspended or cancelled.
- Importation of a clinical trial drug when authorisation is suspended or cancelled.

Amendment
- Information contained in the application for amendment falsified, misleading, or deceptive.
- Failure to notify NPCB after amendment was implemented in cases where the clinical trial endangered the health of trial subject or other person.
- Failure to stop a clinical trial during a suspension or cancellation.

Good Clinical Practices
- Evidence of fraud such as “fabricating” subjects, falsification of study data.

Labeling
- Statement(s) on label is/are false or misleading.

Records
- Sponsor withholding data (e.g. for purpose of deception).
- Failure to report SUSARs which occurred inside and/or outside Malaysia.
- No records in respect of the use of a drug in a clinical trial.
- No records with respect to the enrolment of clinical trial subjects.

Additional Information and Sample(s)
- Providing false, misleading or deceptive sample(s) of the drug or additional information relevant to the drug or the clinical trial.

Interpretation

- Voting members of the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) were not independent of the qualified investigator and/or the sponsor of the clinical trial.
- IEC/IRB membership did not include a minimum of 5 members or IEC/IRB membership and registered with DCA.

APPENDIX B

MAJOR OBSERVATIONS

Interpretation

- Approvals of clinical trials without a quorum of members with the required representation.
- Major changes to previously approved protocol that increase health risks to subjects, were given expedited approval only.
- IEC/IRB membership did not include all of the representative required by the the Malaysian Guidelines for Good Clinical Practice.
- IEC/IRB did not have written procedures in accordance with Good Clinical Practices.
- IEC/IRB approval of the clinical trial was not conducted as per their written operating procedures.
- IEC/IRB did not maintain adequate written minutes of meetings.
- IEC/IRB did not consider the qualifications of qualified investigators before approving trials.
- IEC/IRB did not conduct periodic reviews of continuing clinical trials.

Application for Authorisation/CTIL/CTX

- Information contained in the application was incomplete or incorrect. (↑)
- Failure to report an IEC/IRB that previously refused to approve a trial as requested by NPCB. (↑)

Authorisation/CTIL/CTX

- Failure to disclose all Malaysian clinical trial sites for clinical trial that requires CTIL/CTX or which requires notification to NPCB.
- Failure to provide all necessary information, not previously provided in the application, prior to the importation of a drug at a clinical trial site.

Notification

- Failure to notify NPCB when changes was made to the chemistry and manufacturing information or to the approved protocol.

Amendment

- Implementation of an amendment(s) without obtaining authorisation from IEC/IRB. (↑)
- Failure to implement IEC/IRB approved amendment(s) at a clinical trial site. (↑)

Good Clinical Practices

- Qualified investigator does not have the qualifications to conduct the clinical trial. (↑)
- Medical care and decisions related to the trial are not under the supervision of the qualified investigator. (↑)
- Failure to obtain IEC/IRB approval of the protocol and/or the informed consent forms prior to initiation of a clinical trial. (↑)
- Protocols not amended, informed consents not amended, and/or subjects not advised/re-consented when information becomes available regarding health and safety concerns, or use of the clinical trial drug which endanger the health of the clinical trial subject or other person. (↑)
- Failure to obtain IEC/IRB approval prior to implementation of amendments to protocol or informed consents forms. (↑)
- Informed consent not obtained from subjects before enrolment in the trial or after major amendments to the informed consent form. (↑)
- Informed consents not administered properly or not signed and dated. (↑)
- Inadequate source data to substantiate clinical trial results. (↑)
- Clinical trial was not conducted in accordance with the protocol. (↑)
- Sponsor did not notify the qualified investigator of SUSARs that occurred at other sites. (↑)
- Qualified investigator did not notify the sponsor and/or IEC/IRB in a timely manner of SUSARs. (↑)
- No procedures in place for reporting new safety information to the qualified investigator.
- Significant clinical endpoint data not collected on time, not correctly recorded, or not accurately transcribed/transferred to case report forms. (↑)
- Inadequate systems in place for drug accountability.
- Storage or handling controls in place for drugs were inadequate.
- Source data was not verified for quality, completeness and integrity.
- System(s) and/ or procedure(s) that assure the quality of every aspect of the clinical trial were not implemented.
- The informed consent did not contain all of the required information. (↑)
- Inadequate monitoring of the clinical trial site by the sponsor.
- Individuals involved in the conduct of the clinical trial are not qualified by education, training or experience to perform their respective tasks.
- Incomplete documentation of protocol deviation.
- Lack of documentation that sponsor was informed of protocol deviations.

Records

- No security procedures in place for electronic records or electronic signatures.
- The electronic data system was not validated.
- Sponsor has no or incomplete records of all adverse events which occurred inside or outside Malaysia. (↑)
- Incomplete records respecting the enrolment of clinical trial subjects.

- Incomplete records concerning shipment, receipt, use, disposition, return or destruction of the drug. (↑)
- Quantities of drug not accounted through the various stages of shipment, receipt, disposition, return or destruction of the lot of the drug. (↑)
- No signed/dated qualified investigator undertaking for each clinical trial site prior to the commencement of his/her responsibilities.
- Copies of the protocol/amendments and informed consents approved by the IEC/IRB does not retained for each clinical trial site.
- Absence of IEC/IRB attestation for each clinical trial site stating that it has reviewed and approved the protocol, the informed consent and that it functions in compliance with GCP. (↑)
- No edit trails for changes to electronic records in order to identify who made the changes or when.
- No provisions for retention of records as required by the Malaysian Guidelines for Good Clinical Practice.
- Incomplete records in respect of the use of a drug in a clinical trial.

Suspected Unexpected Serious Adverse Reactions (SUSARs) Reporting

- Sponsor failed to report SUSARs to NPCB. (↑)
- Sponsor did not comply with the prescribed timeline for reports of SUSARs.
- Sponsor did not submit, within the prescribed timeline, an assessment of the importance and implication of any findings made.

Discontinuance of a Clinical Trial

- Sponsor did not inform NPCB that the clinical trial was discontinued in its entirety or at a clinical trial site within 15 working days after the date of the discontinuance.
- Sponsor did not provide NPCB with the reasons for the discontinuance and its impact on the proposed or ongoing clinical trials.
- Sponsor did not inform all qualified investigator(s) of the discontinuance of a trial, the reason for the discontinuation or did not advise them in writing.
- Sponsor did not stop the importation of the drug as of the date of the discontinuance.
- Sponsor, after having discontinued a clinical trial, resumed importing the drug without having submitted the required information to NPCB.
- Clinical trial ongoing at one or more sites after Sponsor stated that the trial was discontinued at those sites. (↑)

APPENDIX C

MINOR OBSERVATIONS

Application for Authorisation/CTIL/CTX

- Sponsor did not maintain copies of previous investigator's brochures pertaining to the clinical trial drug.

Good Clinical Practices

- Delegation of tasks incomplete, signature log incomplete.
- Correction of data not initialed and/or dated.
- Minor errors in transcribing data from source documents to case report forms.
- Source data stored in unsecured location.

Labeling

- Labeling of the products not complying with requirements of the Controls of Drugs and Cosmetics Regulation 1984 and Guidelines for Application of Clinical Trial Import License and Clinical Trial Exemption in Malaysia.

APPENDIX I

CONDUCT OF THE INSPECTION AT INVESTIGATOR SITE

1.0 ORGANISATIONAL ASPECTS

1.1 Implementation of the trial at the site

Organisation and Personnel

- Organisation charts (facility management and scientific organisation charts)
- Documentation of delegation of responsibilities by the principal investigator.
- Systems for QA and QC
- SOP system where available
- Disaster plans, e.g. handling of defective equipment and consequences
- Staff – qualification, responsibilities, experience, availability, training programmes, training records, CV
- Numbers of clinical trials being performed and their nature
- Proportion of time allocated to clinical trial work

Inspect the conditions of implementation of the study at the site

- Contracts between the sponsor or sponsor's representative and the investigator
- Qualifications and experience of the investigator's team in the considered clinical area
- Documentation describing the distribution of duties and functions for the conduct of the trial
- Compatibility of the workload of the investigator and the staff with the requirements of the study
- Organisation of the site for the study (organisation chart, specific training, specific equipment, specific procedures)
- Compliance with the planned time schedule for the study
- Correct implementation of the correct versions of the protocol and its amendments

The inspector should also inspect the dates of the first inclusion/selection of a patient at the site inspected and the last visit of the last patient.

1.2 Facilities and equipment

The aim is to verify the proper use, adequacy and validation status of procedures and equipment used during the performance of the trial. The inspection may include a review of the following:

- Equipment used
- Facilities
- Their suitability for the protocol requirements and the characteristics of the study being inspected

1.3 Management of biological samples

The aim is to examine, conditions and documentation regarding the management of biological samples, if applicable:

- Collection: person in charge of this task, dates and handling procedures
- Storage of the samples before analysis or shipping
- Shipping conditions

1.4 Organisation of the documentation

The aim is to determine whether the general documentation (according to Malaysian Guidelines for GCP), is available, dated, signed and if applicable how it is archived at the trial site.

Also it should be determined if the following trial subjects' documents are available, completed and archived at the trial site.

- Source documents (patient's charts, X-ray,etc.)
- Informed consent documents
- Case Report Form (CRF)
- A sample of data should be verified from the study report and or CRF to the source documents

1.5 Monitoring and auditing

The following points should be examined, if available:

- Monitoring and follow-up by the sponsor. Number of visits at the site, scope and dates of the visits, content of the monitoring visit reports, where these have been requested from the sponsor. Actions required by the monitor. Monitoring visits log. Monitoring plan/SOPs
- Audit certificates (from sponsor file)

1.6 Use of computerised systems

If computerised systems have been used for the trial, it will be necessary to ascertain their validation status.

The elements to evaluate during inspection of computerised systems used in clinical trials are established in a separate document. Computers may be study specific and supplied by the sponsor (eCRFs, e-patient diaries, IVRS, etc.) They may be site specific and part of the routine equipment of the site (medical records, on-line laboratory data, ECG recording, etc.)

2.0 INFORMED CONSENT OF TRIAL SUBJECTS

The aim is to determine whether informed consent was obtained in accordance with Malaysian GCP Guidelines from an appropriate sample of subjects/patients (including the subjects/patients whose medical records are reviewed), or the subjects' legally acceptable representative, prior to their entry into the study. This needs to include the patients whose medical records are reviewed.

It will be necessary to check:

- The signed and self-dated (by the subject and by the person who conducted the informed consent discussion) consent form actually used and approved by the IEC/IRB
- The information sheet actually used and approved by the IEC/IRB, in order to determine whether it includes all the elements required by the Malaysian Guidelines for GCP and current regulations
- The centre practice for giving a copy of the informed consent to the patient
- Consent for access to medical records by the authorities

3.0 REVIEW OF THE TRIAL SUBJECT DATA

The aim is to check whether the investigator team conducted the clinical trial according to the approved protocol and its amendments by source data verification. In the source data verification, it will be necessary to evaluate the source records taking into account their organisation, completeness and legibility. The description of the source data inspected should be reported by the inspector. It will be necessary to evaluate whether corrections to the data recorded in the CRF were done according to Malaysian GCP Guidelines (signed and dated by the authorised person who did it and providing justification, if necessary).

For a number of subjects that will be determined within the inspection plan, (the sample might include the first and last patient enrolled etc) the following should be checked:

3.1 Characteristics of the subjects included in the clinical trial

The aim is to determine whether the inclusion of the subjects in the trial was performed in accordance with the approved protocol and/or that protocol violations are documented and also described in the study report.

It should be checked whether:

- Subjects included in the clinical trial existed and participated in the clinical trial
- Subjects' participation was recorded in their medical records
- Subjects included fulfilled the inclusion criteria and none of the exclusion criteria stated in the protocol were present. Appropriate medical records must support these criteria

3.2 Subjects' visits calendar

The aim is to determine whether the subjects' visits calendar established in the protocol was followed. This check will include a review of the dates when the trial visits took place in order to evaluate whether they were done on the correct dates.

3.3 Efficacy and safety assessment data

The aim is to verify whether the efficacy and safety data recorded in the CRF are in agreement with the source data obtained during the trial and whether adequate data management procedures were in place. All data related to endpoints should be compared with source documents, if applicable.

This check will also include whether adverse events recorded in the site records are also recorded in the CRF and were reported to the sponsor, IEC/IRB and authorities in accordance with current regulations.

In the safety data verification it will be necessary to evaluate the premature discontinuation of treatment and drops outs.

3.4 Concomitant therapy and intercurrent illness

Whether concomitant therapy and intercurrent illnesses were managed in compliance with the protocol and recorded in the CRF and source documents.

4.0 MANAGEMENT OF THE INVESTIGATIONAL MEDICINAL PRODUCT(S)

The aim is to verify whether all the activities related to the Investigational Medicinal Product(s) have been done according to the protocol.

It will be necessary to review the following documents:

- Instructions for handling of Investigational Medicinal Product(s) and trial related materials (if not included in protocol or investigators brochure)
- Shipping records for Investigational Medicinal Product(s) and trial related material. Receipt date(s) of product delivery and quantity. This record should also contain batch numbers (check correspondence with the information kept at the sponsor site), expiration dates and codes assigned to the product and the trial subject
- Documentation regarding allocation of treatment, randomisation and code breaking
- Investigational Medicinal Product(s) accountability at site (pharmacy or investigator)
- Date and quantity dispensed or returned, identification of recipients (patients code or authorized persons). This record should also contain batch numbers, expiration dates and codes assigned to the product and the trial subject
- Documentation about relabeling, if applicable
- Date and quantity returned to the sponsor. Return receipt: this record should also contain batch numbers, expiration dates and codes assigned to the product and the trial subject
- Documentation of destruction of Investigational Medicinal Product(s) (if destroyed at the site), dates and quantity. Documentation of return (if not destroyed at the site), dates and quantity
- Treatment compliance

Other activities, as appropriate:

- Check the suitability of storage conditions and their records (fridge, freezer and controlled substances, etc.)
- Specific SOPs for this activity from the pharmacy or institution should be reviewed
- Check whether there was controlled access to the Investigational Medicinal Product(s) from reception to dispensing
- Verification of the labeling for compliance with applicable regulations

The inspectors should check that where required these documents have been signed and dated by the responsible persons according to the site SOP and/or applicable requirements related to the management of Investigational Medicinal Product(s).

APPENDIX II

CONDUCT OF THE INSPECTION AT CLINICAL LABORATORIES

1.0 GENERAL ASPECTS

1.1 Background

Scope of work and responsibilities.

Accreditation status of the laboratory (the methods) e.g. GLP, ISO

- Fulfillment of national requirements of accreditation
- Relevance of accreditation in the context of clinical trial(s)

Proportion of work in connection to clinical trials.

1.2 Organisation and Personnel

- Organisation charts (facility management and scientific organisation charts)
- Systems for QA and QC, including programme for internal audits
- SOP system (distribution, availability including holidays etc., audit-trail, clinical trials, archiving etc)
- Disaster plans, e.g. handling of defective equipment and consequences
- Staff – qualification, responsibilities, experience, availability, training programme, training records, CV

1.3 Contractual arrangements

- Procedures for example contracts and sub-contracts, protocol, protocol amendments, definition of source data, agreements for reporting
- Methods and procedures (including sample handling)
- Agreed access and availability for monitoring, audit and inspection
- Data recording, handling and archiving
- Security and protection of subject confidentiality

1.4 Facilities/ Premises

- Suitability and adequacy of premises – e.g. adequate degree of separation of work areas to avoid mix-ups, contamination and interference
- Environmental conditions, e.g. temperature, airflow and air pressure, microbiological contamination
- Security and safety, e.g. fire, water and pest control

1.5 Apparatus/ Equipment, Materials, Reagents

- Apparatus available in good working order and complies with relevant specifications
- Quality of general supplies including tap water, analytical water, gases etc.
- Records of operation, maintenance, justification and calibration. Records of the validation for the methods used for the measuring equipment and apparatus (including computerised systems). Log books
- Materials and reagents are prepared, labeled and stored under appropriate conditions and adherence to expiry dates. Labels for reagents indicate their identity, source, concentration and expiry dates
- Apparatus and materials used do not alter to any appreciable extent the samples
- Definition of source data and source documents, retrieval and archiving Data generated in automatic systems e.g. listings, graphs, record traces or computer printouts are archived

2.0 TRIAL RELATED ASPECTS

2.1 Handling of samples

Pre-examination

- Samples obtained from subjects in the clinical laboratory (date and time), identification, labeling, conditions, preparation, storage
- Documentation of receipt (date and time), identification, condition, re-labeling and storage of samples by identifiable person
- Procedures for acceptance or rejection of samples for analysis
- Aliquotting and distribution for examination

Examination

- Compliance with protocol and specified test methods
- Traceability and identification of samples and controls
- Recording of data and acceptance and release of results
- Handling of non-conformance, repeat analysis / re-analysis, and results within critical / alert ranges
- Competence, training and experience of personnel

Procedures for disaster recovery

- Post-examination
- Storage (anonymisation, decoding), retrieval and destruction of samples

2.2 Material and methods

- Material and methods according to the specification stated in the protocol / contract and/or required according European Pharmacopoeia, British Pharmacopoeia, or other established Pharmacopoeia
- Validation status of the methods, appropriately setting of limits of detection / quantification, precision/accuracy, known inferences and specific control measures
- Participation in external control programme, if applicable

3.0 REPORTING

- Various systems for reporting of results may be required according to the protocol/contract e.g. report per sample (i.e. for immediate consideration in medical care of the subject) or on an integrated basis (i.e. to be used in the trial report). This will affect the procedures used by the laboratory and the inspection.

3.1 Procedures for reporting and evaluation of results and for data transfer.

3.2 Systems for alerting results that are unexpected and/or significant deviations from pre-specified limits.

3.3 Transcription of raw data into the report

- Identification of laboratory
- Unique identification and localisation of the subject
- Identification of investigator
- Date and time of sample collection, and time of receipt
- Date and time of examination and release of report
- Source of primary sample type and any comments of its quality
- Description of the examination and of its results
- If applicable, detection limit, uncertainty of each measurements, and reference intervals
- Where appropriate, interpretation of results and other comments
- Identification of the person releasing the report

3.4 Attribution of review and release of the report(s) to responsible personnel.

3.5 Procedures for alterations and amendments of reports.

3.6 Procedures for complaints and corrective actions.

APPENDIX III

CONDUCT OF THE COMPUTER SYSTEMS INSPECTION

The NPCB GCP inspectors agreed to use as the reference for inspection of Computer Systems the published PIC/S Guidance on Good Practices for Computerised Systems in Regulated "GXP" Environments (PI 011-3). The hyperlink to the PIC/S site is http://www.picscheme.org/index.php

APPENDIX IV

CONDUCT OF THE INSPECTION AT SPONSOR SITE AND/OR CONTRACT RESEARCH ORGANISATIONS

1.0 SPONSOR OR CRO QUALITY SYSTEM INSPECTION

The aim of this kind of inspection is to evaluate the quality assurance and quality control systems established by the sponsor/CRO in order to assure that clinical trials are conducted and data are generated, recorded and reported in compliance with the protocol, GCP and applicable regulatory requirements.

The following items should be reviewed in a sponsor/CRO system inspection:

1.1 Organisation and personnel

The aim is to evaluate if the sponsor/CRO has a well-established organisation for clinical research activities and has a sufficient number of properly qualified and trained personnel for each area.

Review:

- Organisational charts that identify the key personnel in each area
- The independence of the quality assurance unit
- The job description, qualifications and training of the individuals involved at any stage of the clinical trial process

1.2 Facilities and equipment

The aim is to identify and evaluate the facilities used for archiving or investigational medicinal product(s) storage as well as the equipment used. Special attention should be paid to computer systems (hardware, software, communications, etc.), in order to evaluate their validation status, and their adequacy for the requirements of the trial(s) being inspected.

1.3 Sponsor/CRO Operating Procedures

Procedures should be reviewed in order to verify their compliance with GCP standards and applicable regulations.

Implementation and termination of the clinical trial

The aim is to evaluate the procedures established for the implementation and termination of the clinical trial.

Review the procedures for:

- Document preparation (format and content and distribution of protocol,

protocol amendments, informed consent documents, investigator brochure, CRF and any other trial documents)
- Investigators selection and training.
- Regulatory compliance (obtaining EC approval/favourable opinion and necessary authorisations, providing notifications and reports as required by GCP and local regulations)

Monitoring

The aim is to evaluate the system established for monitoring clinical trials.

Determine if procedures include:

- Description of monitoring activities (visits, frequency and extent of data review)
- Content and handling of monitoring reports

Agreements for direct access to source documents by the sponsor personnel (or their appointed representatives) and by regulatory authorities and confidentiality of information about subjects.

Investigational Medicinal Product(s)

The aim is to determine if sponsor procedures for different stages of the investigational medicinal product cycle are according to the current GMP, GCP and regulations.

Determine if these procedures establish provisions for:

- Quality control requirements
- Manufacturing, packaging and labeling
- Supplying, accountability, returns and destruction
- Randomisation and code breaking

Sample management

The procedures established for handling **biological samples** obtained in clinical trials should be reviewed.

Safety and adverse events reporting

The aim is to verify procedures for reviewing and communicating findings that could adversely affect the safety of subjects and the reporting of serious adverse events to regulatory authorities, investigators and IECs/IRBs, where applicable.

Review procedures for:

- Expedited Adverse Drug Reaction reporting to regulatory authority(ies), investigators and IEC/IRB, where applicable
- Serious adverse events notification by investigators
- Management of the serious adverse events reported by investigators
- Safety updates and periodic safety reports
- Validation of computer systems used

Data handling and clinical trial report

The aim is to evaluate the system established by the sponsor/CRO for handling the data obtained during the clinical trial and reporting it in the clinical trial report.

Determine if the procedures establish:

- Data handling, data analysis and their control procedures
- Clinical trial report preparation according to ICH standards
- Validation of the computerised systems used
- Audit trails (for paper and computer systems)

Documentation archiving

The aim is to determine whether the system established by the sponsor/CRO guarantees that the general documentation which has to be archived at the sponsor/CRO site (according to Malaysian Guidelines for GCP) is available, complete and maintained in good conditions during the period of time established.

Determine if procedures include:

- System for archiving and retrieval of documents
- Controlled access to the archives

Sponsor audit and quality assurance system

The aim is to determine if the sponsor/CRO has established an audit system, as part of its own quality assurance system in order to evaluate its activities related with clinical trials.

It should be determined if the procedures include:

- Audits of key clinical trial processes including monitoring, data management, safety reporting, clinical study report production, archiving and computer system validation activities
- Audits of contractors/sub-contractors

The inspectors should also review:

- The processes for communicating and addressing audit observations, including the format and distribution of audit reports
- The procedures for dealing with serious and/or persistent GCP non-compliance
- Audit trails
- Procedures for generation and implementation of audit programme(s)/plan(s)

Delegation of duties

The aim is to verify the procedures for contracting/subcontracting of trial-related duties. Inspectors should examine the procedures related with:

- Pre-selection and ongoing assessment of contractor/subcontractors
- Documentation of duty delegation and its time recording
- Handling contract amendments
- Contracts should be reviewed (either specific ones or a sample)

2.0 SPECIFIC CLINICAL TRIAL INSPECTION

The aim of this type of inspections is to verify if the trial has been conducted, data has been generated, documented and reported in compliance with the protocol, GCP principles and sponsor procedures. The procedures and requirements applicable at the time of the trial should be considered, and compared where relevant to those applying at the time of the inspection.

The specific clinical trial inspections could also be conducted to answer questions listed in the request for a GCP inspection.

The aspects that should be checked include:

2.1 Implementation and termination of the clinical trial

The aim is to determine if all legal and administrative aspects of the clinical trial have been accomplished.

Review:

- Distribution of sponsor's duties or functions
- Information given to investigators and/or specific training
- Investigator selection and agreements
- Fulfillment of regulatory requirements (IEC/IRB approval/favourable opinion and necessary authorizations)
- Submission and approval of amendments
- Critical dates: IEC/IRB approval/favourable opinion, regulatory authorisation (where required) initiation of the study, patient enrolment period, closing of the trial sites, termination of the study

2.2 Monitoring

Inspect :

- Monitoring plan/SOPs (availability, content and compliance to it)
- Frequency and extent of the monitoring activities made
- Monitors' qualifications
- Monitoring visit reports and the review of the reports by sponsor/CRO
- Corrective actions induced by monitoring visits

2.3 Investigational Medicinal Product(s)

Inspect the documentation about:

- Manufacturing, packaging, labeling and quality control
- Supplying, accountability, returns and destruction (investigational medicinal product(s) tracking system)
- Randomisation and code breaking
- Blinding
- Shipment
- Condition of shipped product on receipt and during storage

2.4 Safety and adverse events reporting

Inspect:

- Notification, follow up and reporting of serious adverse events and other non-serious adverse events requiring expedited reporting according to protocol
- Safety updates and their communication

2.5 Case Report Form data verification

A selected number of CRFs should be checked to verify:

- Adherence with the protocol as well as data accuracy, completeness, legibility and timeliness
- CRF corrections
- Correspondence of the dates of first patient included and last patient with the dates of the study initiation and completion as well as with investigational medicinal product(s) delivery

2.6 Data handling and clinical trial report (CTR)

Inspect:

- Data tracking system from CRF to the database
- Validation of computer systems used
- Data Management
- Statistical analysis as established in the protocol
- Clinical trial report content
- Quality control applied
- System for review of CTR, including signatures

2.7 Clinical trial documentation and archiving

Determine if all essential documents listed in the Malaysian Guidelines for GCP, are available during the inspection.

2.8 Audit

Determine:

- If the clinical trial was audited and audit reports exist

APPENDIX V

CONDUCT OF INSPECTION OF BIOANALYTICAL PART, PHARMACOKINETIC AND STATISTICAL ANALYSES OF BIOEQUIVALENCE TRIALS

1.0 BIOANALYTICAL PART OF BIOEQUIVALENCE TRIALS

1.1 General organisation of the site

Activity

The main points to consider are the following:
- Nature of the activities carried out at the laboratory
- Proportion of bioequivalence trials in this activity
- The analytical methods used, particularly for complex methods

Personnel

The main points to consider are:
- Organisation charts, valid at the time of the inspection and at the time when the inspected trial was conducted
- Number and categories of people employed
- Qualification, training and experience of the personnel
- Individual work load of people involved

Quality assurance system

The main points to consider are the following:
- Quality assurance system in place at the laboratory
- Existence, availability, accessibility and validity of sops
- List of SOPs used for the trial
- SOP awareness by people in charge

Installations and equipment

The suitability of the facilities and equipment available, their appropriateness for the activity of the laboratory and for the bioequivalence trial inspected should be inspected during the inspection.

Archiving of documentation

The main points to consider are the following:
- Nature of the documents kept
- Place of archiving
- Access control to that place

- Conditions of storage and of protection of the documents
- Person responsible for the archives
- Documentation of file movements
- Duration of retention of the files

1.2 Sample tracking

Receipt

General aspects relating to sample handling at the facility may be inspected including:

- Responsibilities for receipt and handling of biological samples
- Organisation of the receipt system, including outside workdays/hours
- Sample registration
- Controls performed on receipt

The points to consider specifically for the inspected trial(s) are the following:

- Dates and times of receipt of the samples, and acknowledgement of receipt
- List of samples received for each dispatch
- Shipment conditions (temperature)
- Condition of the samples on receipt
- Any anomalies noted
- Known sample stability

Storage

The following points should be inspected for the samples collected for the inspected trial:

- Storage conditions of the trial samples
- Compliance of these conditions with the protocol and the conditions used during
- Method validation
- Assessment of the risk of confusion between samples
- Identification of the freezer(s) used
- Temperature records of the freezer
- Calibration of the thermometer and its traceability to national/international
- Standards
- Alarms and other surveillance measures
- Labeling of the samples, if they are still available
- Documentation of freeze/thaw cycles undergone by the samples

Destruction

Check the date of destruction or return of the samples.

1.3 Sample analysis

Bioanalytical method used

- ***Method description***

Check the consistency of the trial report with the SOP describing the bioanalytical method and other documents available.

- ***Equipment***

The main points to consider regarding the equipment used (including balances and pipettes) are the following:

- Identity of the equipment (make, model)
- Availability of the equipment. If the equipment is no longer visible at the site at the time of the inspection, review the documentation that could show that the equipment needed was indeed available when the trial was conducted
- Availability of instructions for use
- Compliance with specific conditions necessary for the trial, if any
- Documentation relating to the qualification, checks, and maintenance of the equipment.

- ***Reagents***

The main points to consider are:

- Labeling of reagents, including the expiry date
- Traceability of the reagents used
- Compliance with specific storage conditions, if any

- ***Reference substances***

The main points to consider are:

- Availability and contents of the certificates of analysis; - expiry dates
- Storage conditions
- Conditions for access to reference substances

- ***Calibration, control samples***

The main points to consider are:

- Dates and conditions of preparation of the stock and working solutions and of the calibration and control samples, and the number of aliquots prepared for each sample
- Accuracy of the calculation of nominal concentrations
- Conditions and duration of storage of the stock solutions, working solutions

- Calibration and control samples, compared to their stability, as described in the validation report
- Matrix used, including the anticoagulant, if any

The main points to consider regarding the calibration for each run are:

- Number of calibration samples
- Response function used, including weighting, if any
- Acceptance criteria for the calibration curve
- Criteria for exclusion of calibration samples

- ***Development of the method***

A quick overview of the origin and of the development of the bioanalytical method can be helpful to identify critical steps in the procedure.

- ***Method validation***

The main points to consider are:

- Validation protocol
- Dates of the validation
- Adequate documentation of all operations
- Completeness of the validation report, when compared to the various experiments performed
- Consistency of the validation report with the source documents
- Chromatogram integrations
- The exclusion of calibration samples, if any

The main validation parameters are the following:

- Stability:
  - Of the stock solutions
  - Of the samples (bench-top, freeze/thaw cycles, long term)
  - If applicable, of extracted samples before their injection
- Specificity / selectivity
- Accuracy
- Precision
- Limit of quantification
- Response function
- Carry-over
- In case of mass spectrometric methods: matrix effect
- Effect of a dilution, if applicable
- If applicable, effect of the anticoagulant, if the anticoagulant used for the preparation of the calibration and/or QC samples is different from the anticoagulant used to collect samples during the trial

- ***Assays***

The main points to consider are:

- Nature and completeness of the documentation available
- Adequacy of the documentation of all operations
- Completeness of the analytical report
- Number, date and composition of the analytical runs
- Identification of samples and tubes
- Assessment of the risk of sample mix-ups
- Assessment of the risk of sample cross-contamination
- Chromatogram integrations
- Calculation of the concentrations
- Compliance with pre-defined criteria for the exclusion of calibration samples
- Criteria of acceptance of the runs, and compliance with pre-established criteria
- Audit trail settings and information recorded in the audit trails
- Practicalities of repeat analysis and the criteria for choosing the result to be reported
- Maintenance of blinding, if required by the protocol
- Practicalities of data transfer
- Consistency of the analytical report with the source documents

2.0 PHARMACOKINETIC AND STATISTICAL ANALYSES

2.1 Pharmacokinetics

The main points to consider are:

- Quality system in place
- Identity, qualification and responsibilities of the personnel involved
- Software used
- Practicalities and control of data entry
- Sampling times used
- Method used for calculation of pharmacokinetic parameters
- Selection of data for the calculation of the terminal half-life, if applicable
- Consistency of the raw data with the trial report.

Pharmacokinetic parameters can be recalculated before or during the inspection if needed.

2.2 Statistics

The main points to consider are:

- Quality system in place
- Identity, qualification and responsibilities of the personnel involved
- Software used
- Practicalities and control of data entry
- Data line listings and tables of results
- Consistency of the raw data with the calculated pharmacokinetic parameters and with the trial report

The statistical analyses can be repeated before or during the inspection if needed.

APPENDIX VI

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

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

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
- The elements of the review of the application
- The decision-making procedure
- The procedure for communicating a decision
- The follow-up review
- The documentation and archiving procedures; including an inventory of all documents archived and the length of storage of the documents

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, 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
- 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