

GOOD LABORATORY PRACTICE (GLP) COMPLIANCE PROGRAMME MANUAL

NATIONAL PHARMACEUTICAL REGULATORY AGENCY (NPRA)
MINISTRY OF HEALTH MALAYSIA

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1.0 INTRODUCTION

The manual describes the quality system of the National Pharmaceutical Regulatory Agency (NPRA) as the national Compliance Monitoring Authority (CMA) for compliance monitoring of the Organisation for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice (GLP). This manual is supplemented by relevant documents.

The Ministry of Health Malaysia is the coordinator for Good Laboratory Practice (GLP) Compliance Programme in Malaysia. Two (2) Compliance Monitoring Authorities (CMAs) were appointed by the Malaysian Government. The two (2) appointed CMAs are the National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia and the Department of Standards Malaysia, Ministry of International Trade and Industry (MITI), Malaysia.

2.0 OBJECTIVE

The objectives of this manual are to provide:

- Policies and procedures of NPRA as the national CMA in the operation of the national Good Laboratory Practice Compliance Programme
- Mechanism for a listing of test facilities into the NPRA GLP Compliance Programme
- Process on the conduct of inspection on test facilities and study audit.
- Reporting of the inspection and study audit.
- To exchange information with other national CMA according to the provision of OECD.

3.0 SCOPE

NPRA GLP Compliance Programme is a voluntary programme open to test facilities conducting non-clinical health and environmental safety studies and for purpose of registering and/or licensing test items contained in the product in the following categories:

- Pharmaceutical products
- Cosmetics products
- Veterinary drugs
- Food additives
- Medical Devices

For chemicals such as pesticides, feed additives, industrial chemicals and non-pharmaceutical biotechnology products will be inspected by the Department of Standards Malaysia (*Jabatan Standard Malaysia*), Ministry of International Trade and Industry (MITI), Malaysia (<http://www.jsm.gov.my/>) which is the other CMA. There is close cooperation between both CMAs. Mutual cooperation is signed by both CMAs.

Appendix 1: Mutual Cooperation

These test items are frequently synthetic chemicals but may be of natural or biological origin and, in some circumstances may be living organisms. The purpose of the non-clinical safety testing of test items is to obtain data on their properties and/or their safety with respect to human health and the environment. Non-clinical health and environment safety studies covered by the Principles of Good Laboratory Practice include work conducted in the laboratory and in the field.

Type of studies/area of expertise on test item subjected to NPRA GLP Compliance Programme:

- Physical-chemical testing
- Toxicity studies
- Mutagenicity studies
- Analytical and clinical chemistry testing
- Other studies (test facility to specify)

4.0 TERMS AND DEFINITIONS

The manual was prepared based on current documents of the *OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring*. These documents are revised regularly; therefore, the reader of this manual should also refer to the OECD for an updated version.

The following documents were referred to in the preparation for this manual:

- Doc No. 1: OECD Principles of Good Laboratory Practice, 1998.
- Doc No. 2: Guidance for the GLP Monitoring Authorities Procedures for GLP, 1995.
- Doc No. 3: Guidance for the Conduct of Laboratory Inspections and Study Audit, 1995.
- Doc No. 4: Quality Assurance and GLP, 1999 (replaced with Doc No.23)
- Doc No. 5: Compliance of Laboratory Suppliers with GLP Principles, 2000.
- Doc No. 6: The Application of the GLP Principles to Field Studies, 1999
- Doc No. 7: The Application of the GLP Principles to short-term studies, 1999.
- Doc No. 8: The Role and Responsibility of the Study Director in GLP studies, 1999.
- Doc No. 9: Guidance for the preparation of GLP Inspection Reports, 1995.
- Doc No. 10 The Application of the Principles of GLP to Computerised Systems, 1995 (replaced with Doc No. 17)
- Doc No. 11: Advisory document of panel on the GLP: Role and Responsibility of the Sponsor in the Application of the Principles of GLP, 1998.
- Doc No. 12: Advisory document of the Working Group on GLP: Requesting and Carrying out Inspections and Study Audits in another country, 2000.
- Doc No. 13: Consensus document of the Working Group on GLP: The Application of the OECD Principles of GLP to the Organisational and Management of Multi-Site Studies, 2002.
- Doc No. 14: Advisory document of the Working Group on GLP: The Application of the OECD Principles of GLP to in-vitro studies, 2004.
- Doc No. 15: Advisory document of the Working Group on GLP: Establishment and control of Archives that Operate in Compliance with the Principles of GLP, 2007.
- Doc No. 16: Advisory document of the Working Group on GLP: Guidance on the GLP Requirements for Peer Review of Histopathology, 2014.
- Doc No. 17: Advisory document of the Working Group on GLP: Application of GLP Principles to Computerised System, 2016.
- Doc No. 18: OECD Position Paper Regarding the Relationship between the OECD Principles of GLP and ISO/IEC 17025, 2016.
- Doc No. 19: Advisory Document of the Working Group on Good Laboratory Practice on the Management, Characterisation and Use of Test Items, 2018.
- Doc No. 20: Guidance Document for Receiving Authorities on the Review of the GLP Status of Non-Clinical Safety Studies, 2019.

- Doc No. 21: OECD Position Paper Regarding Possible Influence of Sponsors on Conclusions of GLP Studies, 2020.
- Doc No. 23: Quality Assurance and GLP, 2022
- Doc No. 24: Position Paper on Quality Improvement Tools and GLP, 2022

Whenever the OECD publishes a new document relevant to Good Laboratory Practice, it should be read and complied with accordingly.

4.1 Good Laboratory Practice (GLP)

Good Laboratory Practice (GLP) is a quality system concerned with the organisational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

4.2 Terms concerning the organisation of a test facility

Test facility means the persons, premises and operational unit(s) that are necessary for conducting the non-clinical health and environmental safety study. For multi-site studies, those that are conducted at more than one site, the test facility comprises the site at which the Study Director is located and all individual test sites, which individually or collectively can be considered to be test facilities.

Test site means the location(s) at which a phase(s) of a study is conducted.

Test facility management means the person(s) who has the authority and formal responsibility for the organisation and functioning of the test facility according to these Principles of Good Laboratory Practice.

Test site management (if appointed) means the person(s) responsible for ensuring that the phase(s) of the study, for which he is responsible, is conducted according to these Principles of Good Laboratory Practice.

Sponsor means an entity which commissions, supports and/or submits a non-clinical health and environmental safety study.

Study Director means the individual responsible for the overall conduct of the non-clinical health and environmental safety study.

Principal Investigator means an individual who, for a multi-site study, acts on behalf of the Study Director and has defined responsibility for delegated phases of the study. The Study Director's responsibility for the overall conduct of the study cannot be delegated to the Principal Investigator(s); this includes approval of the study plan and its amendments, approval of the final report, and ensuring that all applicable Principles of Good Laboratory Practice are followed.

Quality Assurance Programme means a defined system, including personnel, which is independent of study conduct and is designed to assure test facility Management of compliance with these Principles of Good Laboratory Practice.

Standard Operating Procedures (SOPs) means documented procedures, which describe how to perform tests or activities normally not specified in detail in the study plan or test guidelines.

Master schedule means a compilation of information to assist in the assessment of workload and for tracking of studies at a test facility.

4.3 Terms Concerning the Non-Clinical Health and Environment Safety Study

Non-clinical and environmental safety study, henceforth referred to simply as ‘study’, means an experiment or set of experiments in which a test item is examined under laboratory conditions or in the environment to obtain data on its properties and/or its safety, intended for submission to appropriate regulatory authorities.

Short-term study means a study of short duration with widely used, routine techniques.

Study plan means a document, which defines the objectives and experimental design for the conduct of the study, and includes any amendments.

Study plan amendments mean an intended change to the study after the study initiation date.

Study plan deviation means an unintended departure from the study plan after the study initiation date.

Test system means any biological, chemical or physical system or a combination thereof used in a study.

Raw data means all original test facility records and documentation, or verified copies thereof, which are the result of the original observations and activities in a study. Raw data also may include, for example, photographs, microfilm or microfiche copies, computer-readable media, dictated observations, recorded data from automated instruments, or any other data storage medium that has been recognised as capable of providing secure storage of information for a time period.

Specimen means any material derived from a test system for examination, analysis, or retention.

Experimental starting date means the date on which the first study-specific data are collected.

Experiment completion date means the last date on which data are collected from the study.

Study initiation date means the date the Study Director signs the study plan.

Study completion date means the date the Study Director signs the final report.

4.4 Terms Concerning the Test Item

Test item is defined as an article that is the subject of a study. The conclusion of a GLP study provides information on the properties of the test item which allows an assessment of the risk it presents to the safety of humans, animals or the environment. It should be noted that the test item is also referred to as a “test chemical” in some of the OECD Test Guidelines.

Reference item (control item) means any article used to provide a basis for comparison with the test item.

Batch means a specific quantity or lot of a test item or reference item produced during a defined cycle of manufacture in such a way that it could be expected to be of a uniform character and should be designated as such.

Vehicle means any agent, which serves as a carrier used to mix, disperse, or solubilise the test item or reference item to facilitate the administration/application to the test system.

4.5 Terms concerning to compliance programme

GLP Principles: Principles of Good Laboratory Practice that is consistent with the OECD Principles of Good Laboratory Practice

GLP Compliance Monitoring: The periodic inspection of test facilities and/or auditing of studies for the purpose of verifying adherence to GLP Principles.

(National) GLP Compliance Programme: The particular scheme established by a member country to monitor good laboratory practice compliance by test facilities within its territories, by means of inspections and study audits.

(National) GLP Monitoring Authority: A body established within a Member country with responsibility for monitoring the good laboratory practice compliance of test facilities within its territories and for discharging other such functions related to the good laboratory practice as may be nationally determined. It is understood that more than one such body may be established in a member country.

Test Facility Inspection: An on-site examination of the test facility's procedures and practices to assess the degree of compliance with GLP Principles. During the inspection, the management structures and operational procedures of the test facility are examined, the key technical personnel are interviewed, and the quality and integrity of data generated by the test facility are assessed and reported.

Study Audit: A comparison of raw data and associated records with the interim or final report in order to determine whether the raw data have been accurately reported, determine whether testing was carried out in accordance with the study plan and standard operating procedures, to obtain additional information not provided in the report, and to established whether practices were employed in the development of data that would impair their validity.

Inspector: A person who performs the test facility inspection and study audits on behalf of NPRA.

GLP Compliance Status: The level of adherence of a test facility to the GLP Principles as assessed by the (National) GLP Monitoring Authority.

Regulatory Authority: A national body with legal responsibility for the registration or licensing of pharmaceutical products, cosmetic products, veterinary drugs, food additives, feed additives, pesticide products and industrial chemicals.

5.0 GLP COMPLIANCE MONITORING AUTHORITY (CMA)

5.1 Administration

NPRA (formerly known as National Pharmaceutical Control Bureau) is one of the CMAs appointed by the Cabinet of Malaysia on 13 February 2008 for all studies in the areas of expertise as mentioned in the scope. This was enforced by a Directive issued on 1 June 2009 by the Senior Director of Pharmaceutical Services under Regulation 29, Control of Drugs and Cosmetics Regulations 1984 (Amendment) 2006.

NPRA is one of the five divisions under the Pharmaceutical Services Programme, which is responsible for the GLP Compliance Monitoring Programme. However, the Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) Section, Centre for Compliance and Quality Control, NPRA carries out the daily management of the programme. Under the NPRA current procedures, the Director of NPRA issues a statement of GLP compliance in a form of a certificate.

Appendix 2: Organogram - National Pharmaceutical Regulatory Agency (NPRA)

Office address and further information on NPRA GLP Compliance Programme can be obtained from:

Deputy Director
Centre for Compliance and Quality Control,
National Pharmaceutical Regulatory Agency (NPRA),
Ministry of Health, Malaysia.
Lot 36, Jalan Prof. Diraja Ungku Aziz ,
46200 Petaling Jaya,
Selangor, Malaysia.
Tel : + 603 7883 5400
Website : www.npra.gov.my
NPRA GLP Compliance Programme page :
www.npra.gov.my/index.php/en/glp-main-page.html

As GLP CMA, NPRA has adopted the OECD GLP Principles. The structure, policies and procedures under which NPRA operates are documented to ensure implementation of these policies and procedures are administered in an independent and impartial manner to ensure the smooth operation of all compliance activities. NPRA quality system has been established, documented, implemented and maintained to give confidence in its ability to operate the compliance process in an effective manner.

5.2 Appointment of Inspectors

NPRA is directly responsible for an adequate team of inspectors having the necessary technical/scientific expertise or is ultimately responsible for such a “team”. Details are described in the NPRA procedures for the appointment of inspectors, qualification of inspectors, and training of inspectors.

For each inspection, NPRA shall appoint an inspection team. The names of the inspectors and observers (if any) shall be communicated to the test facility at least one (1) week before the start of the visit. The Deputy Director of the Centre for Compliance and Quality Control will decide the needs of the experts used. Test facilities may object in writing to the use of a particular expert or

observer based on some valid reasons. The test facility shall always accept the inspectors employed by NPRA.

NPRA shall maintain records of test facilities inspected (and their GLP compliance status) and of studies audited for both national and international purposes.

5.3 Confidentiality

NPRA procedures provide adequate arrangements consistent with the laws of Malaysia, to safeguard the confidentiality of the information obtained in the course of its compliance monitoring activities at all levels within the organisation. This arrangement to safeguard confidentiality encompasses all individuals acting on behalf of NPRA.

In the course of an inspection, NPRA inspectors/experts would have access to confidential information relating to individual test facility activities and practices. Except where required by law or permitted by contractual arrangements, the findings of any inspection must be treated as confidential.

Inspectors/experts, observers, staff and individuals acting on behalf of NPRA who have access to test facility files, shall be required to sign an undertaking for maintaining confidentiality. All inspectors/experts/observers shall abide by the “Codes of Ethics” and “Undertaking of Confidentiality” which includes the upholding of confidentiality requirements.

Appendix 3: Codes of Ethics for Inspectors

Appendix 4: Undertaking of Confidentiality

While a directory of GLP Compliance test facilities is available on the NPRA website, confidential information such as inspection reports, particular questions and replies, minutes of internal meetings, etc., which is available on paper, hard discs and/or backup, is only accessible to NPRA.

The confidential information about a particular test facility gathered during the inspection shall not be disclosed to any third party without the written consent of the test facility in question. However, NPRA shall be required to inform the OECD of the GLP status of the test facility and any non-compliant GLP studies. In such cases, the written consent of the test facility shall not be required. The same applies to study audit/facility inspections conducted at the request of national/international authorities.

NPRA would always ensure that sensitive business information shall never be disclosed to any third party. The identification of commercially sensitive information present in the inspection report shall be made in collaboration with the test facility concerned. NPRA may, however, overrule the request from the test facility if needed.

5.4 Personnel and Training

NPRA shall ensure that each inspector/expert is qualified and trained prior to the inspection.

Exchange of information and consultation with staff members of other local/international GLP CMA is practised. This is to promote international harmonisation in the interpretation and application of the Principles of GLP, and in the monitoring of compliance with such principles. In this context, if inspectors from other foreign GLP CMA would like to take part as an observer in an inspection conducted by NPRA, consent from the test facility shall be obtained in advance.

Inspectorate personnel, including experts, shall have no financial or other interests in the test facilities inspected, the studies audited or the firms sponsoring such studies.

The inspector has to show suitable identification at the test facility.

The GLP Inspectors/experts of NPRA may be:

- on the permanent staff
- on the permanent staff of a body separate from NPRA
- hired on case to case basis

6.0 GLP COMPLIANCE PROGRAMME

6.1 General

NPRA GLP Compliance Programme intended to ascertain whether test facilities have implemented requirements as described in documents of the *OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring* according to the Malaysian legal framework. The Programme includes pre-inspection, inspection, surveillance inspection and extra-ordinary inspections (where applicable).

NPRA shall establish and maintain an Annual Overview of the test facilities inspected. This register shall contain information on the name of the test facility, the date of inspection, the area of expertise, the nature of the inspection, compliance status and remarks. The information is submitted to the OECD GLP Working Group secretariat annually.

6.2 Mechanism of entering into the programme

In Malaysia, GLP is a voluntary scheme. There are two (2) mechanisms by which a test facility can be listed in the programme:

1. By submitting an application to NPRA. Test facilities must have at least one completed study before putting up an application to NPRA or;
2. Through the request of inspection received from national or international authorities. The test facility will be invited to submit the application form.

In both cases, the test facility shall be listed in NPRA GLP Compliance Programme only after the test facility has received the GLP compliance certificate.

Appendix 6: Flow Chart for GLP Inspection.

Application procedures and application forms can be obtained and downloaded from the NPRA GLP Compliance Programme webpage.

6.3 Inspection Fee

An inspection fee will be imposed for all the NPRA GLP Compliance Programme activities as stated on the NPRA website.

The fee shall be paid in the form of a Bank Draft/Money Order/Postal Order payable to “*Biro Pengawasan Farmaseutikal Kebangsaan*”. Foreign currencies are not accepted. Once the date of inspection is confirmed, the inspection fee must be made at least two (2) weeks before the inspection. Failure to do so may result in delay / or cancellation of inspection.

6.4 Conduct of GLP Inspections

6.4.1 Notification of GLP Inspection

Notification of inspection shall be sent to the test facility prior to the conduct of the inspection. This notification contains the inspection plan, the name of team members, the date and time of the inspector’s arrival, the objective of their visit and the inspection duration. It is necessary that Test Facility Management (TFM) or its representative, Study Director, Archivist and QA staff are present at the opening meeting and the closing meeting.

6.4.2 Opening Meeting

At the opening meeting, the lead inspector will introduce the inspection team, inform the purpose and outline the scope of the inspection to the test facility management.

6.4.3 Conduct of Inspection

During the inspection, inspectors may interview the Study Director/s, scientist/s and technical staff of the test facility. Documents or records may be asked for and copied for evidence. The test facility shall provide room/s for the review of documents and other activities by the inspectors.

The inspection team will not be concerned with the scientific design of the study, or the interpretation of the findings of the studies, with respect to risks to human health or the environment. These aspects are the responsibility of those regulatory authorities to which the data are submitted for registration/ licensing purposes.

The inspections shall be carried out in accordance with OECD Doc No. 3 *Revised Guidance for the Conduct of Laboratory Inspections and Study Audits*. The criteria described in the OECD Consensus and Advisory Documents shall also be referred to during the test facility inspections and/or study audits, where appropriate.

6.4.4 Closing Meeting

During the closing meeting on the last day of the inspection, the inspectors will present the findings to the test facility management. Copies of any documents retrieved from the test facility during the inspection will be informed to the test facility. A list will be prepared by the test facility and verified by the inspector.

6.4.5 Inspection Report

All findings will be presented for classification in the technical meeting before the issuance of the inspection report. An inspection report will be issued to the test facility after the inspection. The test facility is requested to respond to the findings with corrective action and preventive action (CAPA) within thirty (30) working days.

Subsequent CAPA should be also answered within thirty (30) working days. A maximum of three (3) CAPA correspondences are allowed. The inspection team and Head of the GCP and GLP Section shall consider the need for CAPA 4 on a case-by-case basis only.

6.5 Categories of Test Facility Inspections/Study Audits

The description of each type of inspection is as follows:

6.5.1 Pre-Inspection

Pre-inspection is carried out for the first time to familiarise and verify that the test facility has the resources to undertake GLP studies in respect of management structure, the physical layout of buildings, the range of studies and various documentation available. Test facilities must have at least one completed study per area of expertise during pre-inspection.

Some areas of the test facility will be visited, whereby the overview of activities such as the type and separation of activities, the environmental conditions and the identification and storage of apparatus, test systems, test and reference items and archives are observed.

Inspection is programmed within six (6) months from the date of pre-inspection after considering all corrective actions taken from pre-inspection findings are satisfactory. In cases where the test facility fails to take satisfactory actions within the period [six (6) months], the test facility may submit a new application.

6.5.2 Inspection

The inspection shall be a full inspection that involves both test facility inspection and study audit. The study audit within these inspections would cover both completed and ongoing studies (where applicable) on a sampling basis. The purpose of this inspection is to verify compliance with the Principles of GLP and NPRA GLP Compliance Programme requirements.

For the purpose of this inspection, the test facility is required to submit an updated master schedule of all completed and ongoing studies of both GLP and non-GLP and other relevant documents to NPRA when requested. Preparation for inspection will focus on the information on the master schedule for the selection of the studies to be audited during the inspection.

6.5.3 Surveillance Inspection

Surveillance inspection will be conducted annually for the first two years and subsequent surveillance inspections every two (2) years. Test facility must have at least one (1) completed study per area of expertise per year [at least two (2) completed studies per area of expertise in two (2) years]. The approach used for the surveillance inspection is similar to what is described under Inspection 6.5.2.

6.5.4 Extra-ordinary Inspection

An extraordinary inspection shall be carried out in situations not covered under 6.5.2 and 6.5.3.

The examples of such inspection can be but are not limited to:

- conduct study audits or inspections at the request of national or international authority
- verification of the implementation of the corrective actions
- extension of scope /area of expertise

- significant changes in the test facility (e.g. change of address, renovation, etc.)
- others, where necessary.

Such inspections can be carried out announced or unannounced (e.g. any complaint received) where it is considered necessary. However, the test facility will ensure that its management and other key personnel of the test facility are available during the announced inspection. The approach used for the extraordinary inspection is similar to that described under Inspection 6.5.2.

An Inspection Performed at the Request of other Authorities

A foreign CMA or local/international regulatory authorities (RA) may also request specific study audits. Such requests may sometimes involve test facility inspections. However, it is the responsibility of the RA or the foreign CMA to identify and justify the need for such inspections and study audits.

In cases where local/international RA and/or foreign CMA request for study audit, NPRA will invite the concerned test facility to submit an application for inspection/study audit using the application form. The request for such audits shall be handled as extra-ordinary inspection according to 6.5.4.

6.6 Power of the Inspectors

The NPRA inspectors shall have full access to the test facility and relevant documentation to conduct any type of inspection; otherwise, the test facility would not be listed in the NPRA GLP Compliance Programme.

6.7 Classification of Non-Compliance

During the inspection, the inspection team may come across areas/issues which are not in compliance with the NPRA Compliance Monitoring Programme. Such non-compliances are classified into the following categories:

Major non-compliances:

Deviation from NPRA GLP Compliance Programme that directly affects the integrity of the quality system and/or study data.

Minor non-compliances:

Issues that do not directly affect either the quality system or the integrity of study data. Such deficiencies are normally observed in isolated areas.

6.8 Final Approval of Inspection Results

The inspection team will present the inspection result and make necessary recommendations to the technical meeting committee on whether the test facility is in compliance or not in compliance. The technical meeting committee will review and forward the recommendations to the Director of NPRA in the approval meeting, *Mesyuarat Jawatankuasa Penilaian Pemeriksaan Premis & Kajian (JKPPPK)*.

For a new and existing test facility that is found to be **in compliance**, the Director of NPRA will issue a GLP Certificate.

For a new test facility (which has not been listed in the GLP Programme), that **did not comply** with NPRA GLP Compliance Programme, the inspection report, corrective actions taken by the test facility and justification for rejection, will be tabled for rejection. A letter will be issued by the Director of NPRA to state the reasons for rejection into the programme.

For a test facility which is already in the programme but **not in compliance** with the NPRA GLP Compliance Programme, a notice to remove the test facility from GLP Programme will be issued by the Director of NPRA. The test facility name shall be removed from the NPRA website and the OECD will be notified regarding the removal.

Removal of a test facility from the NPRA GLP Compliance Programme can also be due to other reasons such as out of business, forming a new entity and etc. In this scenario, the test facility shall notify NPRA. The test facility name shall be removed from the NPRA website and the OECD will be notified regarding the removal.

7.0 RIGHTS AND DUTIES

It is in the interest of the test facility to be in compliance with the requirements of the Principles of GLP and to produce data of adequate quality for inspection and decision-making by regulatory authorities. Failure to do so may lead to the non-acceptance of safety data by regulatory authorities.

If the Test Facility Management, QA Staff, Study Director/s, personnel and infrastructure of the test facility, or the types of studies conducted is significantly extended or changed, the test facility is required to inform these changes to NPRA.

The acceptability of safety data is decided by the responsible local/international regulatory authority and not by the NPRA. If a study has not been performed according to the Principles of GLP or the test facility is not operating in compliance with the CP, NPRA will inform the relevant local/international regulatory authorities and/or foreign CMA of the receiving country.

In order to facilitate the communication between sponsors, test facilities, local/international regulatory authorities and CMA, NPRA will provide information on inspections to interested parties in the following formats:

- The conclusions of an inspection and a statement of GLP Compliance where the inspection reveals adequate compliance with GLP are given to the test facility. This information will also be made available on request to the local/international regulatory authority concerned (List of GLP Compliant Test Facility). The same information shall be available on the NPRA GLP Compliance Programme page.
- Annual Overview which includes the test facility inspected and their GLP compliance status shall be submitted to the OECD GLP Working Group Secretariat annually.

8.0 COMPLAINT/ APPEAL PROCEDURES

Any disagreement or difference of opinion between the inspectors and test facility management, arising from the inspection process, will normally be resolved during the inspection or at the closing meeting. However, where problems persist and agreement on differences cannot be reached during the inspection process, test facility management may complaint/s against the findings observed which are communicated in the inspection report. Such complaints against

those findings must be addressed, in writing, to the Director of NPRA within thirty (30) days after the receipt of the inspection report. The Director of NPRA will then take appropriate steps to achieve a mutually acceptable resolution. Therefore, he/she may ask for advice from independent internal or external experts. Based on this advice, the Director of NPRA will make the final decision.

9.0 ARCHIVES

NPRA has its own procedure for archiving all documents related to GLP inspection of the test facilities and documents related to the quality system of NPRA.

Sponsor has a responsibility to ensure the retention period, and storage of records and materials of a study. Retention periods are defined by regulatory (receiving) authorities. The retention period defines the minimal period of time that data must be retained and must be available for review if the safety studies that support the registration of new products need to be verified. It is strongly recommended that records and other sustaining material associated with such safety studies be retained for as long as regulatory authorities might request GLP audits of the respective studies. In Malaysia, it is recommended that the test facility retain the records and material for at least ten (10) years. This is to enable the inspectors to evaluate the compliance of the test facility with the Principles of GLP.

APPENDIX 1





Objective: To ensure that harmonized practices are used in Malaysia with regards to implementation of Organisation for Economic Co-operation and Development (OECD) guidelines on Good Laboratory Practice (GLP) Inspection.

We hereby agree that:

1. National Pharmaceutical Control Bureau (NPCB) as a focal point shall be responsible for organising meetings of the two Compliance Monitoring Authorities (CMAs) and will record the minutes of the meetings.
2. The frequency of the meeting shall be at least once a year.
3. As part of the inspectors training program, inspectors from NPCB may participate as an observer in STANDARDS MALAYSIA inspections, vice versa.
4. If a Test Facility conducts studies that fall under the scope of NPCB and STANDARDS MALAYSIA, the Test Facility may request a joint inspection by both CMAs by submitting a parallel application to both CMAs for GLP certification. Joint inspections of Test Facilities will be carried out together at the request/agreement of Test Facilities (on a same date basis only).
5. Both CMAs shall exchange views on non-compliant GLP issues.
6. Both CMAs shall discuss issues of mutual interest related to GLP.

A stylized signature in black ink, consisting of a horizontal line with a loop and a short vertical stroke at the end.

SELVARAJA SEERANGAM
Director
National Pharmaceutical Control Bureau
Ministry of Health Malaysia

Date: 2 October 2010

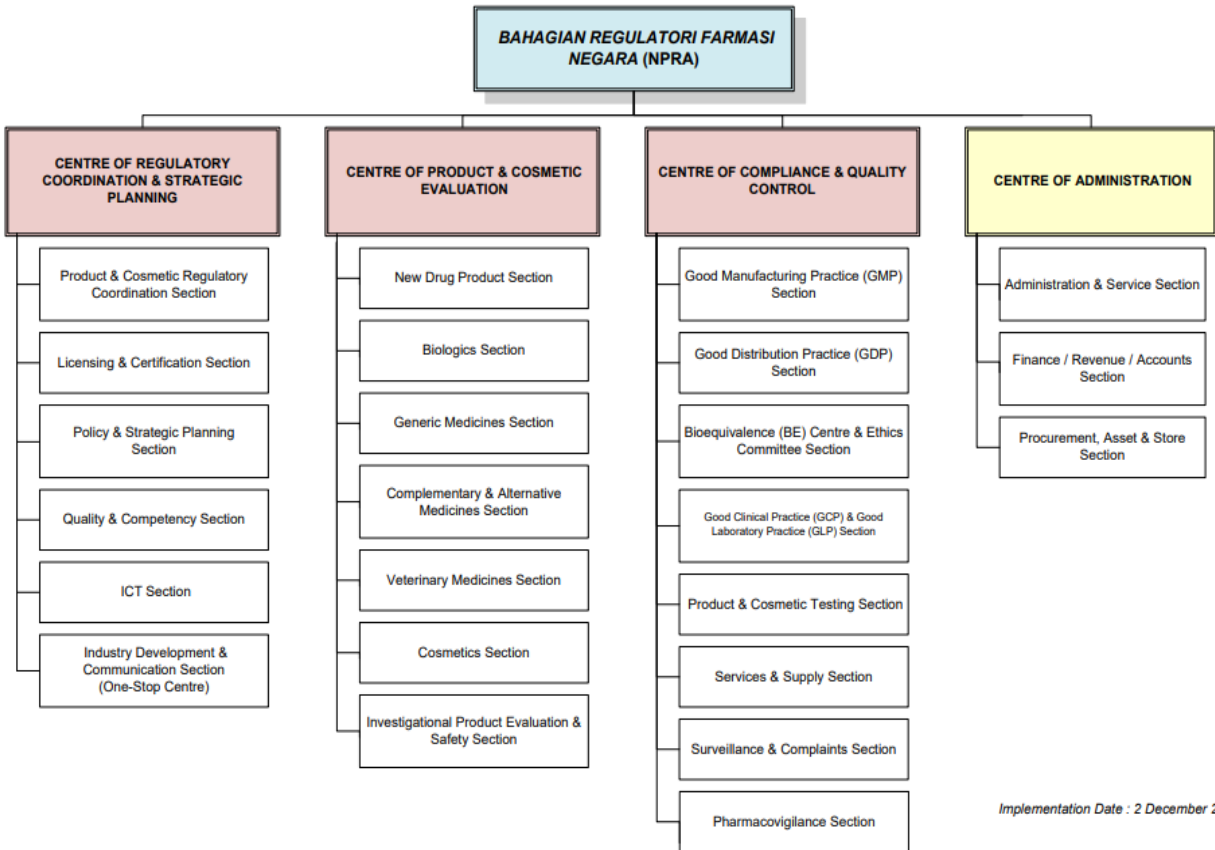
A cursive signature in black ink, starting with a large 'S' and ending with a flourish.

SHAHARUL SADRI BIN ALWI
Director of Accreditation
Department of Standards Malaysia
Ministry of Science, Technology and
Innovation

Date: 2 October 2010

NPCB/GLP/200/001
Version : 1
Date : 1 October 2010

APPENDIX 2



APPENDIX 3

In the context of their inspection activities under GLP, the inspectors undertake to comply with the rules below, which concern the actual activity of inspection as well as the inspectors' attitude to the test facilities inspected, third parties and the National Pharmaceutical Regulatory Agency (NPRA). They must:

- a) Present the facts objectively, honestly, equitably and accurately to all the parties concerned.
- b) Constantly maintain an attitude that welcomes dialogue, avoid arbitrary or authoritarian behaviour and keep their language courteous.
- c) Inform NPRA of any relationship that may exist or have existed in the past two years with the organisation to be inspected and which might cause doubt concerning the independence of their judgment.
- d) Neither accept nor authorise any member of the inspection team under their responsibility to accept for themselves or their entourage any payment, gift, commission or another advantage, even if it is non-pecuniary, from the test facility/ies inspected, their representative or any other party involved or otherwise, to avoid casting doubt on their independence during the inspection.
- e) Take every precaution to avoid informing third parties, whether directly or indirectly as a result of their actions or those of the people under their responsibility, of documents or information which may come to their knowledge in the context of their inspection activities without written authorisation from the parties concerned.
- f) Share their experience with the members of the inspection team with whom they may be called upon to work.
- g) Behave in a manner that does not damage the reputation or interests of the client of the GLP inspection or the organisation inspected.
- h) Act to preserve a positive image of the NPRA and the quality of the inspection.
- i) Cooperate with any requests for information or formal examination procedure if a violation of this code is alleged.
- j) Not take part in any inspection which exceeds GLP purposes /their professional abilities.
- k) Make every effort to improve their own expertise and the effectiveness and quality of their services.
- l) Keep a record of the inspections performed and the training courses attended and transmit copies of these to their files at NPRA.
- m) Know the rules of GLP compliance and contribute to maintaining the reputation of the GLP compliance system.
- n) Accept that the NPRA's staff or authorised representative observes their performance during an inspection carried out after being informed by NPRA and with the agreement of the test facility concerned.

I hereby understand and undertake to comply with the above code of ethics:

Name: Signature:

Date:.....



APPENDIX 4

This undertaking is to safeguard the confidentiality of any information at all levels obtained in the course of compliance monitoring activities under the National Pharmaceutical Regulatory Agency (NPRA) Good Laboratory Practice Compliance Programme.

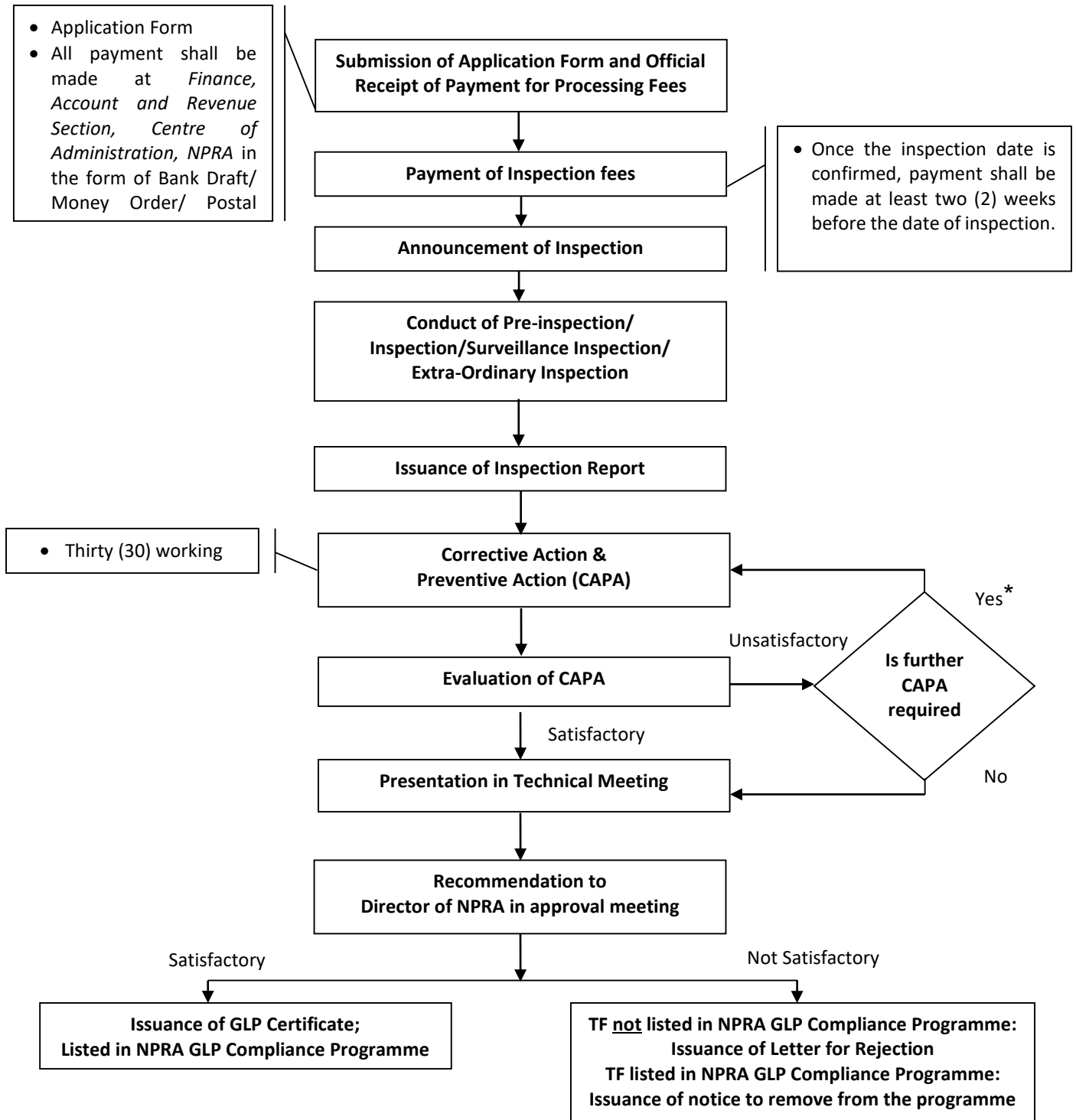
Hereby, I[NRIC:] declare that;

- I. I will not disclose any information gained during the execution of my duties to any person or organization
- II. I am fully aware of the ownership and confidentiality requirement for the protection of intellectual property right
- III. I have no financial or other interest in the test facility inspected, the study audited or the firm sponsoring such study; and
- IV. I have completed this undertaking prior to taking part in any preparation for or actual GLP inspection activity or having access to any document of the GLP compliance program.

Signature: Date:.....

APPENDIX 5

FLOW CHART FOR GLP INSPECTION



*All enquiries should be answered within thirty (30) working days.