ASSOC. PROF. DR. FARAHIDAH MOHAMED

DEPUTY DIRECTOR, INNOVATION & COMMERCIALIZATION UNIT,

RESEARCH MANAGEMENT CENTRE

INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA

GLP: GOOD LABORATORY PRACTICE

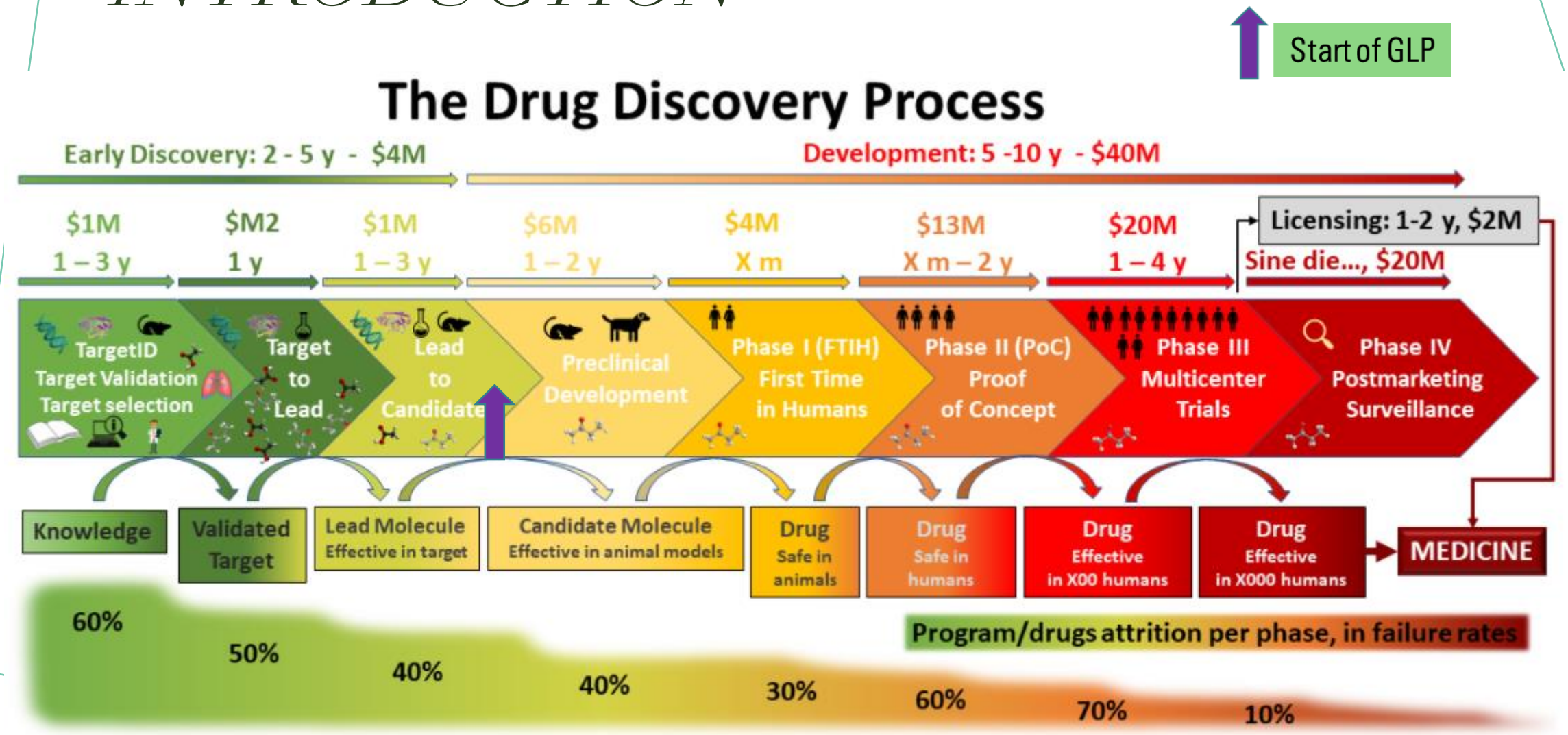
SMBT Institute of Diploma Pharmacy

Jan 2022

OUTLINE

- Introduction – Drug Discovery Process
  - ➢Introduction to OECD & GLP
  - ➢Principles of GLP

INTRODUCTION



https://doctortarget.com/machine-learning-applied-drug-discovery/

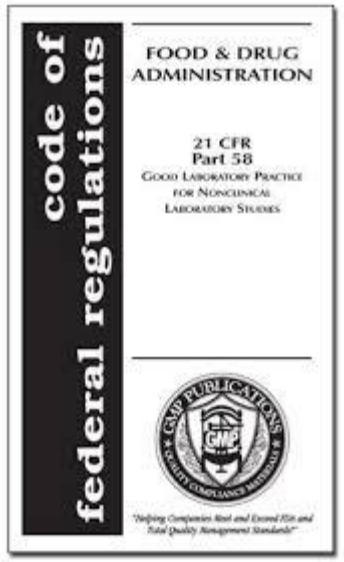
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

OECD

BETTER POLICIES FOR BETTER LIVES

- An intergovernmental organisation of 29 industrialised countries in North America, Europe and Pacific & European Commission
  - > 200 specialised committees & subsidiary groups
- Fxn: coordinate, harmonize policies, discuss issues of mutual concern and respond to international problems
- OECD secretariat is located in Paris, France
- Chemical safety is under Environmental Health and Safety Division

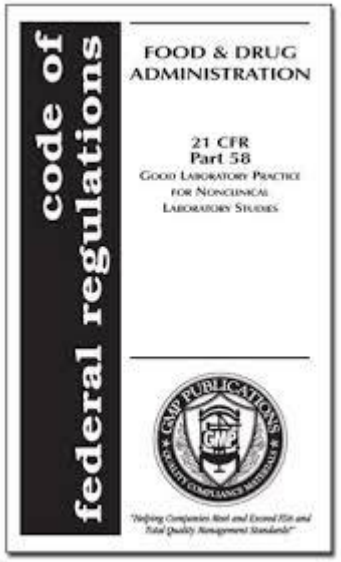
INTRODUCTION TO OECD AND GLP



- GLP principles were developed by OECD
- Adopted by other regulatory authorities: FDA, WHO, NPRA (National Pharmaceutical Regulatory Agency, Malaysia).
- Reason of Existence:

  - ✓ In 70's, several reports concerning fraudulent safety data in US.
  - ✓ FDA found out many labs were poorly organised and maintained
  - ✓ FDA established Final Rule on GLP in June 1979 (21 CFR 58) → GLP regulation
  - ✓ 2 Expert groups (1978 & 1996) under OECD, developed OECD GLP Guideline

INTRODUCTION TO OECD AND GLP



OECD GLP Compliant

- The OECD Principles of Good Laboratory Practice (GLP) ensure the generation of high quality and reliable test data related to the safety of industrial chemical substances and preparations.
- The principles have been created in the context of harmonising testing procedures for the Mutual Acceptance of Data (MAD).

INTRODUCTION TO OECD AND GLP

Argentina*	Australia	Austria	Belgium
Brazil#	Canada	Czech Republic	Denmark
Finland	France	Germany	Greece
Hungary	India#	Ireland	Israel
Italy	Japan	Korea	Luxembourg
Malaysia#	Mexico	The Netherlands	New Zealand
Norway	Poland	Portugal	Singapore#
Slovak Republic	Slovenia	South Africa#	Spain
Sweden	Switzerland	Turkey	United Kingdom
United States of America	*Full adherence only applies to industrial chemicals, pesticides and biocides	Non OECD Member Adhering TO MAD#	

#MAD Mutual Acceptance of Data.
$Total 34 member countries, 6 non-member countries

Home
About NGCMA
Documents of NGCMA
Online Application for GLP Certification
OECD Principles of GLP
OECD Test Guidelines
P Certified Test Facilities

About NGCMA

National Good Laboratory Practice (GLP) Compliance Monitoring Authority {NGCMA}

National GLP Compliance Monitoring Authority (NGCMA) was established by the Department of Science & Technology (DST), Government of India, with the approval of the Union Cabinet on April 24,2002. **India is full-member for Mutual Acceptance of Data (MAD) in the OECD's Working Group on GLP w.e.f March 3, 2011**. As a consequence, the non-clinical health and safety studies/ data of such studies generated by Indian GLP laboratories is acceptable in 36 OECD member countries and 6 non-memberMAD adherent countries. This facilitates export of chemicals,drugs, pesticides etc. to these countriesincluding developed markets of USA, UK, Australia, Japan, European Union, etc.

The National GLP Programme functions through an**Apex Body**, represented by Secretaries of concerned Ministries/ Departments with Secretary, DST being its Chairman. This Apex Body oversees that the National GLP Programme functions as per OECD Principles of GLP &

A number of countries require manufacturers of chemicals viz. Industrial chemicals, Pharmaceuticals (Human and Veterinary), Agrochemicals, Cosmetics Products, Food/ Feed Additives and Medical devices, etc., to establish through data that use of these chemicals does not pose any hazards to human health and the environment. Non-hazardous nature needs to be established through studies and data, which will be examined by the regulatory authorities of the concerned countries. **Good Laboratory Practice (GLP)** is a system, which has been evolved by **Organisation for Economic Co-operation and Development (OECD)** used for achieving the above goals.

National GLP Compliance Monitoring Authority (NGCMA) was established by the **Department of Science & Technology (DST)**, **Government of India**, with the approval of the Union Cabinet on April 24, 2002.

GLP-compliance certification is **voluntary** in nature. Industries/ test facilities/laboratories dealing with above chemicals and looking for approval from regulatory authorities before marketing them, may apply to the NGCMA for obtaining GLP Certification.

49 GLP-CERTIFIED LABS IN INDIA

List of GLP Certified Test Facilities of NGCMA, INDIA

Test Facility	Contact Person	Test Facility Details	Area(s) of Expertise	Test Item(s)	Biological Test System(s)	Validi perio

International Institute of Biotechnology and Toxicology	Dr. A. Ramesh, Test Facility Management	**Address:** Padappai-601301, Kancheepuram District, Tamil Nadu, India
		
		Tel: +91-44-27174246, 27174266
		Fax: +91-44-27174455
		Email: director at iibat dot com
			• **Physical-chemical Testing (Including Five Batch Analysis)**
			• **Toxicity Studies**
			  ○ Acute Toxicity
			  ○ Repeated Dose Toxicity
			  ○ Reproductive Toxicity
			  ○ Carcinogenicity
			  ○ Inhalation Toxicity
			  ○ Neurotoxicity
			• **Mutagenicity Studies**
			  ○ Bacterial Reverse Mutation Test (AMES Test)
			  ○ Chromosome Aberration Test (*In-vivo* and *In-vitro*)
			  ○ Micronucleus Assay (*In-vivo* and *In-vitro*)
			  ○ In-vitro Mammalian Cell Gene Mutation Test
			• **Environmental Toxicity Studies on Aquatic and Terrestrial Organisms**
			• **Studies on Behavior in Water, Soil and Air; Bioaccumulation**
			• **Residue Studies**
			• **Studies on Effects on Mesocosms and Natural Ecosystems**
			• **Analytical and Clinical Chemistry Testing**
			• **Others**
			  ○ ADME Studies
			  ○ Feeding Studies in Livestock (Goat/ Poultry) including Metabolism using ^{14}C labeled chemicals
			  ○ Bioefficacy studies on Household insect pests in the laboratory as per WHOPES and other Standard protocols.
				Industrial Chemicals, Pharmaceuticals (Human and Veterinary), Agrochemicals, Cosmetic Products and Food/ Feed Additives.	Rat, Mice, Rabbit, Guinea Pig, Goat, Dog, *Salmonelia typhimurium* (TA 98, TA 100, TA 102, TA 1535 and TA 1537), Human Peripheral Blood Lymphocytes, Cell Lines (CHO and L5178Y TK+- 3.7.2C), Alga, Duck Weed, Water Flea, Fish, Chicken, Pigeon, Japanese Quail, Honeybee, Earthworm, Mulberry Silkworm, Aquatic Flora - Zooplankton and phytoplankton, Aquatic Fauna - Mosquito Larvae, Mosquito, Cockroach, Housefly, Bed Bug, Dust Mite, Soil, Water and Crop/ Plant.	19-07-201
						18-07-202

INTRODUCTION TO OECD AND GLP

OECD GLP Compliance Monitoring Authority in India

- Pharmaceutical products
- Cosmetics
- Food additive products
- Veterinary products
- Pesticides
- Industrial products other than pharmaceuticals
- Feed Additive products
- Biotechnology (non-pharmaceutical) products

Principles of GLP

- For us to practice GLP
- For authorities to monitor the GLP practitioners

- Series of GLP guidelines:
  - No. 1 – OECD Principles of GLP
  - No. 4, 5, 6, 7, 8, 10, 13 – GLP Consensus Documents
  - No. 2, 3, 9 – Guidance Documents for Compliance Monitoring Authorities
  - No. 11, 12, 14, 15, 16, 17 – Advisory Documents of the Working Group on GLP
  - No. 18 – Position Papers

WHAT

No.	Document
4	Quality Assurance and GLP
5	Compliance of Laboratory Suppliers with GLP Principles
6	The Application of the GLP Principles to Field Studies
7	The Application of the GLP Principles to Short Term Studies
8	The Role and Responsibilities of the Study Director in GLP Studies
10	The Application of the Principles of GLP to Computerised Systems
13	The Application of the OECD Principles of the GLP to the Organization and Management of Multi-Site Studies

GLP Consensus Document -developed by consensus workshops attended by representatives of member countries & relevant stakeholders

WHEN

- During product (test item) registration for the purpose of obtaining the info/data with regard to properties and/or safety of the ‘test items’ of interest
- Test items could be the following:
  - **pharmaceutical products**
  - pesticide products
  - cosmetic products
  - veterinary drugs
  - food additives
  - feed additives
  - industrial chemicals.

WHERE

Non-clinical health and environmental safety studies covered by the Principles of Good Laboratory Practice include work conducted in the laboratory, in greenhouses, and in the field.

Definition of Terms

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

Principal Investigator - 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.

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.

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

Definition of Terms

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

Study Plan Amendment - an intended change to the study plan after the study initiation date.

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

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

Definition of Terms

Test item - an article that is the subject of a study.

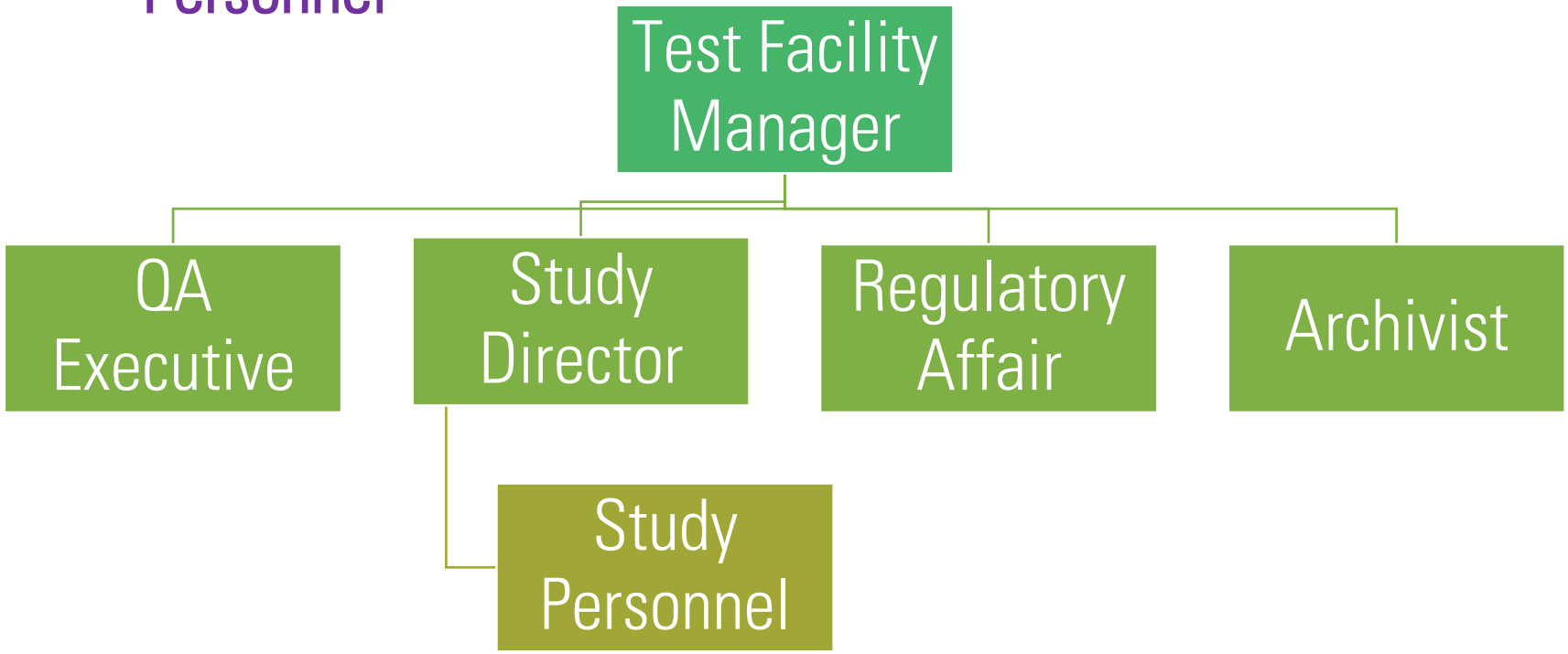
Reference item ("control item") - any article used to provide a basis for comparison with the test item.

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

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

The GLP Principles #1: Test Facility Organisation & Personnel



Basic organisation chart of a GLP-certified centre or lab

The GLP Principles #1: Test Facility Organisation & Personnel

- **Test Facility Management (TFM) responsibilities:**
  - ensure that a statement exists which identifies the individual within a test facility responsible for management
  - ensure that a sufficient number of qualified personnel, appropriate facilities, equipment, and materials are available for the timely and proper conduct of the study
  - ensure the maintenance of a record of the qualifications, training, experience and job description for each professional and technical individual

The GLP Principles #1: Test Facility Organisation & Personnel

➢ **Test Facility Management (TFM) responsibilities:**

- ensure that appropriate and technically valid SOP are established and followed, and approve all original and revised SOP
- ensure that there is a Quality Assurance Programme with designated personnel and assure that the quality assurance responsibility is being performed
- ensure that for each study an individual with the appropriate qualifications, training, and experience is designated by the management as the Study Director before the study is initiated. Replacement of a Study Director should be done according to established procedures, and should be documented.

The GLP Principles #1: Test Facility Organisation & Personnel

➢ Test Facility Management (TFM) responsibilities:

- in the event of a multi-site study, that, if needed, a Principal Investigator is designated, who is appropriately trained, qualified and experienced to supervise the delegated phase(s) of the study. Replacement of a Principal Investigator should be done according to established procedures, and should be documented.
- ensure documented approval of the study plan by the Study Director has made the approved study plan available to the Quality Assurance personnel
- ensure the maintenance of an historical file of all SOPs and of a master schedule
- ensure for a multi-site study that clear lines of communication exist between the Study Director, Principal Investigator(s), the Quality Assurance Programme(s) and study personnel

The GLP Principles #1: Test Facility Organisation & Personnel

➢ Study Director's *(SD)* responsibilities:

- SD is the single point of study control and has the responsibility for the overall conduct of the study and for its final report.
- approve the study plan and any amendments to the study plan by dated signature
- ensure that the QA have a copy of the study plan and any amendments in a timely manner and communicate effectively with the QA as required during the conduct of the study
- ensure that study plans and amendments and SOP are available to study personnel

The GLP Principles #1: Test Facility Organisation & Personnel

➢ Principal Investigator's (PI) responsibilities:

- The Principal Investigator will ensure that the delegated phases of the study are conducted in accordance with the applicable Principles of Good Laboratory Practice, must be knowledgable in GLP and responsible for quality and integrity of data

NOTE #1: For a BE centre, the PI role is specifically for the Clinical Site and it is NPRA regulatory requirement that PI must be from healthcare-taker's background

NOTE #2: For a BE centre that usually involve 1 clinical site instead of multiple sites, SD and PI can be from the same person if the SD is from healthcare-taker's background

The GLP Principles #2: Quality Assurance Programme

➢ General:

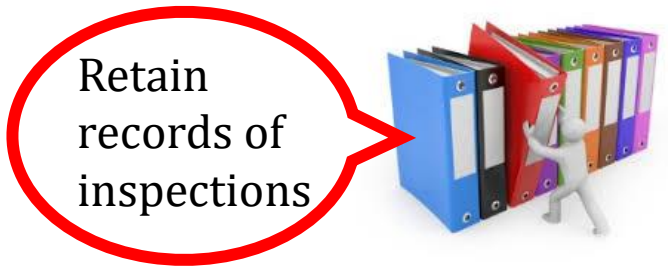
- test facility should have a documented Quality Assurance Programme (QAP), maintain and verify all documents
- should be carried out by an individual or by individuals designated by and directly responsible to management and who are familiar with the test procedures.
- this individual(s) should not be involved in the conduct of the study being assured.

HOW

The GLP Principles #2: Quality Assurance Programme (QAP)

➢ Responsibilities of QA:

- conduct inspections to determine if all studies are conducted in accordance with these Principles of Good Laboratory Practice. Inspections should also determine that study plans and Standard Operating Procedures have been made available to study personnel and are being followed.
- Inspections can be of three types as specified by QAP SOP:
  - ➢ Study-based inspections,
  - ➢ Facility-based inspections,
  - ➢ Process-based inspections.



The GLP Principles #3: Facilities

➢ General:

- The test facility should be of suitable size, construction and location to meet the requirements of the study and to minimise disturbance that would interfere with the validity of the study
- The design of the test facility should provide an adequate degree of separation of the different activities to assure the proper conduct of each study.

HOW

The GLP Principles #3: Facilities

➢ General:

- Archive facilities: should be provided for the secure storage and retrieval of study plans, raw data, final reports, samples of test items and specimens. Archive design and archive conditions should protect contents from untimely deterioration.
- Waste Facilities: Handling and disposal of wastes should be carried out in such a way as not to jeopardise the integrity of studies. This includes provision for appropriate collection, storage and disposal facilities, and decontamination and transportation procedures.

HOW

The GLP Principles #4: Apparatus, Materials and Reagents

➢ General:

- Apparatus, including validated computerised systems, used for the generation, storage and retrieval of data, and for controlling environmental factors relevant to the study should be suitably located and of appropriate design and adequate capacity
- Apparatus should be periodically inspected, cleaned, maintained, and calibrated according to SOP. Records of these activities should be maintained.

HOW

The GLP Principles #4: Apparatus, Materials and Reagents

➢ General:

- Chemicals, reagents, and solutions should be labelled to indicate identity (with concentration if appropriate), expiry date and specific storage instructions.
  - Information concerning source, preparation date and stability should be available.
  - The expiry date may be extended on the basis of documented evaluation or analysis.

The GLP Principles #5: Test Systems

➢ General:

- Records of source, date of arrival, and arrival condition of test systems should be maintained.
- All information needed to properly identify the test systems should appear on their housing or containers; must bear appropriate identification if removed temporarily during testing.

The GLP Principles #6: Test and Reference Items

➢ General:

- Records including test item and reference item characterisation, date of receipt, expiry date, quantities received and used in studies should be maintained.
- Handling, sampling, and storage procedures should be identified in order that the homogeneity and stability are assured to the degree possible and contamination or mix-up are precluded.
- Storage container(s) should carry identification information, expiry date, and specific storage instructions.

HOW

The GLP Principles #6: Test and Reference Items

➢ General:

- Each test and reference item should be appropriately identified (e.g., code, Chemical Abstracts Service Registry Number [CAS number], name, biological parameters).
- For each study, the identity, including batch number, purity, composition, concentrations, or other unique characteristics should be known and recorded.
- The stability of test and reference items under storage and test conditions should be known for all studies.
- A sample for analytical purposes from each batch of test item should be retained for all studies except short-term studies.

The GLP Principles #7: SOP

➢ General:

- A test facility should have written SOP approved by TFM intended to ensure the quality and integrity of the data generated by that test facility.
- SOPs needed for, but not limited to:
  - Receipt, identification, labelling, handling, sampling and storage of *Test and Reference Items*
  - Use, maintenance, cleaning and calibration for ALL instruments
  - Preparation and labelling of *Materials, Reagents and Solutions*
  - Validation, operation, maintenance, security, change control and back-up of ALL computerised systems

The GLP Principles #7: SOP

- SOPs needed for, but not limited to:
  - Coding of studies, data collection, preparation of reports, indexing systems, handling, storage and retrieval of data, including the use of computerised systems.
  - Operation of Quality Assurance personnel in planning, scheduling, performing, documenting and reporting inspections under QAP.

The GLP Principles #8: Performance of the Study

- **Study Plan**

➢ For each study, a written plan should exist prior to the initiation of the study. The study plan should be approved by dated signature of the SD and verified by QA.

➢ The study plan should also be approved by the TFM and the sponsor.

The GLP Principles #8: Performance of the Study

- Content of the Study Plan

1. *Identification of the Study, the Test Item and Reference Item*

a) A descriptive title;
b) A statement which reveals the nature and purpose of the study;
c) Identification of the test item by code or name (IUPAC; CAS number, biological parameters, etc.);
d) The reference item to be used.

The GLP Principles #8: Performance of the Study

- Content of the Study Plan

2. *Information Concerning the Sponsor and the Test Facility*

a) Name and address of the sponsor;
b) Name and address of any test facilities and test sites involved;
c) Name and address of the Study Director;
d) Name and address of the PI(s), and the phase(s) of the study delegated by the Study Director and under the responsibility of the PI(s).

The GLP Principles #8: Performance of the Study

- Content of the Study Plan

3. *Dates*

a) The date of approval of the study plan by signature of the SD, TFM and Sponsor.

b) b) The proposed experimental starting and completion dates.

4. *Test Methods*

Reference to the OECD Test Guideline or other test guideline or method to be used.

The GLP Principles #8: Performance of the Study

- Content of the Study Plan

5. *Issues (where applicable)*

a) The justification for selection of the test system;
b) The method of administration and the reason for its choice;
d) The dose levels and/or concentration(s), frequency, and duration of administration/ application;
e) Detailed information on the experimental design, including a description of the chronological procedure of the study, all methods, materials and conditions, type and frequency of analysis, measurements, observations and examinations to be performed, and statistical methods to be used (if any).

HOW

The GLP Principles #8: Performance of the Study

- General:
  - Content of the Study Plan

6. *Records*

A list of records to be retained.

- Conduct of the Study

- A unique identification should be given to each study. All items concerning this study should carry this identification. Specimens from the study should be identified to confirm their origin. Such identification should enable traceability, as appropriate for the specimen and study.

The GLP Principles #8: Performance of the Study

- **Conduct of the Study**

➢ All data generated during the conduct of the study should be recorded directly, promptly, accurately, and legibly by the individual entering the data.

➢ These entries should be signed or initialled and dated.

➢ Any change in the raw data should be made so as not to obscure the previous entry, should indicate the reason for change and should be dated and signed or initialled by the individual making the change.

The GLP Principles #9: Reporting of Study Results

- **General:**

- A final report should be prepared for each study. In the case of short term studies, a standardised final report accompanied by a study specific extension may be prepared.
- Reports of Principal Investigators or scientists involved in the study should be signed and dated by them.
- The final report should be signed and dated by the SD to indicate acceptance of responsibility for the validity of the data. The extent of compliance with these Principles of GLP should be indicated.
  - Corrections and additions to a final report should be in the form of amendments with clear justification and signed and dated by SD.

The GLP Principles #10: Storage and Retention of Records and Materials

- The following should be retained in the archives:

a) The study plan, raw data, samples of test and reference items, specimens, and the final report of each study;
b) Records of all inspections performed by the Quality Assurance Programme, as well as master schedules;
c) Records of qualifications, training, experience and job descriptions of personnel;
d) Records and reports of the maintenance and calibration of apparatus;
e) Validation documentation for computerised systems;
f) The historical file of all Standard Operating Procedures;
g) Environmental monitoring records.

HOW

The GLP Principles #10: Storage and Retention of Records and Materials

- **Archiving:**

➢ Material retained in the archives should be indexed so as to facilitate orderly storage and retrieval.

➢ Only personnel authorised by management should have access to the archives.

➢ Movement of material in and out of the archives should be properly recorded.

HOW

Summary of GLP Principles

#1 Test Facility Organisation and Personnel
#2 Quality Assurance Programme
#3 Facilities
#4 Apparatus, Material, and Reagents
#5 Test Systems
#6 Test and Reference Items
#7 Standard Operating Procedures
#8 Performance of the Study
#9 Reporting of Study Results
#10 Storage and Retention of Records and Materials

SUMMARY

- GOOD PRACTICES GUIDELINES ARE AVAILABLE AT MANY PLATFORMS
- READING IS THE FIRST STEP TO ACQUIRE THE KNOWLEDGE, THEN SEEK GOOD MENTOR TO STUDY AND PRACTICE WITH OR GET INVOLVE AS INTERN OR PART OF INDUSTRIAL ATTACHMENT
- DEVELOPMENT OF ANY PRODUCTS OR ESTABLISHMENT OF TOXICOLOGY DATA MUST ENSURE THAT REGULATORY REQUIREMENT ARE BEING FULFILLED TO MINIMISE RISK OF REJECTION FROM REGULATORY→ FOLLOW GLP