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AN OVERVIEW ON GOOD LABORATORY PRACTICES

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ABSTRACT

Good Laboratory practice (GLP) governs the quality work in the laboratory. In present study the importance of GLP is covered with special reference to pharmaceutical laboratories. Pharmaceutical laboratories are concerned with life saving drugs, so that it requires strict attention in its manufacturing and testing. In this way GLP is required for quality work in pharmaceutical laboratories.

INTRODUCTION

The purpose of GLPS is to assure the quality, integrity, and durability of the data collected in a study [1]. Good communication must exist between all members of the study team. The Study Director is the control point of the study. SOPS can save considerable time if followed. The Study Plan clarifies the purpose of the study now and in the future [2]. These practices make good technical sense. Remember keep it as simple as possible and communicate effectively to everyone involved [3]. Every laboratory interested in producing quality results is interested in maintaining sound laboratory management practices. Sometimes these practices are referred to, in general terms, as good laboratory practice ("lower case glp"). ISO/IEC 17025, the standard used by NATA to accredit laboratories, is an example of a code of good laboratory practice. NATA has, therefore, been working with codes of good laboratory practice for over 60 years. There is, however, another set of initials, GLP ("upper case GLP"). This article sets out to explain this latter GLP and its applicability to Australian laboratories. The basic document dealing with GLP is the OECD Principles of Good Laboratory Practice, published by the OECD's Environment Directorate, and most recently revised in 1998. This document was produced by the OECD GLP Working Group, on which Australia is represented by NATA. Some countries issue their own versions of the GLP Principles, often as part of national legislation, but the foundation of these documents are the OECD[4].

Principles of GLP. In the US the equivalent legislation is: US (FDA) CFR 21: Part 58 – Good Laboratory Practice for Nonclinical Laboratories studies US (EPA) CFR 40 Vol 7 Part 160 – Good Laboratory Practice Standards (Pesticides Programs) CFR 40 Part 28 Part 792 Toxic Substance Control Act[5]. In EU countries the equivalent legislation is: Directive 2004/10/EC There is a misconception in some quarters that GLP is required for the conduct of clinical studies. The introduction to the OECD Principles of GLP (and the introduction to the USFDA GLPs) make clear that they apply only to non-clinical (pre-clinical) studies. The relevant documents for clinical studies are the various codes of GCP (e.g. ICH) and are most often developed by regulators. Regulators (including those in the US) do require a demonstration of the quality of test data from clinical studies. This could include accreditation of a laboratory to ISO/IEC 17025:2005. In the US, this may well be by means of conformance with CLIA (Clinical Laboratories Improvement Act). In Australia, this can be demonstrated by the testing

laboratory's NATA accreditation (in Medical Testing, Chemical Testing, etc). The basis for the development of GLP was to provide assurance regarding test data related to the hazard assessment of chemicals (pharmaceuticals, veterinary and agricultural chemicals, industrial chemicals) when manufacturers are seeking to register products for use. In Australia the relevant registration authorities are TGA (pharmaceuticals), APVMA (veterinary and agricultural chemicals), and NICNAS (industrial chemicals)[6].

The Principles of GLP are applied to the conduct of non-clinical health and environmental safety studies of test items contained in various chemical products. A study covers work done in a laboratory, in animal houses, in greenhouses, and in the field. The Principles of GLP do not apply to clinical studies. Non-clinical studies include physico-chemical testing, toxicity, mutagenicity, environmental toxicity, bioaccumulation and residue studies; studies of effect on mesocosms and ecosystems, and the analytical chemistry associated with such studies.

The OECD Principles of GLP describe a quality system concerned with the organisational process and the conditions under which non-clinical studies are planned, performed, recorded, archived and reported. It does not concern itself with the technical validity of the studies themselves. The Principles can be quite prescriptive about some aspects of the conduct of the studies, especially in relation to the role of the Study Director (and any Principal Investigators), the role of the Quality Assurance unit, the content of study plans (protocols) and reports, and the way in which all data related to each study is archived. The OECD Principles are an integral part of the OECD Council Directives on Mutual Acceptance of Data in the assessment of chemicals. Annex II of this document states that data generated in a facility that adheres to the OECD Principles of GLP and that is recognized as GLP compliant by a national GLP

compliance monitoring authority must be accepted internationally. NATA, as the Australian GLP compliance monitoring authority, only inspects Australian facilities for compliance with the OECD Principles of Good Laboratory Practice (GLP). An inspection of an overseas facility by NATA would not mean that the data generated would be accepted by regulatory authorities. For data generated under GLP in another country to be accepted internationally under these directives, the relevant government would need to set up a compliance monitoring program and apply for provisional adherence to the Directives. Recognition of overseas facilities by NATA would not obliged overseas regulators to accept data from that country [6].

Good Laboratory Practice is defined in the OECD Principles as *"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"*.The purpose of the Principles of GLP is to promote the development of quality test data and provide a tool to ensure a sound approach to the management of laboratory studies, including conduct, reporting and archiving. The Principles may be considered as a set of standards for ensuring the quality, reliability and integrity of studies, the reporting of verifiable conclusions and the traceability of data the GLP Principles, in their regulatory sense, apply only to studies which :

- are non-clinical, i.e. mostly studies on animals or in vitro, including the analytical
- aspects of such studies;
- are designed to obtain data on the properties and/or the safety of items with respect
- to human health and/or the environment;
- are intended to be submitted to a national registration authority with the purpose of
- registering or licensing the tested substance or any product derived from it.
- Depending on national legal situations, the GLP requirements for non-clinical laboratory

The discovery phase often involves thousands or even tens of thousands of new molecular entities (NMEs) being screened for activity against a target disease. GPL is concerned with: - the organizational process, the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, reported, and archived[3,11].

Products tested under GLP

GLP is a requirement in regulatory nonclinical safety testing of the following test items:

• Pharmaceutical products

• Pesticide products

• Cosmetic products

• Veterinary drugs

• Food additives

• feed additives

• Industrial chemicals

Purpose of the GLP principles

• Obtain reliable and reproducible data

• Obtain comparable quality between countries

• Avoid repetition of studies

• Enable reconstruction of studies

• Optimise animal conditions

• Shorten the registration time of the drug

DRUG DEVELOPMENT STAGES

Stage 1 - DISCOVERY

Stage 2- NON-CLINICAL

Stage 3- CLINICAL

Stage 4- POST-APPROVAL MANUFACTURING

TIME LINE APPROXIMATELY 12 YEARS

Stage 1

The first stage, the discovery of a potential NME, is not covered by a regulatory standard, nor is studies that demonstrate proof of concept. The WHO has recently published guidance on this early research phase: Quality Practices in Basic Biomedical Research – QPBR.

Stage 2

The position of GLP studies within the drug development process is specific to the second stage. These studies are termed “non-clinical” as they are not performed in humans. Their primary purpose is safety testing. Toxicology and safety pharmacology studies, with a potential extension to pharmacokinetics and bioavailability, are those studies where compliance with GLP is required.

Stage 3

The third stage, following on from safety studies of stage 2, encompasses clinical studies in human subjects. Here, GCP is the basic requirement for quality standards, ethical conduct and regulatory compliance. GCP must be instituted in all clinical trials from Phase I (to demonstrate tolerance of the test drug and to define human pharmacokinetics) through Phase II (where the dose-effect relationship is confirmed) to Phase III (full scale, often multi-centric, clinical efficacy trials in hundreds or thousands of subjects).

Stage 4

The fourth stage is post-approval. Here the drug has been registered and is available on the market. However, even after marketing approval, the use of the drug is monitored through formal pharmacovigilance procedures. Any subsequent clinical trials (Phase IV) must also comply with GCP[7].

Good Laboratories Practice (GLP) in Pharmaceuticals

- Laboratory should be located designed, customized and maintained to suit the performance of all Q.C. test and analysis required.
- Conveniently located to service the Mfg. Dept. but preferably separate to avoid vibration, dust, internal and external traffic to protect the delicate instruments.
- As far as possible there must be separate wings for analytical, instruments, microbiology and sterility etc. and all wings may be interconnected with internal door.
- There must be effective air lock, provisions for A.C. and fumigation chamber, laboratory should be so designed that not only adequate provision of space but provision for utility, water, solvent storage, extraction dust collection etc. were covered.
- Laboratory furniture so designed to provide for adaptability, tabletop must be covered properly resistant to acid, alkali and solvent etc. Floor should be smooth, easy to clean and adequate drainage facility. [7,8]

Equipment's

- There must be a written standard operating procedure for each instrument. Instrument should be located with adequate place in a separate room under controlled temperature, Instrument must be handle with almost care and keep it clean all the times. The surrounding also required to be cleaned.
- The calibration and maintenance / service record must be kept and must be done periodically.
- The glassware must be calibrated with certified one before use. Particularly the glassware which are to be utilized for measuring purpose need calibration before use. All the necessary instruction regarding operating, handling and care should be display near the instruments.
- Light should be adequate.
- Electrical system in laboratory must not be over loaded. Voltage stabilizer must be provided to protect delicate instruments [9].

Chemicals and Reagents

- Storage of chemicals and reagent should be done in a manner it involved in the use, container of all chemicals and reagents must be properly labeled. Transfer of chemical must be done almost care. All analytical reagents and prepared solution must be labeled. Records of Molar Solutions entered in register prepared for the same.
- "No chemical reagents pipettes out by mouth, rubber bulb must be use."

Organisation and Personnel

- Every individual who is a part of the laboratory and engaged in conduct of testing shall have the requisite educational qualification, training, and experience to enable the individual to perform the assigned function.
- There shall be sufficient and number of personnel for proper conduct of the studies in accordance with protocols.
- The personnel should be provided with appropriate clothing suiting to their needs and the clothing should be of a nature, which will prevent microbiological, chemical contamination.
- The personnel should be subjected to proper medical examination to ensure that there will not be a source of contamination and their health status.

Documentation

- The document is critical factor of the good laboratory Practice Documentation is the accepted method of recording information for future reference. The major documents that need to be provided are protocols, logbook for usage, maintenance and calibration of equipment there should be well established SOPs.
- Receipt and storage of samples [11].

Use of GLP

• Fraud and serious findings were discovered during "for cause inspections" by FDA in the 1970s

• Inspections performed in 40 toxicology laboratories

• Industrial Biotest Corporation, Illinois conducted more than 20.000 studies concerning drug development [10].

GLP Regulations

• Improve data quality

• Obtain reliable and reproducible data

• Obtain comparable quality between countries

• Avoid repetition of studies

• Enable reconstruction of studies

Purpose of the GLP principles 'The rules of ones

• ONE Study

• ONE Study Plan

• ONE Study Director

• ONE Compliance Claim

• ONE Final Report

Study

• Test facility management and personnel

• Quality assurance programme

• Facilities

• Apparatus, materials and reagents

• Test systems

Elements of GLP Test facility

• Study Plan

• Amendments

• Deviations

• Notes to file

• Standard Operating Procedures (SOP)

Study Personnel

• Documented GLP/SOP training

• Comply with study plan and SOPs

• Document deviations and communicate these to SD

• Record raw data in GLP compliance

Data recording

All data should be recorded:

• Directly

• Promptly

• Accurately

• Legibly

• Indestructibly

• Signed and dated by the individual entering the data

• Study documentation

• SOPs/guidelines

Archiving

• Quality Control (QC)

• Quality Assurance/audit (QA)

Quality Assurance System

Quality Control (QC)

• Quality review of operational techniques and procedures ensuring correct data collection, transfer and reporting:

- Planning

- Study conduct

- Data collection and recording

- Reporting

- Archiving

Quality Assurance (QA)

• QA is an independent function with no direct line of authority to a project, a study or an operational unit

• The QA Manager reports directly to the top management

• QAs role is advisory

Role of Quality Assurance

• Assure management compliance with GLP

• Assess whether adequate QC procedures have been used to ensure reliable data

Quality Assurance audits

Audits should verify compliance between the GLP study and:

• National legislation

• Current international guidelines

• Study Plan

• Company SOPs

Certifications and accreditations

• Certification: Assessment by a third part if a product or a system fulfils certain specifications.

• Accreditation: Recognition of competence by a third part

• A signal to clients about quality and competence

• International recognition

• Voluntary in most cases

• Required by authorities some cases (i.e. food products)

ISO certification and accreditation

• ISO: non-governmental organisation

• ISO 9001 (certification)

- first published in 1987

- generic quality management system

- applies to various products and systems [11].

CONCLUSION & DISCUSSION

As seen above that the GLP are the important part of manufacturing industries. Especially in case of pharmaceutical company they are backbone of production of pharmaceutical products. Remember that

- Is used internationally to describe a set of principles and procedures, which, when followed by manufacturers help in ensuring that the products manufactured will have the required quality.
- GLP cannot be tested into a batch of product.
- It must be built into each batch of product during all stages of the manufacturing process.

The product are manufactured by following above parameters (GLP) in a manufacturing industries are of good quality, high therapeutic index(in case of pharmaceuticals) and industries is having high production rate. So these must be implemented in manufacturing firm especially in case of pharmaceuticals because these are given to human being. Life is a precious so there is a need of standard product which can be manufactured by applying GLP.

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