COMMISSION DIRECTIVE 1999/11/EC

of 8 March 1999

adapting to technical progress the principles of good laboratory practice as specified in Council Directive 87/18/EEC on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances

(Text with EEA relevance)

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community,

Having regard to Council Directive 87/18/EEC of 18 December 1986 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances [1], and in particular Article 4 thereof,

Whereas the principles of good laboratory practice (GLP) referred to in Directive 87/18/EEC have been modified by OECD Council Decision [C(97)186(Final)];

Whereas it is necessary to adapt the reference to the principles of GLP as specified in Directive 87/18/EEC so as to take account of these modifications, and, by publishing the full text of the revised principles of GLP, to facilitate the uniform interpretation and application thereof;

Whereas the measures provided for in this Directive are in accordance with the opinion of the Committee for the adaptation to technical progress of the Directives concerning the elimination of technical barriers to trade in dangerous substances and preparations,

HAS ADOPTED THIS DIRECTIVE:

Article 1

Article 1(1) of Directive 87/18/EEC is replaced by the following:

'1. Member States shall take all measures necessary to ensure that laboratories carrying out tests on chemical products, in accordance with Directive 67/548/EEC, comply with the principles of good laboratory practice as laid down in the Annex to this Directive.'

Article 2

The Annex hereto is added as Annex to Directive 87/18/EEC.

Article 3

1. Member States shall adopt the laws, regulations and administrative provisions necessary in order to comply with this Directive not later than 30 September 1999 and shall forthwith inform the Commission thereof.

2. When Member States adopt these provisions, these shall contain a reference to this Directive or shall be accompanied by such reference at the time of their official publication. The procedure for such a reference shall be adopted by Member States.

Article 4

This Directive is addressed to the Member States.

Done at Brussels, 8 March 1999.

For the Commission

Martin BANGEMANN

Member of the Commission

[1] OJ L 15, 17. 1. 1987, p. 29.

ANNEX

THE OECD PRINCIPLES OF GOOD LABORATORY PRACTICE (GLP)

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Section I

INTRODUCTION

Preface

Government and industry are concerned about the quality of non-clinical health and environmental safety studies upon which hazard assessments are based. As a consequence, OECD Member countries have established criteria for the performance of these studies.

To avoid different schemes of implementation that could impede international trade in chemicals, OECD Member countries have pursued international harmonisation of test methods and good laboratory practice. In 1979 and 1980 an international group of experts, established under the special programme on the control of chemicals, developed the 'OECD principles of good laboratory practice' (GLP), utilising common managerial and scientific practices and experience from various national and international sources. These principles of GLP were adopted by the OECD Council in 1981, as an Annex to the Council Decision on the mutual acceptance of data in the assessment of chemicals. [C(81)30(Final)].

In 1995 and 1996, a new group of experts was formed to revise and update the principles. The current document is the result of the consensus reached by that group. It cancels and replaces the original principles adopted in 1981.

The purpose of these principles of good laboratory practice is to promote the development of quality test data. Comparable quality of test data forms the basis for the mutual acceptance of data among countries. If individual countries can confidently rely on test data developed in other countries, duplicative testing can be avoided, thereby saving time and resources. The application of these principles should help to avoid the creation of technical barriers to trade, and further improve the protection of human health and the environment.

1. Scope

These principles of good laboratory practice should be applied to the non-clinical safety testing of test items contained in pharmaceutical products, pesticide products, cosmetic products, veterinary drugs as well as food additives, feed additives, and industrial chemicals. 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 testing these test items is to obtain data on their properties and/or their safety with respect to human health and/or the environment.

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.

Unless specifically exempted by national legislation, these principles of good laboratory practice apply to all non-clinical health and environmental safety studies required by regulation for the purpose of registering or licensing pharmaceuticals, pesticides, food and feed additives, cosmetic products, veterinary drug products and similar products, and for the regulation of industrial chemicals.

2. Definition of terms

2.1. *Good laboratory practice*

Good laboratory practice (GPL) 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.

2.2. *Terms concerning the organisation of a test facility*

1. *Test facility* means the persons, premises and operational unit(s) that are necessary for conducting the non-clinical health and environmental safety study. For multisite studies, those which 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.

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

3. *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.

4. *Test site management* (if appointed) means the person(s) responsible for ensuring that the phase(s) of the study, for which he is responsible, are conducted according to these principles of good laboratory practice.

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

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

7. *Principal investigator* means an individual who, for a multisite 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.

8. *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.

9. *Standard operating procedures (SOPs)* means documented procedures which describe how to perform tests or activities normally not specified in detail in study plans or test guidelines.

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

2.3. *Terms concerning the non-clinical health and environmental safety study*

1. *Non-clinical health 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.

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

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

4. *Study plan amendment* means an intended change to the study plan after the study initiation date.

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

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

7. *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 as stated in section 10 below.

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

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

10. *Experimental completion date* means the last date on which data are collected from the study.

11. *Study initiation date* means the date the study director signs the study plan.

12. *Study completion date* means the date the study director signs the final report.

2.4. *Terms concerning the test item*

1. *Test item* means an article that is the subject of a study.

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

3. *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.

4. *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.

Section II

GOOD LABORATORY PRACTICE PRINCIPLES

1. **Test facility organisation and personnel**

1.1. *Test facility management's responsibilities*

1. Each test facility management should ensure that these principles of good laboratory practice are complied with, in its test facility.

2. At a minimum it should:

(a) ensure that a statement exists which identifies the individual(s) within a test facility who fulfil the responsibilities of management as defined by these principles of good laboratory practice;

(b) ensure that a sufficient number of qualified personnel, appropriate facilities, equipment, and materials are available for the timely and proper conduct of the study;

(c) ensure the maintenance of a record of the qualifications, training, experience and job description for each professional and technical individual;

(d) ensure that personnel clearly understand the functions they are to perform and, where necessary, provide training for these functions;

(e) ensure that appropriate and technically valid standard operating procedures are established and followed, and approve all original and revised standard operating procedures;

(f) ensure that there is a quality assurance programme with designated personnel and assure that the quality assurance responsibility is being performed in accordance with these principles of good laboratory practice;

(g) 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;

(h) ensure, in the event of a multisite 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;

(i) ensure documented approval of the study plan by the study director;

(j) ensure that the study director has made the approval study plan available to the quality assurance personnel;

(k) ensure the maintenance of a historical file of all standard operating procedures;

(l) ensure that an individual is identified as responsible for the management of the archive(s);