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(Acts whose publication is not obligatory)

COMMISSION

COMMISSION DIRECTIVE

of 18 December 1989

adapting to technical progress the Annex to Council Directive 88/320/EEC on the inspection and verification of good laboratory practice (GLP)

(90/18/EEC)

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community,

Having regard to Council Directive 88/320/EEC of 9 June 1988 on the inspection and verification of good laboratory practice (GLP) (1), and in particular Article 7 (2) thereof,

Whereas it is necessary to adapt the Annex to Directive 88/320/EEC in order to facilitate uniform interpretation throughout the Community by replacing the reference to the OECD guidance documents by the full text of the documents concerned,

HAS DECIDED AS FOLLOWS:

Article 1

The Annex to Directive 88/320/EEC is hereby replaced by the Annex hereto.

Article 2

1. The Member States shall adopt the laws, regulations and administrative provisions needed in order to comply with this Directive not later than 1 July 1990 and in conjunction with Council Directive 88/320/EEC. They shall fort with inform the Commission thereof.

2. Member States shall ensure that the text of the provisions of internal law which they adopt in the field of the Directive is communicated to the Commission.

Article 3

This Directive is addressed to the Member States.

Done at Brussels, 18 December 1989.

For the Commission
Martin BANGEMANN
Vice-President

(1) OJ No L 145, 11. 6. 1988, p. 35.

ANNEX

'ANNEX

The provisions for the inspection and verification of GLP which are contained in Annexes A and B to this Directive are those contained in Annexes 1 (guides for compliance monitoring procedures for good laboratory practice) and 2 (guidance for the conduct of laboratory inspections and study audits) respectively to the draft Council recommendation on compliance with principles of good laboratory practice (OECD ENV/CHEM/CM/88/15 (first revision).'

ANNEX A

GUIDES FOR COMPLIANCE MONITORING PROCEDURES FOR GOOD LABORATORY PRACTICE (GLP)

To facilitate the mutual acceptance of test data generated for submission to regulatory authorities of OECD member countries, harmonization of the procedures adopted to monitor good laboratory practice compliance, as well as comparability of their quality and rigour, are essential.

The aim of this Annex is to provide detailed practical guidance to OECD member countries on the structure, mechanisms and procedures they should adopt when establishing national good laboratory practice compliance monitoring programmes so that these programmes may be internationally acceptable.

It is recognized that member countries will adopt GLP principles and establish compliance monitoring procedures according to national legal and administrative practices, and according to priorities they give to, e.g. the scope of initial and subsequent coverage concerning categories of chemicals and types of testing.

Since member countries may establish more than one good laboratory practice monitoring authority due to their legal framework for chemicals control, more than one good laboratory practice compliance programme may be established. The guidance set forth in the following paragraphs concern each of these authorities and compliance programmes, as appropriate.

DEFINITIONS OF TERMS

The definitions of terms in the 'OECD principles of good laboratory practice', adopted in Article 1 of Council Directive 87/18/EEC (1) are applicable to this document. In addition, the following definitions apply:

GLP principles: Principles of good laboratory practice, that are consistent with the OECD principles of good laboratory practice as adopted in Article 1 of Directive 87/18/EEC.

GLP compliance monitoring: The periodic inspection of laboratories 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 laboratories within its territories, by means of inspections and study audits.

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

Laboratory inspection: An on-site examination of the test facility's procedures and practices to assess the degree of compliance with GLP principles. During inspections, the management structures and operational procedures of the laboratory are examined, key technical personnel are interviewed, and the quality and integrity of data generated by the 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, to 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 establish whether practices were employed in the development of data that would impair their validity.

Inspector: A person who performs the laboratory inspections on behalf of the (national) GLP monitoring authority.

GLP compliance status: The level of adherence of a laboratory to the GLP principles as assessed by the (National) GLP monitoring authority.

Regulatory authority: A national body with legal responsibility for aspects of the control of chemicals.

(1) OJ No L 15, 17. 1. 1987, p. 29.

COMPONENTS OF GOOD LABORATORY PRACTICE COMPLIANCE MONITORING PROCEDURES

Administration

A (national) GLP compliance programme should be the responsibility of a properly constituted, legally identifiable management body adequately staffed and working within a defined administrative framework.

Member countries should :

— ensure that the (national) GLP monitoring authority is directly responsible for an adequate 'team' of inspectors having the necessary technical/scientific expertise or is ultimately responsible for such a 'team',

— publish documents relating to the adoption of GLP principles within their territories,

— publish documents providing details of the (national) GLP compliance programme, including information on the legal or administrative framework within which the programme operates and references to published acts, normative documents (e.g. regulations, codes of practice), inspection manuals, guidance notes, etc.,

— maintain records of laboratories inspected (and their GLP compliance status) and of studies audited.

To foster international understanding and liaison, member countries should inform the OECD and other member countries (e.g. through the OECD complementary information exchange procedure) of the nature and availability of the documentation on GLP which has been produced, together with the addresses and telephone numbers of the (national) GLP monitoring authorities.

Confidentiality

(National) GLP monitoring authorities will have access to commercially valuable information and, on occasion, may even need to remove commercially sensitive documents from a laboratory or refer to them in detail in their reports.

Member countries should :

— make provision for the maintenance of confidentiality, not only by Inspectors but also by any other persons who gain access to confidential information as a result of GLP compliance monitoring activities,

— ensure that, unless all commercially sensitive and confidential information has been excised, reports of laboratory inspections and study audits are made available only to regulatory authorities and, where appropriate, to the laboratories inspected or concerned with study audits and/or to study sponsors.

The names of laboratories subject to laboratory inspections within a (national) GLP compliance programme, their levels of compliance with the national GLP principles and the date(s) the inspections were conducted should be made available to national) GLP monitoring authorities in other member countries upon request.

Personnel and training

(National) GLP monitoring authorities should :

— *ensure that an adequate number of Inspectors is available*

The number of inspectors required will depend upon :

(a) the number of laboratories involved in the (national) GLP compliance programme ;

(b) the frequency with which the GLP compliance status of the laboratories is to be assessed ;

(c) the number and complexity of the studies undertaken by those laboratories ;

(d) the number of special inspections or audits requested by regulatory authorities,

— *ensure that inspectors are adequately qualified and trained*

Inspectors should have qualifications and practical experience in the range of scientific disciplines relevant to the testing of chemicals. (National) GLP monitoring authorities should :

(a) ensure that arrangements are made for the appropriate training of Inspectors, having regard to their individual qualifications and experience,

(b) encourage consultations, including joint training activities where necessary, with the staff of (national) GLP monitoring authorities in other member countries in order to promote international harmonization in the interpretation and application of GLP principles, and in the monitoring of compliance with such principles,

— *ensure that inspectorate personnel have no financial or other interests in the laboratories inspected, the studies audited or the firms sponsoring such studies,*

— *provide inspectors with a suitable means of identification (e.g. an identity card).*

Inspectors may be :

— on the permanent staff of the (national) GLP monitoring authority,

— on the permanent staff of a body separate from the (national) GLP monitoring authority, or

— employed on contract, or by another way, by the (national) GLP monitoring authority to perform laboratory inspections or study audits.

In the latter two cases, the (national) GLP monitoring authority should have ultimate responsibility for determining the GLP compliance status of laboratories and the quality/acceptability of a study audit, and for taking any action based on the results of laboratory inspections or study audits which may be necessary.

(National) GLP compliance programmes

GLP compliance monitoring is intended to ascertain whether laboratories have implemented GLP principles for the conduct of studies and are capable of assuring that the resulting data are of adequate quality. As indicated above, member countries should publish the details of their (national) GLP compliance programmes. Such information should *inter alia :*

— *define the scope and extent of the programme*

A (national) GLP compliance programme may cover only a limited range of chemicals, e.g. industrial chemicals, pesticides, pharmaceuticals, etc., or may include all chemicals. The scope of the monitoring for compliance should be defined, both with respect to the categories of chemicals and to the types of tests subject to it, e.g. physical, chemical, toxicological and/or ecotoxicological,

— *provide an indication as to the mechanism whereby laboratories enter the programme*

The application of GLP principles to health and environmental safety data generated for regulatory purposes may be mandatory. A mechanism should be available whereby laboratories may have their compliance with GLP principles monitored by the appropriate (national) GLP monitoring authority,

— *provide information on categories of laboratory inspections/study audits*

A (national) GLP compliance programme should include :

(a) routine laboratory inspections — i.e. the regular monitoring of laboratories, in principle on a two-year cycle. These inspections include both a general inspection of the laboratory and a (limited) study audit of an on-going or completed study ;

(b) special laboratory inspections/study audits at the request of a regulatory authority — e.g. prompted by a query arising from the submission of data to a regulatory authority,

— *define the powers of inspectors for entry into laboratories and their access to data held by laboratories*

While inspectors will not normally wish to enter laboratories against the will of the laboratory management, circumstances may arise where entry and access to data are essential to protect public health or the environment. The powers available to the (national) GLP monitoring authority in such cases should be defined,

— *describe the laboratory inspection and study audit procedures for verification of GLP compliance*

The documentation should indicate the procedures which will be used to examine both the organizational processes and the conditions under which laboratory studies are planned, performed, monitored and recorded. Guidance for such procedures is available in Annex B to this Directive,

— *describe actions that may be taken as follow-up to laboratory inspections and study audits*

Follow-up to laboratory inspections and study audits

When a laboratory inspection or study audit has been completed, the inspector should prepare a written report of the findings.

Member countries should take action where deviations from GLP principles are found during or after a laboratory inspection or study audit. The appropriate actions should be described in documents from the (national) GLP monitoring authority.

If a laboratory inspection or study audit reveals only minor deviations from GLP principles, the laboratory should be required to correct such minor deviations. The inspector may need, at an appropriate time, to return to the facility to verify that corrections have been introduced.