Good Laboratory Practice (GLP)

Working document

(does not necessarily represent the views of the Commission services)
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Guideline developed within the Standing Committee on Plant Health with regard to the acceptability of data, whether or not performed in accordance with the principles of Good Laboratory Practice (GLP).

INTRODUCTION

Document 7109/VI/94 rev.6 provides detailed guidance for the applicability of the principles of Good Laboratory Practice (GLP) to individual studies of Annexes II and III, part A, of Directive 91/414/EEC concerning the placing of plant protection products on the market.

However further guidance was considered necessary in order to clarify the acceptability of old studies which are not performed in accordance with the principles of GLP. This document therefore intends to give guidance to Member States and applicants concerning the acceptability of studies and data submitted in accordance with the requirements of Annexes II and III of Directive 91/414/EEC in relation to the application of the principles of GLP.

I. LEGAL PROVISIONS

1. 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]provides in article 1 (1) that 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 GLP.

Member States shall apply this Directive not later than 30 June 1988.

The principles of GLP are explained in detail in the relevant OECD documents; summarised GLP is concerned with the organisational process and the conditions under which studies are planned, performed, monitored, recorded, retained and reported.

2. Directive 87/18/EEC provides in article 1 (2) that paragraph 1 shall apply also where other Community provisions provide for the application of GLP in respect of test on chemical products to evaluate their safety for man and/or the environment.

3. Article 13 (1) of Directive 91/414/EEC provides that applicants for the authorization of a plant protection product have to submit a dossier satisfying the requsirements of Annexes II and III.

Annexes II and III detail the data to be submitted. This covers:

- reference to test guidelines which intends to ensure that the data submitted are scientifically acceptable (addressing the right questions in an appropriate way) and
- the circumstances in which studies have or have not to be submitted
- the application of GLP (introduction to the Annexes provides in point 2(1) : "Tests and analyses must be conducted in accordance with the principles laid down in Directive 87/18/EEC where testing is done to obtain data on the properties and/or safety with respect to human health or the environment").

Member States shall apply this Directive not later than 25 July 1993.

4. The Commission adopted temporary derogations for the application of the principles of GLP for residue trials started at the latest on 31.12.1997 and for honeybee and beneficial arthropod testing started at the latest on 31.12.1999 (Directives 93/71/EEC and 95/35/EC both amending Directive 91/414/EEC).

5. Since the Directive provides in general terms for the application of GLP to studies on the properties and/or safety with respect to human health or the environment, the Standing Committee on Plant Health agreed that guidance document 7109/VI/94 rev. 6 contains the correct interpretation of which studies referred to in Annexes II and III are related to human health or the environment and therefore should be subject to the GLP requirements.

6. Article 13(6) provides that Member States may continue to apply previous national rules concerning data requirements for existing active substance as long as such substances are not included in Annex I.

This provision provides flexibility for Member States concerning:

- the circumstances under which they require or do not require the submission of particular data;
- the test guidelines to be followed for generating data;
- the application of the principles of GLP.

II. ACCEPTANCE OF STUDIES AND DATA FOR AN APPLICATION FOR INCLUSION OF AN ACTIVE SUBSTANCE IN ANNEX I OR FOR AN AUTHORISATION OF A PLANT PROTECTION PRODUCT

7. It should be borne in mind that in the introduction to the Annexes II and III, Directive 91/414/EEC provides some flexibility for the acceptance of studies not performed according to the provisions of test guidelines referred to in the Annexes provided an acceptable justification is provided. However, the introduction does not provide a similar flexibility concerning the application of GLP.

It is also important to note that Directive 91/414/EEC emphasises that needless repetition of tests on animals should be avoided.

The situations as described in points 8 and 9 may arise:

8. Studies initiated after 25 July 1993

All relevant studies should be performed in accordance with GLP (document 7109/VI/94 rev.6 provides detailed guidance in this respect) because mutual acceptance of GLP-studies ensures that studies should not be repeated unnecessarily.

This also applies to studies performed in countries outside the EU intended to be used for the authorization of a plant protection product within the EU.

For third countries where the E.U. or a Member State has an agreement on mutual recognition of GLP, GLP compliance statements have to be accepted if the test facility is certified by the national GLP authority.

GLP compliance statement: is terminology used in dossiers (statement or compliance statement); in Directive transposing GLP also the word statement is used.

For third countries where no such agreement exists GLP statements have to be accepted only in those cases where inspection on compliance with GLP has been performed in the third country by an official GLP monitoring authority of one of the Member States.

However the following problem arises:

For active substances already on the market Member States can, according to article 13 (6), continue to apply national data requirements as long as the active substance is not included in Annex I. Until inclusion of the active substance in Annex I, Member States might still accept non-GLP data.

However, in order to avoid that non-GLP data generated after 25 July 1993 would be accepted in a limited number of Member States or be rejected in the review programme for inclusion of the active substance in Annex I, applicants should be encouraged to generate all relevant data after 25 July 1993 in accordance with GLP.

9. Studies initiated before 25 July 1993.

Before Directive 91/414/EEC entered into force there was no requirement for GLP at EU level for the authorization of plant protection products and therefore studies can not be rejected if GLP was not applied provided that they are valid scientifically.

III. EXTENSION OF AN AUTHORISATION FOR MINOR USES

10. Article 9 (1) of Directive 91/414/EEC provides for an extension of the field of application of an already authorized plant protection product to the extent that:

- documentation and information to support this extension has been submitted
- Member States have established that the use of the product has no harmful effect on human health, directly or indirectly
- the intended use is minor in nature.

11. There is no reference to Annex III in article 9 (1) and hence neither to GLP. Although there is no specific provision for mutual recognition of such extensions of use, Member States may take advantage of the possibility to grant extensions of use based on authorizations granted in another Member State.

Nevertheless the case of residue data (in particular residue trials and livestock feeding studies) merits a specific approach.

12. For minor uses granted by Member States in the framework of Article 9, Member States have to be satisfied that the use has no harmful effect on human health; they can rely on several types of information concerning residues (residue trials might be carried out in Member States or in third countries):

1. (a) residue trial data carried out according to GLP and satisfying Annex III requirements.

2. (b) extrapolation from data on other crops as far as sufficient reliable data are available for these crops.

3. (c) residue trial data not carried out according to GLP but otherwise satisfying Annex III requirements.

4. (d) residue trial data not carried out according to GLP and not satisfying Annex III requirements.

13. For certain minor crops there is Community trade and hence it may be necessary to establish Community MRLs in the framework of the residue directives (Directives 86/362/EEC, 86/363/EEC and 90/642/EEC). At that stage it could become very difficult to establish a Community MRL if the available data accepted by a Member State would not be considered acceptable at Community level.

Depending on the type of data as mentioned under point 12 the following situations arise:

1. (a) Residue trial data carried out according to GLP and satisfying Annex III requirements would facilitate the establishment of Community MRLs. However, the availability of such data will probably be more the exception than the rule.

2. (b) extrapolation from data on other crops as far as sufficient reliable data are available and according to extrapolation possibilities as provided in document 7034/VI/95 last revision or further guidance documents to be developed. Since this document reflects an agreement between all Member States there would be no problems with mutual recognition of data and establishment of a Community MRL.

3. (c) residue trial data satisfying the Annex III requirements (except GLP): where such trials are carried out by official or officially recognised testing facilities meeting the requirements of points 2.2 and 2.3 of the introduction to Annex III, there should be no problem with mutual recognition of data and establishment of a Community MRL

4. (d) Data which were not performed according to the test guidelines of Annex III and for which neither a quality control has taken place should not be accepted by Member States. In any case establishment of a Community MRL on the basis of such data would not be possible.