Guideline to the Implementation of Act No. 356/2003 Coll.

and Decree No. 219/2004 Coll. on the procedures required for awarding the Good Laboratory Practice Certificate and on the integration of the test facilities into the GLP National Programme

The purpose of this guideline is setting up the procedures for awarding the GLP Statement according to the OECD Principles (hereinafter referred to as Statement) as well as the procedures for GLP inspections. The guideline constitutes necessary activities both of the applicant or the Statement holder, and of the GLP National Inspection Authority. It is based in the Act No. 356/2003 Coll., in the wording of later regulations, in the Decree No. 219/2004 Coll., as well as in the GLP National Programme.

1. Explanation of terms

1.1 **Full-routine inspection** of the test facility shall be conducted

a) when the test facility has applied for integration into the National Programme and issuing of the GLP Statement (an essential document for this is a submitted application for verification of compliance with the GLP Principles, hereinafter referred to as an Application) or in the event if the test facility integrated into the National Programme is changing or extending your its activities,

b) during the follow-up inspection in the due maximum interval of three years (Application not necessary, test facility is given notice before the inspection),

c) upon request made by the Regulatory Authority (Ministry of Environment) or by a Regulatory Authority of OECD or EU member state (the test facility is usually given notice before the inspection).

1.2 **Target inspection** serves as a control inspection of removal of deviations from GLP Principles found during a full-routine inspection when the conclusion is „pending“. It may occur on request made by the Regulatory Authority (Ministry of Environment) or by a Regulatory Authority of OECD or EU member state. In the event of more of minor deviations inspector may also prescribe the Target inspection.

1.3 **Study audit** is always a part of the full-routine inspection, however, it may be conducted independently. It may be requested by Regulatory Authority (Ministry of Environment), by Regulatory Authority of a member state of OECD or EU, or it may be conducted upon request submitted by a sponsor. The purpose of the study audit is reconstructing the study by comparing the final report with the study plan, by verification of standard

operating procedures relevant at the time of conducting the study and of other recorded data concerning a running or concluded study.

1.4 Decisions made by the inspectors concerning the compliance with the GLP Principles:

a) **in compliance** (none or minor deviations),

b) **pending** (serious deviations, which have no influence on the integrity of the study; target inspection is necessary),

c) not in compliance (serious deviations, which affect integrity of the study, or, if the test facility does not permit the inspectors entering and conducting the inspection – Article 4, or, if it does not provide the filled in questionnaire within a determined term – Par. 2.4 and 2.4.1).

2. Application for the GLP Certificate and inclusion into the National Programme

2.1 The test facility submits application when:

2.1.1 applying for inclusion into the GLP National Programme (follow the first inspection)

2.1.2 if changing or extending scope of activities, changing site of action and/or of own decision .

2.2 A filled application (a request example is shown in Annex No. 2 of the Decree No. 219/2004 Coll.) including annexes mentioned in the Decree (§ 3, Art. 2 and 3) are to be sent by the management of the test facility to the Ministry of Environment and a copy to the GLP National Inspection Authority.

2.3 GLP National Inspection Authority shall confirm to the test facility the reception of the application within 15 days and shall forward a questionnaire to the applicant.

2.4 Test facility shall deliver a filled questionnaire to the GLP National Inspection Authority within one month.

2.4.1 In well-founded cases, the GLP National Inspection Authority may prolong the term upon request made by the test facility, however, by a maximum of one additional month.

2.5 In general, GLP National Inspection Authority will conduct an inspection within 3 months after taking over a filled in questionnaire.

3. Announcement of inspection

3.1 GLP National Inspection Authority shall announce the term of the inspection to the manager of the test facility in writing together with the names of the inspectors, inspection date, a preliminary programme of the inspection, and it shall set the requirement that all personnel who may be concerned should be present during the inspection.

3.1.1 If an external specialist is a member of an inspection team, the GLP National Inspection Authority shall make a request to the management of the test facility for a written statement as to his participation.

3.2 The inspection may also be conducted without any previous notice (see the National GLP Programme).

4. Authorisation of inspectors to entering the test facility as well as to perform associated activities is defined by § 9 Art. 3 Act No. 356/2003 Coll.

4.1 Inspectors are authorised pending the inspections pursuant to Act No. 552/1991 Coll., i.a.:

a) to enter objects, facilities and plants, plots and other areas of the legal entities inspected, bearing on the subject of inspection; immunity of residences being guaranteed,
b) to ask inspected persons for presenting authentic documents and other papers, electronic records and their printouts, and programme source codes, product samples, or another commodities in due terms,
c) to get acquainted with classified matters provided they are certified for the particular degree of security according to special Act,
d) to require inspected persons to provide with true and complete information about investigated and related facts,
e) to safeguard documents in reasonable cases; their receipt shall be confirmed in writing and copies of the respective documents retained to the inspected person,
f) require the inspected persons to deliver a written report on rectification of deficiencies in a due time limit,
g) to impose disciplinary fines in cases set out by Act No. 552/1991 Coll.,
h) to use telecommunication devices of inspected persons provided the necessity of their using to secure the inspection.

4.2 If the test facility would not permit demonstrably the inspectors to enter and conduct inspection, the decision would be “not in compliance”.

5. Inspection procedure

5.1 The purpose of a pre-inspection is to familiarize the inspectors with the organisation scheme, layout of the test facility, construction and extent of activities of the test facility.

5.1.1 In case the data submitted in the questionnaire or any additional information requested by the inspector are not sufficiently conclusive, the inspector may visit the test facility prior to the inspection itself.

5.2 The proper inspection is opened by a starting conference, during which the inspectors present their authorisation, make their acquaintance with the organisation of the test facility and draw up a time schedule of the inspection. Starting conference involves above all:

a) identification of inspectors,

b) reason and category of the test facility inspection or study audit,

c) more detailed information on test facility (spaces, personnel, activities and studies),

d) agreement on a rough time schedule of the inspection ,

e) assignment of persons, who will accompany the inspectors.

5.3 During the conduct of the test facility inspection the inspectors examine all points defined by the “Principles of Good Laboratory Practice OECD” (Annex No. 1 of the Decree No. 219/2004 Coll.), especially:

a) organisation and staff,

b) quality assurance programme,

c) biological test systems (care, housing, containment),

d) instrumentation, materials, computer systems, samples,

e) test and reference items,

f) standard operating procedures,

g) performance of the study,

h) final report,

i) storage and retention of records and other items,

j) at least one study in form of study audit.

5.4 Closing conference

5.5 In the course of closing conference, management of the test facility is informed of the details of the inspection and of the findings made by the inspection team.

5.6 The management of the test facility may raise objections during the discussion regarding the decisions of the inspection team.

5.7 The inspection team leader presents a draft of the final report, especially of the detected deviations from the principles and their significance. The management of the test facility shall define the way and term of corrections. The term may be determined by an inspector as well.

5.8 The deadline for the removal of minor deviations is one month. A target inspection is not necessary.

5.9 Serious deviations, which do not affect the integrity of the study, should be removed within six months after termination of the inspection. A target inspection is necessary in case of the decision “pending”.

6. Final report on the inspection

6.1 The final report on the inspection is to be compiled by the inspection team leader in three weeks at the latest after the termination of the inspection and is to be forwarded to the management of the test facility for signature and comments.

6.2 The manager of the test facility shall elaborate and forward to the GLP National Inspection Authority his statement regarding the final report within 14 days after the reception thereof along with a note regarding the way and the terms of corrective actions. A written statement of test facility manager is an integral part of the final report.

6.3 The final report includes relevant data mentioned under the points 6.3.1 to 6.3.15.

6.3.1 Names of inspectors including their authorisation

6.3.2 Name, place, address and identification number of the test facility, in case of study audit the name of study

6.3.3 Scope of activities of the test facility

6.3.4 Names of key personnel of the test facility, who were present at the inspection

6.3.5 Declaration confirming that the inspectors had announced the start of the inspection and presented their authorisations

6.3.6 Place and duration (time data) of the inspection

6.3.7 Reason of the inspection

6.3.8 Subject of the inspection

6.3.9 Legal documents, on the basis of which the inspection has been conducted

6.3.10 Conclusion of the inspection (including stated serious, systematic and repeated deviations)

6.3.11 Deadlines to document corrective actions

6.3.12 Decision of inspectors on compliance with the GLP Principles (see Par. 1.4, Points a to c)

6.3.13 Findings made the inspectors concerning the points of Par. 4.3

6.3.14 Information on possibilities and procedures of appeal

6.3.15 Date, signature of the inspection team leader as well as of authorised representatives of the test facility management including their comments regarding the final report.

6.4 Counterpart of the final report with all annexes is to be sent by the GLP National Inspection Authority to the Ministry of Environment and to the test facility.

7. The appeal procedures

7.1 Appeal against the decision of the inspection team

7.1.1 The subject, when being inspected, may raise objections against the proceeding of the inspection to the team leader.

7.1.2 The subject, when being inspected, may raise objections in written against the final report together with a supporting substantiation within 15 days after delivery.

7.1.3 In case of refusal, the test facility has the right to appeal to the head of ASLAB.

7.1.4 As to the objections, the head of the ASLAB shall decide within 30 days. The decision taken by the director of the GLP National Inspection Authority is ultimate.

7.2 In case of disagreement with the decision of the head of ASLAB, one can call for rectification in form of administrative proceeding at the Ministry of Environment or by legal proceedings.

8. GLP Statement

8.1 The Statement confirms that the test facility has been in compliance with the GLP Principles at the time of the inspection. At the same time the test facility is included into the GLP National Programme.

8.2 Introducing the test facility into the GLP National Programme means that the inspected test facility has been found in compliance with the Decree of the Ministry of Environment No. 219/2004 Coll. and, thus, with the "OECD Principles of Good Laboratory Practice" as well.

9. Decision on GLP non compliance

9.1 If during the conduct of the inspection the test facility integrated in the GLP National Programme (i.e. the facility to which a Certificate has already been issued) proofs will be found demonstrating that the facility is not in compliance with the GLP Principles, the inspector pronounces the decision "not in compliance" (serious deficiencies affecting the integrity of the studies have been found).

9.2 In the case corresponding to Par. 9.1, the final report presented by the GLP National Inspection Authority shall include the decision "not in compliance" together with recommendation for exclusion from the National GLP Programme and deprivation of the Statement. On the basis of the GLP National Inspection Authority recommendation, the Ministry of Environment shall withdraw the Statement according to § 9 (6) Act No. 356/2003 Coll. The Ministry shall promulgate this fact similarly as the preceeding issue of the Statement in the Bulletin of the Ministry of Environment. Further, GLP National Inspection Authority informs ~~it notifies~~ the appropriate OECD Authority on the exclusion from the National Programme.
Use of an invalid certificate is considered to be a deception of the thirds.

10. Ways of informing and publishing

10.1 Information on all test facilities integrated in the GLP National Programme (i.e. those, to which a Statement has been issued) are published in the Bulletin of the Ministry of Environment and include: name and address of the test facility, extent of activities, dates of the first and the last inspection and the degree of compliance with the principles.

10.2 Information on the test facilities newly integrated into the GLP National Programme are published to the extent mentioned in Par. 10.1 in the Bulletin of the Ministry of Environment.

10.3 Information on the test facilities which are no more in compliance with the GLP Principles are published without any delay in the Bulletin of the Ministry of Environment to the extent given in Par. 10.1.

10.4 According to the principles of membership of the Czech Republic in OECD, the GLP National Inspection Authority informs annually the monitoring bodies of the OECD member countries to an extent according to Par. 10.1

Information included in Par. 10.1 – 10.3 and 11.1 are also available at the Internet address: http://aslab.vuv.cz/slp.php.

11. Removal from and resignation on the GLP National Programme

11.1 If the test facility is not wishing any more to be further integrated into the GLP National Programme, it shall notify in written both the Ministry of Environment and the GLP National Inspection Authority about its resignation from the GLP National Programme. The resignation is published in the Bulletin of the Ministry of Environment and announced to the monitoring bodies of the OECD member countries.

11.2 The test facility which has resigned from the GLP National Programme (Par. 11.1) is regarded as a facility not in compliance with the GLP Principles.

11.3 The test facility having received the decision “not in compliance” from the inspection team is to be removed from the GLP National Programme. After publishing the information (Art. 10) on exclusion from the GLP National Programme, such a facility is removed from the list.

11.4 The test facility, which resigned to or has been removed from the GLP National Programme may request again for being integrated according to the procedure mentioned in Art. 2.