LATAK-D.040 Assessment of the quality of work in good laboratory practices laboratories

1. Introduction

The Cabinet of Ministers of the Republic of Latvia Regulation No. 398 of 3 September 2002 “Requirements for the quality of laboratory work and laboratory inspection” (hereinafter the Regulations) includes legal provisions arising from Directive 2004/9/EC of the European Parliament and of the Council of 11 February 2004 on the verification and approval of good laboratory practice (hereinafter - GLP) and Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of the application of these principles in relation to the testing of chemical substances. The Regulations apply to studies, inspections (except clinical) and tests (hereinafter referred to as studies) carried out to obtain information on the properties of biocides, chemical substances and mixtures, as well as on the properties of preparations of biological origin or living organisms intended to be used in the composition of medicinal products, plant protection products, cosmetic products, veterinary medicinal products, food additives and animal feed additives (hereinafter referred to as the substance or organism to be tested), and their hazards to human health and the environment, and are intended for submission to the Ministry of Welfare, the Ministry of Health, the Ministry of Climate and Energy and the Ministry of Agriculture, as well as to institutions subordinate to these ministries. In accordance with the Regulations, the state agency “Latvian National Accreditation Bureau” (hereinafter referred to as the Agency) must periodically monitor laboratories in accordance with the requirements of the Regulations.

2. Criteria for good laboratory practice

The GLP laboratory work quality assessment criteria are outlined in the Regulations. These require adherence to the OECD's principles of good laboratory practice when conducting research (Annex 4).

3. Confidentiality

As stipulated in Regulation Point 55, agency employees are entitled to access restricted information, including trade secrets related to laboratory research, and may reference them in their reports. The Agency keeps restricted information, including trade secrets, confidential during quality control of lab work. Agency employees may enter laboratories and obtain necessary information with prior approval from laboratory management or the person responsible, as stated in Regulation Point 57 – Authorized employees are entitled to access laboratories and obtain essential data for the protection of human health or the environment. This right is granted upon invitation from the research manager or another representative of the laboratory management, without requiring prior approval from the laboratory management or the individual in charge. Inspection reports are accessible to the assessed institution, designated agency personnel, and relevant authorities.

4. Scope of the Regulations

The Regulations apply to studies, inspections (except clinical) and tests (hereinafter referred to as studies) carried out to obtain information on the properties of biocides, chemical

substances and chemical products, as well as on the properties of preparations of biological origin or living organisms intended to be used in the composition of medicinal products, plant protection products, cosmetic products, veterinary medicinal products, food additives and animal feed additives (hereinafter referred to as the substance or organism under test), and their hazard to human health and the environment, and are intended for submission to the Ministry of Welfare, the Ministry of Health, the Ministry of Climate and Energy and the Ministry of Agriculture, as well as to institutions subordinate to these ministries.

5. Personnel involved in the inspection

The inspection may be conducted by a single inspector from the Agency or in collaboration with another inspector or expert. Foreign specialists may be invited for the inspection if needed. In all cases, the task/role of the lead inspector shall be performed by an inspector from the Agency. The Agency oversees the training and competence of its inspectors. The Director of the Agency makes the formal decision regarding the compliance of the GLP laboratory with the requirements.

6. Inclusion of the laboratory in the Agency's GLP Compliance Program and GLP Register

Laboratories in Latvia subject to GLP requirements must comply with them. Prior to submitting an application, the laboratory must evaluate whether its operations fall under the Regulations' stipulations and provide documentation of at least one completed study. A laboratory must submit an application (F.003) and supporting documents (F.002.LLP) to the Agency to prove compliance with the criteria. The forms are available on the Agency's website https://www.latak.gov.lv/lv/visparejie-dokumenti-ieskait-pieteuka-formu and https://www.latak.gov.lv/lv/labas-laboratorijas-prakses-laboratorijam.

Once documents are submitted, the initial assessment can begin. Should it be required, an initial site visit may be conducted. The tentative schedule for this visit is outlined in Annex 2.

7. Laboratory inspection and research verification procedure

1. The Agency's GLP compliance program involves inspecting Latvian GLP laboratories, assessing their operations, and reviewing studies.
   a) inspections can be initial/routine (planned), additional or specially requested (for example, by Latvian competent authorities, GLP laboratory monitoring institutions of other countries);
   b) the laboratory is usually informed in advance of the upcoming visit. An approximate program of the planned assessment is provided in Annex 3. The content and duration of the specified programs may vary depending on the size of the institution being assessed, the number of locations and other factors;
   c) prior to the inspection, the inspector reviews all relevant existing information pertaining to the matter at hand, such as previous inspection reports, research studies, and other pertinent documents, see also the list of documents to be submitted);

d) the inspector shall briefly discuss with the laboratory's authorized representatives the purpose and course of the visit, request access to certain documents and other information necessary for a complete inspection and/or audit of the study. The laboratory management is responsible for providing the Agency inspector with all necessary original data and other materials on the studies to be performed, and shall, upon request, provide samples and copies of documents and other materials necessary for the inspection, including copies of documents to be attached to the assessment file and/or report.

2. A full inspection covers the following:
   a) **Organization and personnel.** Purpose: To determine whether the laboratory has sufficient qualified personnel, personnel resources and support services, taking into account the variety and number of studies performed; whether the organizational structure is appropriate and whether the management has established a work plan for training and medical supervision of personnel that is appropriate for the studies performed in the institution.
   b) **Quality assurance.** Purpose: To assess how laboratory management ensures that studies are conducted in accordance with GLP principles and whether studies are conducted in accordance with GLP principles.
   c) **Premises.** Purpose: To determine whether the premises, their area, design, location are suitable for conducting research in accordance with the principles of GLP.
   d) **Equipment, materials, reagents and samples.** Purpose: To assess whether the laboratory has the necessary equipment and facilities, they are suitably located and properly operated, their capacity is sufficient to perform the work; to check whether the equipment is maintained and operated in accordance with the tests to be performed, to check whether the materials and reagents used are appropriately labeled, used and stored and that they do not contaminate the system under test.
   e) **Test system.** Purpose: To determine whether appropriate procedures are in place for handling and controlling the various test systems (physicochemical test systems and biological test systems). To verify whether the test systems (animals, plants, tissues, chemical and physical systems) are appropriately located and controlled. In cases where the test systems include animals, whether the care and handling of the animals is appropriate to minimize the risk of uncontrolled influences that could affect the results of the study.
   f) **Care, housing, and containment of biological test systems** (if applicable). Purpose: To determine whether the laboratory, if involved in research involving animals or other biological test systems, has facilities and conditions for their care, housing, and containment that are adequate to prevent stress and other problems that may affect the test systems and, consequently, the quality of the data.
   g) **Test substances or organisms and reference substances or organisms.** Purpose: To verify that procedures are in place to ensure that the identity, potential potency, quantity and composition of test substances or organisms and reference substances or organisms are as specified, that test and reference materials are properly received and stored, that substances are introduced into the test systems in accordance with the study plan, and that the identity, quantity and composition of test and reference materials are assured and controlled.

h) **Standard Operating Procedures.** Purpose: To verify that the laboratory has documented, approved, and used all standard operating procedures (SOPs) and methods relevant to the research.
i) **Research plan.** Purpose: To verify that the research plan has been written, approved and reviewed in accordance with GLP principles.
j) **Conduct of studies.** Purpose: To verify that studies are conducted in accordance with GLP principles.
k) **Handling of records.** Purpose: To verify whether appropriate handling of records, safe storage of records and materials, and appropriate accounting have been established.
l) **Study results report.** Purpose: To assess whether the study report has been prepared in accordance with GLP principles, to verify the traceability of data from the original data to the final report.
m) **Research reviews.** Purpose: Reconstructing the research by comparing the final report with the research plan, relevant standard operating procedures, source data, and other archived materials.

8. Inspection results and conclusions

The results of the inspection and study audit, including any non-conformities found, are discussed with the laboratory's responsible persons. An oral and written laboratory inspection report (F.041.LLP) and a report on non-conformities found (F.040.LLP) are provided at the final meeting of the inspection visit. A detailed annex to the GLP laboratory inspection report (F.042.LLP) follows within one month. If non-conformities are found during the visit, the laboratory must take corrective action within the agreed deadlines. After the initial assessment and a positive decision, the GLP laboratory is included in the Agency's GLP laboratory programme, by entering it in the GLP laboratory register (F.058.LLP) and issuing the laboratory a certificate of compliance with the GLP principles. From now on, after regular and additional visits to laboratories included in the GLP laboratory program, its status (compliant, undecided, non-compliant) and the date(s) of the inspection performed are recorded in the register, informing the competent GLP Monitoring institutions of the OECD and/or EU Member States annually.

9. Inspection frequency

Regular inspection visits of all laboratories included in the GLP laboratory program take place approximately once every two years. If necessary, visits are organized in shorter periods. Additional visits may take place. Laboratory inspections and study audits are also possible at the request of competent authorities. In cases where studies or parts thereof are conducted in several countries (multi-site study), inspections and study audits may also be requested by other national GLP monitoring institutions.

10. Violations

If a laboratory included in the Agency's GLP Laboratory Register does not comply with the requirements of the GLP regulations, it may be excluded from the GLP Laboratory

Programme, specific studies may be excluded from the programme, or all reports may be rejected. In such cases, the laboratory's status is noted accordingly in the GLP Laboratory Register.

Annex 1

Terms and definitions

A. Terms and definitions can be found in Directive 2004 /10/EC of the European Parliament and of the Council.

NOTE: In Latvian version terms and definitions in this document are provided by the Translation and Terminology Centre. For better understanding, some terms are given in brackets with their English equivalent.

1. Good Laboratory Practice (GLP) - a quality system associated with organizational processes and regulations according to which non-clinical health and environmental safety studies are planned, conducted, controlled, documented, archived and reported

2. Terms relating to the organization of the testing facility

2.1. Test facility - the personnel, facilities and operational unit/s necessary for the conduct of a non - clinical health and environmental safety study. For studies conducted at multiple sites, the test facility is the site where the study director is located, as well as all other separate test sites that are collectively or individually considered to be test facilities.

2.2. Locations - where a stage/s of research is/are carried out.

2.3. Test facility management – person/s with authority and formal responsibility for its organization and operation in accordance with these principles of good laboratory practice.

2.4. Test site management (if appointed) - the person/s responsible for ensuring that the stage of the study for which it is responsible shall be carried out in accordance with these principles of good laboratory practice.

2.5. Sponsor - an entity that commissions, supports *and*/or proposes to conduct a non-clinical health and environmental safety study.

2.6. Study director - a person whose competence includes the overall management of health and environmental safety research.

2.7. Principal investigator - a person who, in a multi-site study, acts on behalf of the study director and has responsibility for specific phases of the study. The study director 's responsibility for the conduct of the study as a whole cannot be delegated to the principal investigator/s; it includes approving the study plan and its amendments, approving the final report, and ensuring that all applicable principles of good laboratory practice are followed.

2.8. Quality Assurance Program - A defined system, including staff who are free to conduct research, designated to ensure compliance with these Good Laboratory Practices by the management of the testing facility.

2.9. Standard Operating Procedures (SOPs) - documented procedures that describe how to perform testing or activities that are not typically described in detail in study plans or testing instructions.

2.10. Master schedule - a collection of information used by the testing institution to assess the scope of work and monitor the progress of research.

3. Terms relating to non-clinical health and environmental safety studies

3.1. Non-clinical health and environmental safety studies (hereinafter referred to as studies) - trials or a set of trials in which the test item is examined in a laboratory or under natural

conditions to obtain data on its properties and/or safety, and the results of which are intended for submission to regulatory authorities.

3.2. Short-term studies - studies that are conducted for a short period of time using widely used, generally accepted methods.

3.3. Study plan - a document that sets out the research objectives and the scheme of experiments required for the study, and their possible amendments.

3.4. Amendments to the research plan – changes to the research plan made after the start date of the research plan implementation.

3.5. Test system - the biological, chemical or physical system, or a combination of these systems, used for the study.

3.6. Output data - all original records and documentation of the testing institution or certified copies thereof, obtained in the original observations and activities of the study. Output data may also include, for example, photographs, copies of microfilm or microfiche, computer-readable recordings on data carriers, dictated notes or observations, data recorded by automatic operating instruments or data on other data carriers recognized as safe for the storage of information for the period specified in Article 10 of Directive 2004/10/EC of the European Parliament and of the Council.

3.7. A specimen - material removed from a testing system for testing, analysis, or preservation.

3.8. Trial start date - the day on which the first data of a particular study is obtained.

3.9. Trial end date - the day on which the last data for a particular study is obtained.

3.10. Research start date - the day when the research director signs the research plan.

3.11. Study end date - the day the study director signs the final report.

4. Terms related to the item being tested

4.1. Test item - the product on which the research is being conducted.

4.2. Reference item - a product used for comparison with the item being tested.

4.3. Batch - a defined quantity of a test item or reference material obtained in one specific production cycle so that it can be considered homogeneous and is designated accordingly.

4.4. Vehicle - a substance used to mix, disperse, or dissolve a test item or reference material so that it can be introduced/used in a test system.

B. Definitions of terms provided in the OECD Principles of Good Laboratory Practice.

1. GLP compliance monitoring - periodic inspection of research facilities and/or review of studies to confirm compliance with GLP principles.
2. National *GLP* compliance program – a specific scheme established by a Member State to monitor the compliance of research establishments with GLP in its territories through inspection and study verification.
3. National GLP Monitoring Authority – *an authority established in a Member* State which is responsible for monitoring the compliance of research establishments with GLP within its territory and for performing such other functions in relation to GLP as may be prescribed by the State. More than one such authority may be established in a Member State.
4. Test facility inspection - an on-site examination of the procedures and practices of research establishments to assess the level of compliance with the principles of GLP. During the inspection, the management structure and operating procedures of the research establishment are examined, key technical personnel are interviewed, and the quality and integrity of the data provided by the establishment are assessed and reported on.

5. Study audit - a comparison of the baseline data and related records with the interim or final report to determine whether the baseline data have been reported accurately, whether the studies have been conducted in accordance with the study design and standard operating procedures, to obtain additional information not provided in the report, and to determine whether practices were used to obtain the data that could reduce their validity.
6. Inspector - a person who carries out inspections of a research institution and verification of studies on behalf of the national GLP supervisory authority.
7. GLP compliance level - the level at which the research institution complies with the principles of GLP, as assessed by the national GLP supervisory authority.
8. Regulatory Authority – a government body that is legally responsible for aspects of chemical control.

Annex 2

Sample agenda for the first visit

Agenda for the first visit to the GLP laboratory

Laboratory name_____
Laboratory address_____
Date of visit_____

Introductory conversation

- Introduction
- Purpose and scope of the visit
- Laboratory management presentation
- Appointment of accompanying persons

Discussion on the research area

Laboratory management structure

- Organizational chart
- Documentation
- List of studies
- Research plan
- Standard Operating Procedures (SOP)
- Research reports
- Quality Assurance Program

Laboratory inspection

- Infrastructure
- Archives
- Equipment
- Test and reference substances
- Systems to be tested

Closing meeting

Annex 3

Sample agenda for a laboratory inspection visit

Laboratory name_____
Laboratory address_____
Dates of visit_____

First day
Introductory conversation

- Introduction
- Purpose and scope of the visit
- Approval of inspection/research audit agenda
- Laboratory management presentation
- Appointment of accompanying persons

Inspection

- Organization and personnel
- Documentation
- Quality Assurance Program
- Archives
- Premises and technical equipment
- Equipment
- Test and reference substances
- Systems to be tested
- Execution

Consultation between inspectors
Closing discussion with laboratory management on the first day

Second day
Research audit
Consultation between inspectors
Closing discussion with laboratory management on the second day

Third day
Research audit
Discussion among inspectors, summarization of results, preparation for the final meeting
Inspection closing meeting, discussions

Annex 4

Publications

OECD publications (www.oecd.org) on the principles of good laboratory practice and compliance monitoring :

1. OECD Principles there Good Laboratory Practice (1997)

2. Guidance for GLP Monitoring Authorities . Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practice (1995)

3. Guidance for GLP Monitoring Authorities . Revised Guidance for the Conduct of Laboratory Inspections and Study Audits (1995)

4. Advisory Document of the Working Party there Good Laboratory Practice there Quality Assurance and GLP (2022)

5. GLP Consensus Document . Compliance of Laboratory Suppliers with GLP Principles (2000)

6. GLP Consensus Document . The application of the GLP Principles to Field Studies (1999)

7. GLP Consensus Document . The application of the GLP Principles to Short -Term Studies (2003)

8. GLP Consensus Document . The Role and Responsibilities of the Study Director in GLP Studies (1999)

9. Guidance for GLP Monitoring Authorities . Guidance for the Preparation of GLP Inspection Reports (1995)

10. GLP Consensus Document . The Application of the Principles of GLP to Computerized Systems (1995)

11. Advisory Document . The Role and Responsibilities of the Sponsor in the Application of the Principles of GLP (1998)

12. Advisory Document . Requesting and Carrying Out Inspections and Study Audits in Another Country (2002)

13. GLP Consensus Document . The Application of the OECD Principles of GLP to the Organization and Multi -Site Management Studies (2002)

14. Advisory Document . The Application of the Principles of GLP to in in vitro Studies (2004)

15. Advisory Document . Establishment and Control of Archives that Operate in Compliance with the Principles of GLP (2007)

16. Guidance there the GLP Requirements for Peer Review of Histopathology (2015)

17. Application of GLP Principles to Computerized Systems (2016)

18. OECD Position Paper Regarding the Relationship between the OECD Principles of GLP and ISO/IEC 17025 (2016)

19. Position paper. Outsourcing of Inspection Functions by GLP Compliance Monitoring Authorities (2014)

20. OECD Position Paper on Good Laboratory Practice and IT Security (2024)

21. GLP Data Integrity (2021)

22. OECD Position Paper Regarding Possible Influence of Sponsors on Conclusions of GLP Studies (2022)

Register of changes made

Version	Content of changes	Date
03	Updated publications	16.01.2018.
04	The state agency "Latvian National Accreditation Bureau" and the Ministry of Climate and Energy is presented	23.04.2025.
	Section 6 lists the Agency 's internet links	
	The section “Terms and definitions” includes numbering	
	“break” removed from Annexes 2 and 3	
	Updated Annex 4 Publications	