On approval of the Rules for the implementation of principles of good laboratory practice

Unofficial translation

Order of the Minister of Trade and Integration of the Republic of Kazakhstan dated June 17, 2021 No. 414-RL. Registered with the Ministry of Justice of the Republic of Kazakhstan on June 18, 2021 No. 23092

Unofficial translation

This order shall come into force on July 1, 2021.

In accordance with subparagraph 7 of paragraph 1 of Article 7 of the Law of the Republic of Kazakhstan "On Technical Regulation", **I HEREBY ORDER:**

1. To approve the attached Rules for the implementation of principles of good laboratory practice.

2. The Committee for technical regulation and metrology of the Ministry of Trade and Integration of the Republic of Kazakhstan shall ensure:

1) state registration of this order in the Ministry of Justice of the Republic of Kazakhstan;

2) placement of this order on the Internet resource of the Ministry of Trade and Integration of the Republic of Kazakhstan.

3. Control over the execution of this order shall be entrusted to the supervising Vice-Minister of Trade and Integration of the Republic of Kazakhstan.

4. This order shall come into force on July 1, 2021 and shall be subject to official publication.

Minister of Trade and Integration
of the Republic of Kazakhstan — *B. Sultanov*

"AGREED"
Ministry of Agriculture
of the Republic of Kazakhstan

"AGREED"
Ministry of Industry
and Infrastructural Development
Republic of Kazakhstan

"AGREED"
Ministry of Healthcare
of the Republic of Kazakhstan

Approved
by the order of the Minister of
Trade and Integration of
the Republic of Kazakhstan
dated June 17, 2021 No. 414-RL

Rules for the implementation of principles of good laboratory practice

Chapter 1. General provisions

1. These Rules for the implementation of principles of good laboratory practice (hereinafter-the Rules) have been developed in accordance with subparagraph 7) of paragraph 1 of Article 7 of the Law of the Republic of Kazakhstan “On Technical Regulation” and shall determine the procedure for implementing the principles of good laboratory practice.

2. The following basic concepts are used in these Rules:

1) data register of the state system of technical regulation (hereinafter - the register of technical regulation) - an electronic database of technical regulations, accreditation subjects, issued documents on conformity assessment, expert auditors for conformity assessment, equipment, information about products that do not meet the requirements of technical regulations, and other information in the field of technical regulation;

2) a testing centre (laboratory) (hereinafter - laboratory) - a legal entity or a structural subdivision of a legal entity, acting on its behalf, carrying out tests (researches);

3) information system of technical regulation - an automated information system designed to store, process, search, distribute, transfer and provide data and information contained in the technical regulation registers, the state system for ensuring the uniformity of measurements, the national standardization system and unified registers issued or adopted documents on conformity assessment of the Eurasian Economic Union;

4) principles of good laboratory practice - a system of requirements aimed at ensuring the quality of preclinical laboratory research, including the processes of organizing, planning, conducting and monitoring preclinical laboratory researches in the field of human health protection, environmental safety, registration, archiving and presentation of results of such researches;

5) monitoring of compliance with good laboratory practice - within the framework of contractual relations periodic inspection of laboratories and (or) audit of the results of their researches to confirm compliance with the principles of good laboratory practice.

3. The procedure for monitoring compliance with good laboratory practice shall be carried out in accordance with Article 16 of the Law of the Republic of Kazakhstan "On Technical Regulation", GOST (State Standard) 31879 "Principles of good laboratory practice (GLP). Guidance on procedures for monitoring compliance with the GLP Principles.

Chapter 2. The procedure for the implementation of principles of good laboratory practice

Paragraph 1. Requirements for the organization and personnel of laboratories

4. The administration of laboratory to comply with the requirements of principles of good laboratory practice shall:

1) approve the regulations determining the person(s) performing the duties of management in accordance with principles of good laboratory practice;

2) provide a sufficient number of staff of competent personnel, appropriate premises, equipment and materials for the timely and proper conduct of the research;

3) maintain up to date documentation on the level of qualifications, education, work experience and job responsibilities of specialists and technical personnel;

4) determine the rights and obligations, the form of education and training of laboratory employees;

5) prior to the start of the research, appoint an employee with the appropriate education, qualifications and work experience as the head of the research (replacement of the head of the research shall be conducted in accordance with the established procedure and shall be documented);

6) appoint a responsible investigator who has the appropriate education, qualifications and experience to control the implementation of this stage (stages) of the research (replacement of the responsible investigator shall be conducted in accordance with the established procedure and shall be documented) when conducting a research at several test sites;

7) approve the plan of the research by the head of the research;

8) provide the access service with an approved plan of the research;

9) ensure the preservation of historical files of all standard operating procedures;

10) appoint a person responsible for managing the archive(s);

11) control the implementation of the main schedule;

12) control the compliance of laboratory resources with the requirements for their use in the research;

13) ensure clear and consistent communication between the head of the research, responsible investigator(s), quality assurance service and specialists performing this research when conducting researches at several test sites;

14) control the correctness of the design of tests and the standard test object;

15) approve the procedures for computerized systems for validating, managing and maintaining the principles of good laboratory practice.

5. To organize the research conduct, the laboratory administration shall appoint the head of the research, who:

1) carries out general management of the research;

2) is responsible for preparing the final report;

3) approves the research plan;

4) controls the activities of the quality assurance service throughout the research;

5) controls access to information to the specialists performing researches;

6) controls the progress of the research, in terms of implementation of the research plan and preparation of a final report on the results of the research performed at several test sites,

with determining the role of each responsible executor (s) at each of the test centres and test sites involved in the research process;

7) controls the performance of work in accordance with the research plan, with the organization of assessment and documentation of the impact of any deviations from the research plan on the quality and integrity of conducting the research, and takes corrective actions (to recognize the acceptability of deviations from standard operating procedures during the research);

8) controls the registration of all primary research data in full;

9) controls the validation of computerized systems used in the research;

10) approves the final report on the reliability of information and performance of researches in accordance with the principles of good laboratory practice;

11) after completion (including termination) of the research, controls the procedure for drawing up and archiving the research plan, final report, primary research data and related materials.

6. To conduct the research, the administration of the laboratory shall appoint a responsible researcher who:

1) performs the assigned stages of research in accordance with the principles of good laboratory practice;

2) follows the instructions of the research plan and standard operating procedures used in the research;

3) registers and sends to the management the identified deviations from the instructions and procedures of the research;

4) keeps records of the primary data of the research;

5) carries out works on the reliability of the research.

Paragraph 2. Requirements for a quality assurance program

7. Laboratories in their activities shall be guided by a documented quality assurance program in accordance with the principles of good laboratory practice.

8. The laboratory administration shall appoint an authorized person competent in the methods of conducting testing quality assurance programs.

9. An authorized person responsible for quality assurance shall not be involved in the conduct of the research.

10. The quality assurance service shall perform the following functions:

1) keeping copies of the approved research plans and standard operating procedures, used in the laboratory, including the current version of the master schedule;

2) applies documented procedures for checking the content of the research plan for compliance with the principles of good laboratory practice;

3) conducts inspections to verify the conduct of research for compliance with the principles of good laboratory practice;

4) checks the final reports for compliance with the primary researches data of methods, procedures, observations and results of researches;

5) submit data on inspections to the laboratory administration, the head of the research, responsible investigator(s);

6) in order to achieve verification of reliability of the primary research data shall enter the data on the stage (stages) of the research being checked and the date of transmission of the inspection data to the laboratory administration, the head of the research and the responsible researcher into the final report on the types of inspections and dates of their conduct.

7) for the traceability of results of long-term tests conducted in the laboratory, including tests not completed for the calendar year, approves an annual summary report on the status of all preclinical researches and activities of the department conducted over the past year in the laboratory.

11. Verification of compliance with the procedures of the quality assurance program shall be carried out through:

1) inspection of individual researches;

2) inspection of testing centres;

3) inspection of individual processes.

Paragraph 3. Requirements for premises

12. Dimensions, equipment and location of laboratory premises shall be taken into account, depending on the objectives of the research during researches.

13. When conducting kinds (types) of researches that differ from each other, the requirements for the layout of premises for each kind (type) of the planned research shall be taken into account.

14. Researches using substances or organisms classified as biologically hazardous shall be carried out in the rooms or areas of the laboratory, provided with separate sectors and isolation of test systems.

15. The stability and safety of test systems for the diagnosis, treatment and control of diseases shall be provided with suitable premises or areas.

16. To ensure adequate protection against invasion, pollution and/or contamination the laboratories shall be equipped with isolated storage rooms (areas for resources and equipment containing test systems).

17. To prevent pollution in the laboratory, separate rooms or zones shall be equipped for receiving and storing test objects and standard (control) objects and mixing test objects with carriers.

18. Stores for test items shall be isolated from rooms or areas containing test systems and meet the requirements for ensuring identity, concentration, purity and stability, as well as the safe storage of hazardous substances.

19. To ensure the safe storage and retrieval system of research plans, primary research data, final reports, test objects and samples, archive rooms shall be equipped with conditions for long-term storage of archival materials.

20. For the safe conduct and reliability of research results, the procedures for decontamination, transportation, processing, disposal, collection, storage and disposal of waste shall be applied.

Paragraph 4. Requirements for equipment, materials and reagents

21. When conducting researches, the equipment, validated computerized systems used to create, store and retrieve data, as well as to control environmental parameters according to their characteristics and location, corresponding to the goals and objectives of the research shall be taken into account.

22. The laboratory conducts periodic maintenance of the equipment used in the research, including regular periodic inspection, maintenance, calibration and verification in accordance with standard operating procedures, with appropriate records, calibration and verification in accordance with the Law of the Republic of Kazakhstan "On ensuring the uniformity of measurements".

23. When conducting researches, the influence of equipment and materials on the state of test systems shall be excluded.

24. When using chemicals and their mixtures, reagents and solutions, labels and markings, indicating information about the name of the substance, concentration, expiration date of the shelf life and storage instructions, including information about the manufacturer, production date and stability shall be checked.

25. For uninterrupted operation and continuity of the process, the laboratory shall be provided with autonomous power supplies.

Paragraph 5. Requirements for test systems

26. When conducting researches, physical and chemical test systems shall be used.

27. To obtain physical and chemical data, the laboratory uses equipment, the technical characteristics and location of which satisfy the goals and objectives of the research.

28. When conducting researches, the laboratory shall ensure the safety of physical and chemical test systems.

29. When conducting researches, biological test systems shall be used.

30. The laboratory establishes the conditions for storage, placement, processing and protection of biological test systems.

31. To assess the state of health, the laboratory shall ensure isolation for each new incoming test system of animal and plant origin. If a disease or mortality occurs, this batch of animals shall not be used in the research and shall be painlessly euthanized. At the start date

of the research experiment, the laboratory shall control all test systems to exclude diseases or conditions that serve as an obstacle to the purpose of the research. Test systems that have diseases or injuries detected during the course of the research shall be isolated and treated to ensure the completeness of the research. Diagnoses and treatment of any diseases, both during the research and before its start shall be documented.

32. The laboratory shall ensure registration of data on the sources of test systems, the dates of their receipt and condition.

33. The laboratory shall ensure an acclimatization period sufficient to adapt to the conditions of the research before the initial introduction of the test object or standard object of biological test systems.

34. The laboratory shall ensure the measures for proper identification of the test system, indicating information on the entrance doors of the premises or containers, when transferring individual test systems from one room to another or from one container to another, marking shall be provided.

35. The laboratory shall ensure the measures for cleaning and sanitizing the rooms or containers used to contain the test systems. To prevent the detection of contaminants in quantities that can affect the course of the research, the laboratory shall control the materials that come into contact with the test system. All cases of pesticides use shall be documented.

36. When using test systems in the field, it is ensured that spraying liquids (for killing insects) and pesticides do not affect the course of the research.

37. When using biological test systems in the form of cell cultures of animal origin, used in in vitro researches (in vitro), a periodic identity verification procedure and a test for mycoplasma infection shall be ensured. To prevent introduction into the original pure culture of animal cells, such test systems shall be duplicated. One batch is used as a working test system, from which further passages shall be obtained by subculturing for testing. The other batch serves as a standard for cell identification and quality control of the working test system .

Paragraph 6. Requirements for test objects and standard objects

38. The laboratory maintains records that indicate the characteristics of test objects and standard objects of the research, the dates of their receipt, expiration dates, initial quantity and information on accounting for consumption.

39. When conducting works on the processing, sampling and storage procedures of test objects and standard objects, homogeneity and stability, as well as contamination control or mixing of these objects shall be ensured.

40. The laboratory shall ensure that test objects or standard objects shall be properly stored, with identification information on the container(s), expiration dates and instructions for their storage.

41. The laboratory shall ensure the identification of each test object and standard objects.

42. For conducting of each research, the laboratory indicates such general characteristics of the test object and the standard object as lot (batch) number, purity, composition, concentration and individual characteristics for each research.

43. When the test object comes directly from the customer, the customer and the laboratory shall establish a mechanism to identify it. The customer submits a document describing the results of preliminary laboratory tests that allow to compare the aggregate state , colour, viscosity, solubility in water, organic solvents, bases and acids.

44. The laboratory shall ensure the stability of the test object and the standard object during their storage under experimental conditions.

45. The laboratory shall establish the homogeneity, concentration and stability under environmental conditions of the test object for introduction or application in the carrier.

46. The laboratory shall ensure the safety of the analysis of the sample from each batch (series) of the test object for all researches.

Paragraph 7. Requirements for standard operating procedures

47. The laboratory administration shall approve standard operating procedures (hereinafter- SOP), as well as revised SOP, which are designed to ensure the quality and completeness of the data obtained during the research.

48. The laboratory administration shall ensure that each unit and/or each site of the laboratory has access to valid SOP relevant to their activities. In addition to the SOP, it is also allowed to use printed publications, normative and technical documents, normative documents, international and national methodological manuals, reference books and special articles.

49. Information about deviation from the SOP during the research shall be registered, recorded by the head of the research and the responsible researcher(s).

50. Standard operating procedures shall be used for the activities of following types (but not limited to them) of researches on:

1) test objects and standard objects, including receipt, identification, labelling, processing, sampling and storage;

2) equipment, materials and reagents, including use, maintenance, care and calibration;

3) quality assurance procedures;

4) computerized systems, including validation, operation and maintenance procedures, security, change control and backup creation;

5) materials, reagents and solutions, including preparation and labelling;

6) storage of records, reporting, storage and retrieval of information, coding of researches, data collection, preparation of reports, indexing systems, data processing, including using computerized systems;

7) test systems, including the preparation of premises and creation of environmental conditions for the placement of test systems, procedures established for the receipt,

transportation, placement, characterization and identification of test systems, as well as their care, preparation of test systems, observations and examinations before, during and after completion of the research, handling of test systems dying or deceased during the research, collection, identification and handling of samples, including necropsy and histopathology, placement of test systems on test sites;

8) quality assurance procedures, including planning, scheduling inspections, conducting inspections, documenting and reporting on inspections.

Paragraph 8. Requirements for conducting researches

51. The laboratory administration shall develop a research plan for each research separately prior to the start of the research.

The research plan shall be approved by the laboratory administration and the research head and verified in accordance with the principles of good laboratory practice.

52. Changes and justified amendments to the research plan shall be approved by the dated signature of the research head, with subsequent storage along with the research plan.

In case of deviation from the research plan, the responsible researcher shall describe, explain and communicate the information to the research head in a timely manner, indicating the date. Information about deviations from the research plan shall be stored along with the primary research data.

53. The main research plan shall be complemented by special annexes for short-term researches.

54. The following shall be included in the research plan, but not limited to:

1) data on the research, the test object and the standard object;

2) description of the research;

3) the essence and purpose of the research;

4) description of the test object, indicating the code or name;

5) description of the standard (control) object used;

6) information about the research customer;

7) the dates of researches, indicating the date of approval of the research plan signed by the head of the research, the laboratory manager and the customer;

8) the expected start and end dates of the experiment;

9) test methods with references to the relevant guidelines on test methods of the Organization for Economic Cooperation and Development (hereinafter referred to as the OECD), international and national regulations, guidelines and methods;

10) justification for the choice of the test system;

11) characteristics of the test system: species, genus, strain, substrain, source of acquisition, quantity, body weight ranges, sex, age;

12) rationale for the choice of test systems and method of administration;

13) dose and/or concentration levels, frequency and duration of administration;

14) detailed information about the design of the experiment, including a description of the research procedures in chronological order, all methods used, materials and conditions, types and frequency of analyses, measurements, observations and checks, statistical methods of data processing.

15) a list of all records and documents to be kept.

55. Each research and all objects related to this research shall be assigned a unique identification number (code).

56. To ensure the traceability of the relevant sample and research, the samples used in the research shall be identified to confirm their origin.

57. The laboratory administration controls the recording of data obtained during the research, with the appropriate identification of the person who maintains these records.

58. Changes to the primary data shall be recorded when saving the previous data, indicating the reasons for making the changes, with certification of the record of the changes by the person who made them.

59. The data registered by direct input into the computer shall be identified during their input by the person responsible for this procedure. To track changes, a computerized system shall ensure that all audit reports are saved, taking into account changes and initial data.

Paragraph 9. Requirements for reports on the results of researches

60. At the end of each research, a final report shall be prepared.

61. Responsible researchers, as well as scientific employees participating in the research shall sign reports with the appropriate identification (date, time, surname, name, patronymic (if any) of the employee, seal of the organization (if any)).

62. The final report shall be signed and dated by the research head, indicating the compliance of the report with the principles of good laboratory practice.

63. Corrections and additions to the final report shall be approved in the form of amendments, with clearly identified reasons. Each of the amendments shall be approved and dated by the research head.

64. Formatting/ corrections of the final report identified in the form of an appendix in accordance with the requirements of national legislation or the national regulatory body shall not be considered an action to make corrections, additions or amendments to the final report.

65. The final report includes the following, but is not limited to:

1) materials about the research, the test object and the standard object;

2) full name of the research;

3) description of the code, name and test object;

4) the name of the standard test object;

5) characteristics of the test object, including purity, stability and uniformity;

6) data of the research customer;

7) start and end dates of the experiment;

8) information about the types and dates of inspections carried out, the stage (s) of the research, the inspections passed, the results of the inspection, indicating the dates, which were submitted to the laboratory administration, the research head and the responsible researcher (s);

9) description of materials and test methods used in the research;

10) references to the OECD methodological guidelines, international and national regulations that were used in the research;

11) summary of results;

12) information obtained during the implementation of the research plan;

13) presentation of results, including calculations and statistical processing of the obtained data;

14) assessment and discussion of the results, conclusions and opinions.

66. The laboratory administration shall ensure the storage of the research plan, test objects and standard objects, samples, primary research data and final reports in a specially designated place (s).

Paragraph 10. Requirements for storing records and materials

67. The laboratory administration shall ensure the orderly storage of documents and materials in archives, by approving documented procedures for access to archives, taking into account the registration, acceptance and issuance of archival materials, conditions and terms of storage.

68. The laboratory administration shall ensure the storage of documents and materials in the archive:

1) the research plan, primary data, samples, test object and standard object, final report of each research;

2) records of all inspections performed in the area of the quality assurance program, as well as major schedules;

3) information about the education, training, qualifications and work experience of the personnel;

4) records and reports of equipment maintenance and calibration;

5) documents on validation of computerized systems;

6) historical files of all standard operating procedures;

7) monitoring records of environmental parameters.

The laboratory administration shall conduct works on the destruction of samples, test objects and standard objects before the expiration of the established period, indicating the reasons and conditions.

The laboratory administration in order to ensure the reliability of traceability of the results of the research shall control the storage of samples, test objects and standard test objects, taking into account the quality, timing and storage conditions.

69. Upon termination of activities, the laboratory or organization in which the archive is located shall transfer archival materials to the successor, and in his/her absence to the customer (s) of the research (es).