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If a whole or part of a paragraph has been amended, the date of the amending regulation appears in square brackets at the end of the paragraph. If a whole paragraph or sub-paragraph has been deleted, the date of the deletion appears in square brackets beside the deleted paragraph or sub-paragraph.

Republic of Latvia

Cabinet
Regulation No. 398
Adopted 3 September 2002

Requirements for the Work Quality of Laboratories and Inspections of Laboratories

Issued pursuant to
Section 6, Paragraph two of the Chemical Substances Law
and Section 7, Paragraph one of the Law On Conformity Assessment
[26 January 2010]

I. General Provisions

1. This Regulation prescribes:

1.1. the requirements for the work quality of laboratories in determining the physical, chemical, toxicological or ecotoxicological properties of chemical substances and mixtures or in studies on the impact of such substances and mixtures on the environment or human health;

1.2. the conditions for inspections of laboratories, also in relation to the assessment and monitoring of the work quality of laboratories (good laboratory practice), study audit (in order to ensure study data that are comparable with the studies conducted in other countries, and to prevent technical barriers to trade) and monitoring of laboratories (in order to avoid the overlapping of tests, to save time and resources, as well as to improve the protection of human health and the environment).
[26 January 2010]

2. The Regulation shall apply to studies, trials (except clinical) and tests (hereinafter – studies) that are conducted in order to obtain information regarding the properties of biocides, chemical substances and mixtures, as well as the properties of such agents of biological origin or live organisms, which are intended for the use as the constituent parts of medicinal products, plant protection products, cosmetic products, veterinary medicinal products, food supplements and animal feed supplements (hereinafter – test substance or organism), and the hazards that they pose to human health and the environment. The study results are provided for submitting to the Ministry of Welfare, the Ministry of Health, the Ministry of Environment and the Ministry of Agriculture, as well as to the institutions subordinated to such ministries (hereinafter – competent authorities).
[18 October 2005; 26 January 2010]

3. The properties of test substances and organisms, as well as their hazards shall be studied in laboratory settings, greenhouses or in the environment, using biological, chemical or physical systems or combinations thereof (hereinafter – test systems). In conducting studies, the recommendations of the Organisation for Economic Co-operation and Development (OECD) on good laboratory practice principles shall be taken into consideration.

4. Certifications or confirmations issued in the European Union Member States, the European Economic Area states, member states of the European Free Trade Association and the Organisation for Economic Co-operation and Development in accordance with the norms laid down in the European Union Member States, which certify that the respective study has been conducted and is monitored in accordance with the requirements of good laboratory practice, shall be recognised in Latvia.
[18 October 2005]

5. The studies shall be conducted by the laboratories that are monitored by the Latvian National Accreditation Bureau of the limited liability company "Standardisation, Accreditation and Metrology Centre" (hereinafter – Latvian National Accreditation Bureau) in accordance with the requirements laid down in this Regulation.
[26 January 2010]

II. Requirements for the Work Quality of Laboratories

6. If studies are conducted at several sites (hereinafter – study sites), the conformity with the provisions of this Regulation shall be ensured at all study sites.

7. A person who organises the management of all studies and is responsible for them and who owns the laboratory or who heads the laboratory (hereinafter – responsible person), shall ensure the monitoring and control of the work quality of the laboratory. The responsible person shall:

7.1. appoint the study director and control his or her work;

7.2. ensure sufficient number and qualification of laboratory employees, premises, equipment and materials for prompt and correct conduct of studies;

7.3. appoint an employee who ensures the creation of the archives and storing of the following information:

7.3.1. regarding the approved study plans;

7.3.2. regarding the qualification of laboratory employees (including job descriptions and information regarding training and experience of employees);

7.3.3. regarding work schedules;

7.3.4. regarding the methods for the conduct of studies and the amendments made thereto;

7.4. check whether a laboratory employee has clearly understood the functions to be performed and whether personnel training is ensured;

7.5. appoint one or several persons who are responsible for quality assurance (hereinafter – quality assurance personnel);

7.6. appoint a person who is responsible for the conduct of each particular study (hereinafter – responsible specialist);

7.7. approve a laboratory work quality assurance programme and check whether the study director ensures the work quality of laboratory in accordance with this Regulation;

7.8. assess and approve appropriate and technically justified methods for the conduct of studies and amendments thereto, as well as ensure their introduction.
[26 January 2010]

8. The methods for the conduct of studies approved by the responsible person shall be used in order to carry out activities that are not governed by study plans and documents. Methods that are commonly used in laboratory practice shall be used for simple, frequently conducted studies.

9. The study director shall approve the work schedule, as well as the study plan in which the course of the intended study is documented, in order to evaluate and plan the work load of employees and to implement sequential conduct of the studies. The study plan shall be co-ordinated with the quality assurance personnel, which checks its conformity with the requirements of this Regulation. A study plan, which includes the basic study questions and corresponding explanations, shall be used for short-term studies.

10. Observations and readings that are obtained in direct observations and activities and recorded in study protocols or original documents, or in copies of the referred-to documents approved by the study director, are the original data. Photographs, microfilms or copies of microfilm fragments, information in electronic form, audio cassettes, data recorded by automatic instruments, as well as other information carriers, which can ensure the storage of information, may also be original data.

11. The date when the study director approves the study plan shall be considered the date of commencement of studies.

12. If amendments to the study plan are required after commencement of studies, they shall be approved by the study director and stored together with the study plan.

13. If unplanned deviations from the study plan arise after commencement date of studies, the person conducting the studies shall describe and explain them, while the study director shall approve them as deviations from the study plan and store together with the original data.

14. The date when the study director approves the final review shall be considered the date of completion of the studies.

15. The date when the first characteristic results of the study have been obtained shall be considered the commencement date of an experiment.

16. The date when the study results are summarised shall be considered the completion date of an experiment.

17. The study director shall be responsible for the management of studies, their conformity with this Regulation, the credibility and validity of the study results, as well as perform the following duties:

17.1. ensure premises, equipment and device constructions that are appropriate for the conduct of studies and situate them in a way that would reduce the interference which could affect the credibility of the studies to the minimum;

17.2. provide for actions in the study plan, which guarantee correct conduct of each study;

17.3. provide for sufficient area of premises or fields to guarantee isolation of separate studies, taking into consideration the test substances or organisms known to or potentially capable to cause biological hazard, in order to ensure the conduct of studies;

17.4. approve the study plan and all amendments thereto with a signature and date;

17.5. co-operate with the quality assurance personnel, as well as ensure prompt issue of the study plan and all amendments to the quality assurance personnel;

17.6. ensure the availability of the study plans and amendments thereto, as well as the approved methods for the conduct of studies to the laboratory personnel;

17.7. if the study is conducted at several sites, ensure that the role of each responsible specialist, all testing equipment required for the conduct of the study and the sites of conduct of studies are indicated in the respective study plan and final review;

17.8. ensure the conformity with all procedures provided for in the study plan, evaluate and document the effect of the deviations from the study plan on the quality and credibility of studies;

17.9. approve amendments to the methods for the conduct of studies made during studies;

17.10. ensure documenting and minute-taking of all original data obtained;

17.11. ensure the validation of information systems used for studies;

17.12. approve the final review, indicating the date and the deviations from the requirements of this Regulation that have occurred;

17.13. ensure the transfer of the study plan, the final review, the original data and materials that substantiate such data to the archives after completion of studies.
[26 January 2010]

18. Employees who conduct the studies have the following duties:

18.1. to acquire the quality assurance fields of laboratory work, which are necessary for activities of the respective employee during studies;

18.2. to become acquainted with the study plan and such methods for the conduct of studies, which are required for work in the respective studies, to take into account the conditions laid down in the study plan and methods;

18.3. to document the deviations from the study plan or the methods for the conduct of studies and to submit the respective information to the study director or the responsible specialist;

18.4. to immediately and precisely take minutes of the original data and to be accountable for their quality;

18.5. to conform to the labour safety and health protection measures in order to minimise the risks, and to report to the study director on the required additional conditions of labour safety or health protection.

19. The quality assurance personnel have the following duties:

19.1. to become acquainted with the approved study plans, work schedule and the methods for the conduct of studies;

19.2. to check whether the study plan contains such information which is necessary in accordance with the requirements of this Regulation, to document the results of inspections and to keep the protocols of inspections;

19.3. to check the studies, work process, equipment and devices in order to determine whether all studies conform to the requirements of this Regulation, to assess whether the study plans and approved methods for the conduct of studies are accessible to the persons conducting studies and whether they are conformed to;

19.4. to check the final reviews and to confirm that observations, as well as methods and procedures have been described and that the recorded results precisely reflect the original data;

19.5. to immediately report to the responsible person and to the study director on all results of inspections;

19.6. to draw up a report (for inclusion in the final review), indicating the types of inspections and their dates, checked stages of studies, as well as the dates when the inspection results are reported to the responsible person and the study director.

20. Individual warehouse premises or field areas, which are separated from the premises or areas where the test substances and organisms are stored, shall be arranged for the material stocks and equipment in order to ensure their protection against infections, contamination, becoming damaged or invasions of foreign organisms.

21. The premises or field areas for storage of the test substances or organisms shall be equipped in a way that preserves the identity, concentration, purity degree and stability of the test substances or organisms, as well as guarantees safe storage of the hazardous substances.

22. In order to prevent infections, contamination or mixing of the test substances or organisms and standard substances or reference organisms (substance or organism, which is used as the basis for comparison with the respective test substance or organism), separate premises or field areas shall be established for their receipt and storage, as well as for mixing standard substances or reference organisms with the carrying substance (transport substance) (a substance that is used for mixing, dispersion or dilution of the test substance or organism or also a standard substance or reference organism in order to enable its introduction into the test system).
[26 January 2010]

23. Appropriate premises or areas that prevent infection or becoming ill shall be set up in order to diagnose and treat the diseases of the test organisms.

24. Appropriate archival and sample storage premises shall be established in order to ensure safe storage of study plans, original data, final reviews, samples (all materials, which have been obtained from the test system and are intended for examination, analyses or storage) and samples of the test substances.

25. Activities involving waste generated by the laboratory shall be carried out in a manner that does not endanger human life and health, environment, as well as does not affect the work quality of laboratories.

26. The equipment used for studies shall be periodically checked, cleaned, serviced and calibrated in accordance with laws and regulations or the instructions approved by the study director (if the respective issue is not governed in laws and regulations).

27. The equipment and materials used for the studies may not cause such negative impact on test substances or organisms, which has not been determined in the study plan.

28. Chemical reactants and solutions shall be labelled with a label bearing the name, term of validity, storage conditions and, if possible, concentration thereof. Information regarding the origin, date of manufacture and stability of such mixtures must be accessible to the personnel.
[26 January 2010]

29. The study director may extend studies on the term of validity of chemical reactants and solutions on the basis of documented results of analyses only.

30. The equipment used for physical and chemical studies must be appropriately located, designed and sufficiently powerful in order to ensure the wholeness (integrity) of the respective test substances or organisms.

31. In order to guarantee the quality of data, the conditions that are appropriate for the storage, keeping, servicing and operations with biological systems shall be ensured, as well as the following provisions shall be conformed to:

31.1. animal and plant systems just received and to be tested shall be isolated until the moment when their health status has been assessed. If a non-characteristic instance of death occurs, the test animals and other biological systems may not be used in studies. If required, the animals shall be subject to euthanasia;

31.2. the test systems may not be ill or infected on the commencement date of the studies. The individuals that are infected or injured during the studies shall be isolated and treated, if integrity of the studies must be preserved. All diagnoses and treatment for each disease shall be documented either before the studies or during the studies;

31.3. the information regarding the origin, date of receipt and condition of the test systems at the moment of receipt shall be preserved;

31.4. before treatment or use of biological test systems, they shall be acclimatised in the testing environment for an appropriate period of time;

31.5. all information that is required to correctly identify the test systems (including information regarding the conducted studies) shall be indicated on enclosures, premises, cages or containers;

31.6. during experiments, the premises for keeping the test systems, cages or containers shall be cleaned and the bedding of animals shall be changed with appropriate intervals in accordance with the laws and regulations laying down the procedures and methods for keeping, use, sale and disposal of animals used for experiments and scientific purposes, as well as welfare requirements for the use of such animals;

31.7. none of the materials that some in contact with the test system may contain substances in the amount that could interfere with the studies;

31.8. plant protection products and biocides used shall be recorded in the protocol;

31.9. the test systems that are studied in their environment shall be located in a way that would prevent interference caused by the use of sprays or pesticides before the conduct of studies.

32. The study director shall ensure the storage of all those protocols that provide the characterisation of the test substances and standard substances, the date of receipt thereof, the term of validity and the quantities received and used during the studies.

33. Actions with the test substances or organisms and standard substances or reference organisms, as well as the procedures for sample collection and storage shall be organised in a way that ensures the homogeneity and stability of such substances, prevents poisoning, infection or mixing of the substances.

34. The information regarding the name, term of validity and special storage conditions of the substance, mixture or organism shall be indicated on the storage container.
[26 January 2010]

35. Each test substance or organism and standard substance or reference organism shall be identified by indicating its name in accordance with the nomenclature of the International Union of Pure and Applied Chemistry (hereinafter – IUPAC), its code or number in the reference magazine *Chemical Abstracts* (CAS number) and biological parameters.

36. Name, batch (including batch number), purity degree, composition, concentration and other special characteristics of each test substance or organism and standard substance or reference organism shall be documented.

37. If the test substance or organism is introduced into the test system by using a carrying substance (transport substance), the homogeneity of the test substance or organism, its concentration and stability in this carrying substance (transport substance) shall be determined prior to such introduction. For the test substances and organisms that are used in their environment, these parameters shall be determined in separate laboratory experiments.
[26 January 2010]

38. Samples for control analyses shall be stored from each batch of the test substance or organism.

39. Methods for the conduct of studies approved by the responsible person that apply to the actions to be performed at this site shall be used during each study.

40. If deviations from the methods for the conduct of studies arise during the studies, they shall be indicated in the protocol, and if these changes are useful for the conduct of studies, they shall be approved by the study director.

41. The approved methods for the conduct of studies shall be used:

41.1. for the receipt, identification and labelling of the test substances or organisms, standard substances or reference organisms and for actions with them, sampling and storage;

41.2. for the use, servicing, cleaning and calibration of equipment;

41.3. for the validation, servicing, use, security, control of changes of the information system and backup of information;

41.4. for the production and labelling of materials, reactants and solutions;

41.5. for the drawing up, storage and amendments (including the coding of studies) to protocols, data collection, drawing up of reports, indexation of systems, data processing, as well as the use of information system;

41.6. for the actions with the test systems, including:

41.6.1. preparation of premises, provision of microclimate and clean air in the premises;

41.6.2. receipt, transfer, placement, characterisation, identification and care for the test system;

41.6.3. preparation of the test system, as well as observations and tests before commencement of the studies, during the studies and at the end of the studies;

41.6.4. actions with those individuals of the test system, which have been found dying or dead during the studies;

41.6.5. sampling, identification and actions with samples (including dissection and histopathology);

41.6.6. insertion and placement of the test systems into study schemes;

41.7. quality assurance procedures (including actions of the quality assurance personnel during planning of inspections, drawing up of schedules and execution thereof, drawing up of documents and submission of reviews).
[26 January 2010]

42. The following information shall be indicated in the study plan:

42.1. name of the studies, test substances or organisms and standard substances or reference organisms:

42.1.1. a brief description of the studies;

42.1.2. type and objective of the studies;

42.1.3. name of the test substance or organism according to IUPAC nomenclature, code or number in chemical reference magazine *Chemical Abstracts* (CAS number), biological parameters;

42.1.4. standard substances or reference organisms used;

42.2. the name and address of the client that ordered the studies;

42.3. the name and address of the responsible person;

42.4. the given name, surname and address of the study director;

42.5. the given name, surname and address of the responsible specialist, study phases delegated to the responsible specialist by the study director;

42.6. the date when the study plan was approved;

42.7. the date when the study plan was co-ordinated with the client;

42.8. the planned dates of commencement and conclusion of experiments;

42.9. references to generally accepted study methods;

42.10. the substantiation for choosing the test system;

42.11. the characterisation of the test system (for instance, species, family, subfamily, number, origin, sex and age, body weight);

42.12. the method of administration (for instance, by inhaling, by oral administration) and the justification of the choice thereof;

42.13. the quantity or the concentration of the dose, frequency of administration, duration of use;

42.14. detailed information regarding the experiment project by including a description of the chronological procedure of the studies, all methods, materials and conditions, type and frequency of tests, measurements to be taken, observations, inspections and statistical methods used;

42.15. the list of protocols to be kept.

43. The studies shall be conducted in accordance with the study plan, considering the following conditions:

43.1. a special name shall be granted to each study and each substance or organism that refers to this study;

43.2. the origin of the sample shall be indicated on the labelling of each sample;

43.3. all data shall be recorded in the protocols by precisely and legibly recording every reading and observation separately. The person who conducts the study shall approve these records by his or her signature;

43.4. the amendments to the original data shall be made in a way that enables the legibility of the previous record, indicating the reason for the amendment. The person who conducts the study shall approve these records by his or her signature.

44. The initial data, all changes in the data and causes thereof shall be indicated upon entry of the study data into the information system, as well as the date and time of each information entry and data of the person who made the record in the information system.

45. The final review shall be drawn up regarding each study. Shortened final reviews shall be drawn up regarding short-term studies, adding the respective explanations to them.

46. The reviews signed by the responsible specialists shall be enclosed with the final review, indicating the date.

47. The final review, as well as amendments thereto shall be signed by the study director, indicating the date (for amendments – also the reason for amendment).

48. The following information shall be provided in the final review:

48.1. name of the studies, test substances or organisms, standard substances or reference organisms:

48.1.1. a brief description of the studies;

48.1.2. name of the test substance or organism according to IUPAC nomenclature, code or number in chemical reference magazine *Chemical Abstracts* (CAS number), biological parameters;

48.1.3. names of the standard substances;

48.1.4. characterisation of the test substance or organism (including its purity degree, stability and homogeneity);

48.2. information regarding the client and the person who conducts the studies:

48.2.1. the name and address of the customer;

48.2.2. names and addresses of all sites where the studies were conducted;

48.2.3. name, surname and address of the study director;

48.2.4. name, surname and address of the responsible specialist, as well as the phases of the studies delegated to him or her;

48.2.5. given names, surnames and addresses of those persons conducting the studies, who have prepared the reports for the final review;

48.3. the dates of commencement and conclusion of experiments;

48.4. the report of the person responsible for the quality assurance programme, which includes information regarding inspections related to the quality assurance programme and the dates thereof, dates of inspections, information regarding when the results of inspections were reported to the responsible person and the study director or when the responsible specialist was informed confirming that the final review reflects original data;

48.5. the description of materials and study methods:

48.5.1. the description of the methods and materials used;

48.5.2. references to the respective approved study methods;

48.6. study results:

48.6.1. summary of the results;

48.6.2. information and data required by the study plan;

48.6.3. explanation of the results, indicating the statistical methods used;

48.6.4. evaluation of the results and conclusions;

48.7. the site where samples of the study plans, the test substance or organism and standard substance or reference organism, original data and the final review are stored.

49. The following materials shall be stored in the archives:

49.1. study plans, work schedules, original data, samples of test substances or organisms and standard substances or reference organisms and final reviews regarding each study;

49.2. inspection protocols related to the quality assurance programme;

49.3. information regarding the qualification, training, experience and job descriptions of the personnel;

49.4. protocols and reviews on the servicing and calibration of equipment;

49.5. documents on the validation of the information system;

49.6. documentation related to the drawing up of the methods for the conduct of studies;

49.7. environmental monitoring protocols.

[26 January 2010]

50. If samples of the test substances or organisms, standard substances or reference organisms and mixtures obtained during experiments are destroyed before expiry of the determined storage period, such action shall be substantiated and an appropriate document shall be drawn up.

[26 January 2010]

51. The samples of test substances or organisms, standard substances or reference organisms and mixtures obtained during experiments shall be stored only for as long as the quality of these mixtures permits assessment thereof.
[26 January 2010]

III. Monitoring of the Work Quality of Laboratory and Assessment of Laboratories

52. Upon implementation of the monitoring of the work quality at assessed laboratories, the Latvian National Accreditation Bureau shall periodically control the laboratory by inspecting the means of studies (including the required personnel, equipment and other material resources for the conduct of studies), procedures and practices on sites, by questioning the leading technical personnel and assessing the management system and work process of the responsible person, as well as by evaluating the quality and body of the data obtained at the laboratory and the conformity with this Regulation. Employees of the Latvian National Accreditation Bureau may attract experts in order to perform inspections or evaluations.

53. The Latvian National Accreditation Bureau shall draw up a written inspection protocol (in two copies) regarding each inspection performed. The incompatibilities and deviations that have been detected, as well as instructions on the required corrections shall be indicated in the protocol.

54. The Latvian National Accreditation Bureau shall ensure theoretical and practical training of its employees, as well as provide information regarding the requirements and methods used for assessment of the work of laboratories.

55. Employees of the Latvian National Accreditation Bureau have the right to access classified information (including commercial secrets) related to the studies conducted at the laboratory and to include references to such information in their reviews. The Latvian National Accreditation Bureau shall ensure protection of the classified information (including commercial secrets), which has been obtained during performance of quality control of laboratory work.

56. Employees of the Latvian National Accreditation Bureau shall not participate in the conduct of studies and interpretation of the study results.

57. Employees of the Latvian National Accreditation Bureau have the right, by receiving a prior approval of the responsible person, to enter laboratories and obtain the required information. If access to the data is materially significant for the protection of human health or environment, the authorised employees have the right, by inviting the study director or another representative of the laboratory management, to enter laboratories and obtain the required information without approval of the responsible person.
[26 January 2010]

58. If classified information (including commercial secrets) is stored at the laboratory, the Latvian National Accreditation Bureau shall guarantee that the reviews on laboratory inspections and study audits are accessible to the competent authorities only.

58.[1] The competent authorities, the client that ordered the studies, as well as any other person that has access to classified information (including commercial secrets) obtained during monitoring of the work quality of laboratory shall ensure non-disclosure of such information.
[26 January 2010]

59. The Latvian National Accreditation Bureau shall draw up a programme for assessment (control) of the work quality of laboratory, which shall include:

59.1. conditions for inspections of laboratories (including general inspection of laboratories), as well as for study audit (assessment of data, study methods, procedure and results) of one or several current or completed studies;

59.2. conditions for inspection of laboratories and study audits upon request of the competent authorities;

59.3. rights and obligations of the authorised employees during laboratory inspections and in acquisition of data, during inspections of samples, approved methods for the conduct of studies and other documentation;

59.4. descriptions of laboratory inspections and study audit procedures;

59.5. descriptions of repeat laboratory inspections and study audit procedures.

60. A study audit shall be performed in order to assess the course of the current or completed studies and receive additional information that has not been indicated in the final review. Upon conducting a study audit the original data shall be compared with the final review and other information, facts shall be evaluated in order to determine whether methods that may reduce the credibility of results have been used during data collection or processing, and assessment of whether inspections have been conducted in accordance with the study plan and approved methods for the conduct of studies.

61. Before performance of a laboratory inspection or a study audit, employees of the Latvian National Accreditation Bureau shall:

61.1. plan their work and receive approval for the times of their visits and inspected sectors with the study director;

61.2. review information regarding the test substance or organism, management structure, physical location of the buildings and the scope of the studies;

61.3. examine the reviews of the previous inspections, location of laboratories, work organisation, reviews on studies, protocols and *Curriculum vitae* of the study personnel.

62. Special attention during evaluation shall be paid to the deviations and violations detected during the previous inspection or evaluation, as well as the measures taken in order to eliminate such deviations or violations.

63. The Latvian National Accreditation Bureau shall inform the laboratory on the date and time of arrival of its employees, the purpose of the visit and the duration of the inspection in order to ensure that the respective personnel and documentation is accessible to employees of Latvian National Accreditation Bureau. If individual documents or reviews must be inspected, the authorised representative shall indicate them before their visit.

64. Upon commencement of a laboratory inspection or a study audit, an employee of the Latvian National Accreditation Bureau shall inform the management and personnel of the laboratory regarding the reason for inspection or study audit to be performed, inspected areas and laboratory departments, studies and documents selected for auditing and employees that must be involved, as well as discuss the course of the laboratory inspection or study audit with the management of the laboratory, including the following issues:

64.1. agreement on access to documentation and, if necessary, copying of the respective documents;

64.2. request of information regarding the management structure, work organisation and employees of the laboratory;

64.3. request of information regarding the conduct of studies that are not subject to this Regulation at the premises of the laboratory, where the inspection or study audit is performed;

64.4. identification of the documents and samples that are required in order to perform the auditing of the selected current or completed studies;

64.5. agreement on the allocation of special premises for inspection of the documents and other actions;

64.6. conduct of interviews with the quality assurance personnel.

65. In order to evaluate whether a laboratory has sufficient number of qualified personnel, staff positions and fixed assets to ensure the variety and quantity of the studies to be conducted, whether the organisation structure is appropriate and whether the management has drawn up a policy of personnel training and health protection in accordance with the requirements of the study conducted at the laboratory, employees of the Latvian National Accreditation Bureau shall examine the following documents:

65.1. plans of the floors of the building;

65.2. the documents on work organisation in administrative and scientific issues;

65.3. *Curriculum vitae* of the employees involved in the studies selected for auditing;

65.4. lists of current and completed studies with information regarding the type of the study, commencement and completion dates, test system, type of administration of the test substance and the given name and surname of the study director;

65.5. personnel health protection plans;

65.6. job descriptions, instructions, personnel training programmes and protocols;

65.7. list of approved methods for the conduct of studies used at the laboratory;

65.8. approved methods for the conduct of studies within the framework of inspected or audited studies.

66. In order to evaluate whether the mechanism provided for by the quality assurance programme sufficiently controls the conduct of studies in accordance with the quality requirements for laboratory work, the employee of the Latvian National Accreditation Bureau shall request the person responsible for quality assurance to demonstrate quality assurance and study control systems and methods, as well as to demonstrate the protocols prepared during the quality assurance procedure.

67. An employee of the Latvian National Accreditation Bureau shall check the following information regarding the quality assurance personnel:

67.1. qualification documents of the quality assurance personnel manager and personnel;

67.2. independence of the quality assurance personnel from the studies;

67.3. work of the quality assurance personnel, while planning and performing inspections, monitoring the pre-determined critical phases of the studies, as well as the resources available for these actions;

67.4. the procedures by which samples are used to control such short-term studies where control of each study is impossible;

67.5. the scope of quality assurance monitoring during the studies;

67.6. quality assurance procedures, checking the conformity of the final review with the original data;

67.7. reports of the quality assurance personnel on the problems that may affect the quality or credibility of studies;

67.8. measures implemented by the quality assurance personnel, if deviations from the requirements of this Regulation are discovered;

67.9. the role of the quality assurance personnel, if the studies or parts thereof are conducted at other laboratories;

67.10. participation of the quality assurance personnel in the checks of approved methods for the conduct of studies, amendments to and specification of these methods.

68. Upon the inspection of a laboratory an employee of the Latvian National Accreditation Bureau shall check whether:

68.1. the test substances, animals, food, samples and other materials of an individual study are situated in a way that prevents mixing thereof with the substances, samples, animals and food of other studies;

68.2. environmental control and monitoring at the storage areas of the test substances, laboratory premises, premises of animals and other biological systems are carried out appropriately;

68.3. the required parasite control procedures are being implemented.

69. Upon assessment of the care for the test biological systems and living conditions at the laboratory, the conformity of such conditions with the laws and regulations laying down the procedures and methods for keeping, use and sale of animals used for experiments and scientific purposes and the welfare requirements for the use of such animals, the procedures and methods for slaughtering thereof shall be checked.

70. If studies that require variety of animal or plant species, as well as microbial or another cell or cell-like systems are conducted at the laboratory, the control of care, living conditions and maintenance shall be determined depending on the test systems.

71. As regards the biological systems an employee of the Latvian National Accreditation Bureau shall check whether:

71.1. the test systems that are indicated in the study plans are being used;

71.2. the test systems have been appropriately identified during the studies, whether protocols or log entries on the receipt of the test systems are present, whether thorough registration of the received, used, transferred or eliminated systems has been performed;

71.3. premises of the test systems, enclosures, cages or tanks have been identified precisely and whether all required information regarding them has been indicated;

71.4. studies on the same animal species or the same biological test system, but with different substances are sufficiently separated;

71.5. the animal species and other biological test systems are sufficiently separated;

71.6. the temperature of the environment of biological test systems, the light and darkness cycle conforms to the study plan or the standardised methods for the conduct of studies;

71.7. records in logs regarding the receipt of test systems, their living conditions, maintenance, care and health status assessment conform to the actual test systems;

71.8. records in logs regarding the examination, quarantine, morbidity and mortality rate of animals and plant test systems, their behaviour, diagnoses and treatment or other similar aspects, in accordance with each biological system, are made;

71.9. conditions for an appropriate disposal or elimination of the test systems at the end of the inspection exist.

72. For biological systems, employees of the Latvian National Accreditation Bureau shall check the following:

72.1. suitability of the premises, equipment and materials to the needs of the test systems and studies;

72.2. quarantine measures for animals and plants that are introduced at the laboratory and the functionality of such measures;

72.3. the procedures by which animals or other elements of test systems shall be isolated, if it is known or a possibility exists that they are either ill or carriers of the disease;

72.4. whether each test system is appropriately controlled and whether respective protocols exist (regarding health, behaviour and other aspects);

72.5. cleanliness of animal cages, feeding racks, water tanks, other tanks and auxiliary equipment;

72.6. suitability and efficiency of the analysis of environmental conditions and the equipment for the maintenance of environmental conditions;

72.7. clearing and removal of animal excrements and waste – whether operations with such waste are performed in a way that reduces smell, spread of diseases and environmental pollution;

72.8. the storage areas of animal feed or similar materials for all test systems – whether these areas are used for storage of inappropriate materials (for instance, test substances, chemical substances for parasite control, disinfection agents) or not and whether these materials are stored separately from the areas where animals are kept or other biological test systems are located;

72.9. the protection of stored feed and bedding materials from decay due to unfavourable weather conditions or as a result of invasions or infections.

73. Upon assessment of the equipment, materials, chemical reactants and samples, it shall be checked whether the laboratory premises and equipment are suitable for the conduct of studies, whether the equipment used is available in sufficient quantity, whether it is sufficiently powerful in order to conform to the requirements of the studies conducted at the laboratory, whether the materials, chemical reactants and samples are appropriately labelled, used and stored, the following shall also be checked:

73.1. cleanliness and work order of the equipment;

73.2. records in the logs regarding the operation, servicing, verification, calibration and validation of measuring equipment and apparatus, including information systems;

73.3. labelling of the materials and chemical reactants, conformity of storage temperatures, conformity with the terms of validity, data on the labels of chemical reactants;

73.4. conformity of the samples with the test system, type of the study and date of collection;

73.5. the impact of the equipment and materials used on the test system.

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74. For physical and chemical systems it shall be checked whether the stability of the test substances and standard substances has been determined, if required by the study plan, whether standard substances indicated in the study plan are used, whether graphs obtained from automatic systems, printouts of automatic recording devices and computer printouts are documented in the logs as original data and submitted to the archives.

75. Upon assessment of the test substances or organisms and standard substances or reference organisms, the procedures for the determination and guaranteeing of the conformity of the identity, efficiency, quantity and composition of such substances with the labelling and the receipt and storage of such substances shall be evaluated, as well as it shall be checked whether:

75.1. written protocols on the receipt of test substances and standard substances, on all actions, sample-taking, use and storage are available, as well as whether the responsible employee is indicated in the protocols;

75.2. the test substances and standard substances are labelled in accordance with the requirements laid down in the laws and regulations;

75.3. the tanks, vessels and containers of the test substances and standard substances are labelled correctly;

75.4. the storage conditions are appropriate for the preservation of the concentration, degree of purity and stability of the test substances and standard substances;

75.5. written protocols or records in the logs on determination of the identity, degree of purity, composition and stability of the test substances and standard substances and, if necessary, on elimination of infections are available;

75.6. there are procedures for determination of homogeneity and stability of the mixtures containing the test substances and standard substance;

75.7. the containers, tanks and vessels containing the mixtures or solutions of the test substances and standard substances are labelled, as well as whether records in the logs on their homogeneity and stability are made;

75.8. samples for control tests from each batch of the test substances and standard substances are available for such studies. The duration of the studies does not exceed four weeks, these samples are stored for appropriate periods of time;

75.9. the methods for mixing of substances ensure avoidance of substance identification errors or unfavourable arbitrary mixing of such substances;

75.10. detailed quantitative and qualitative information regarding the test organism and reference organism – microbiological purity, characteristics, identity, properties, impurity content and quantity of extraneous organisms.

76. Upon assessment of the methods for the conduct of studies, it shall be checked whether:

76.1. copies of the approved methods for the conduct of studies are available at each study site;

76.2. the procedures for the review and updating of the methods for the conduct of studies are determined;

76.3. all amendments to the methods for the conduct of studies or changes therein are approved and the date of approval is indicated;

76.4. the documentation of the drawing up of methods for the conduct of studies is stored;

76.5. methods for the conduct of studies are determined for the following actions:

76.5.1. receipt of the test substances and standard substances, determination of the identity, degree of purity, composition and stability, labelling, sample-taking, use and storage;

76.5.2. use, servicing, cleaning, calibration and checking of measuring equipment, information systems and environmental control equipment;

76.5.3. preparation of reactants and dose;

76.5.4. recording of the data into logs, completing protocols, reporting, storing of records and reviews;

76.5.5. preparation of the premises, areas and zones containing the test systems and environmental control;

76.5.6. receipt, transfer, placement, characterisation, identification and care for the test systems;

76.5.7. actions with the test systems before studies, during studies and after completion of the studies;

76.5.8. removal or elimination of the test systems;

76.5.9. use of parasite control agents and cleaning agents;

76.6. quality assurance programme is available.

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77. Upon assessment of the conduct of studies, it shall be checked whether:

77.1. the study plan is signed by the study director;

77.2. all amendments to study plans are signed by the study director, indicating the date;

77.3. the date when the study plan was co-ordinated by the client that ordered the studies is indicated;

77.4. measurements, observations and inspections conform to the study plan and the approved methods for the conduct of studies;

77.5. the results of measurements, observations and inspections are directly, correctly, precisely and legibly recorded in the logs and signed, indicating the date;

77.6. after amendments to the original data (including data stored on computers) the previous records shall be retained, the reasons for changes, the person responsible for changes and the date when such changes were made shall be indicated;

77.7. the data received from the computer or the data stored on the computer are identified and secured against unauthorised amendments or loss;

77.8. the information systems used for the studies are safe, precise and validated;

77.9. all unforeseeable scenarios in the original data have been studied and evaluated;

77.10. the results that are included in the study reviews are appropriate, complete and correctly reflect the original data.

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78. Upon assessment of the final review, an employee of the Latvian National Accreditation Bureau shall check whether:

78.1. the review is signed by the study director, indicating the date, and thus accepting the liability for the credibility of the studies and certifying that the studies have been conducted in accordance with the requirements of this Regulation;

78.2. the reviews are signed by the respective employees, indicating the date, if the reviews on the studies conducted at other laboratories have been included;

78.3. the review contains the report of the quality assurance personnel and whether it has been signed, indicating the date;

78.4. amendments are signed, if such have been made by the responsible employees;

78.5. a list on the placement of all samples, models and original data in the archives and the premises for the storage of samples is available.

79. Upon assessment of the storage of reports, protocols and reports, the following shall be checked:

79.1. whether a person responsible for the archives is appointed;

79.2. equipment of the archives for the storage of study plans, original data, final reviews, samples and models, personnel training models and practice protocols;

79.3. the procedures for the receipt of the materials submitted to the archives;

79.4. the procedures laying down access to the archives for authorised personnel only, as well as the procedures for the registration of such employees who have been granted access to the original data and other documents;

79.5. records in the log or a card catalogue regarding the materials that are taken from or returned to the archives;

79.6. whether the reviews and the materials are stored for the established time period, whether they are protected against damage by fire, unfavourable weather conditions or other factors.

80. A study audit, which inspects the current or completed studies, may also be included into an inspection of laboratories.

81. The Latvian National Accreditation Bureau (irrespectively of the inspection for ensuring studies) shall conduct special, specific study audits, if they are required by State institutions, in order to assess the applications regarding the test substances or organisms or also to determine the risk posed thereby to human health and environment.

82. Employees of the Latvian National Accreditation Bureau and the invited experts who participate in the auditing of studies have the right to take a decision on both the method of inspection and the degree of inspection. The study audit shall be performed in order to evaluate the progress of the studies, comparing the final review with the study plan, the methods for the conduct of studies, the original data and other materials of the archives.

83. Upon performance of the study audit, an employee of the Latvian National Accreditation Bureau shall:

83.1. become acquainted with job descriptions of the respective study director and responsible specialists, their Curriculum vitae and work experience;

83.2. check whether the number of the personnel trained in the respective areas of the studies to be conducted is sufficient;

83.3. identify the individual items of equipment or special devices used during the studies and check the records in device calibration, operation and maintenance logs;

83.4. check the reviews on the stability of the test substances, analyses of the test substances and recipes, feed analyses;

83.5. check (if possible, by questioning the employees) the work objectives of the selected participants of the studies in order to determine whether they have had sufficient amount of time in order to implement the tasks indicated in the study plan or review;

83.6. compile the copies of all documents on control procedures or significant stages of the studies, including:

83.6.1. the study plan;

83.6.2. the approved methods for the conduct of studies for the time period when the studies were being conducted;

83.6.3. logs, laboratory record books, files, work schedules, printouts of the data stored on computers, calculation checks, if such were used;

83.6.4. the final review;

83.7. for studies involving mammals, check a pre-determined percentage of individual animals starting from the moment they were received until dissection, paying special attention to protocols that refer to:

83.7.1. the body mass of the animals, intake of food and water, formulation of the dose and method of administration;

83.7.2. clinical observations and findings during dissection;

83.7.3. clinical biochemistry;

83.7.4. pathology.

84. After completion of the laboratory inspection or study audit employees of the Latvian National Accreditation Bureau shall discuss the established facts with representatives of the laboratory and the institution conducting the studies in a closed session and draw up a written inspection review.

85. If assessment and study audits reveal only insignificant violations in the work quality of the laboratory, which cannot affect the overall results of the studies, an employee of the Latvian National Accreditation Bureau shall request elimination of such violations and indicate a time period within which the violations must be eliminated. Repeat inspection shall be performed after expiry of the determined time period.

86. If no violations the requirements for the work quality of the laboratory are detected or if they are insignificant, the Latvian National Accreditation Bureau shall:

86.1. issue a certification that the laboratory has been assessed and operates in accordance with the quality requirements of laboratory work. The date of inspection and the inspected studies shall be indicated in certification;

86.2. submit a copy of certification, together with an inspection protocol, to the competent authority, which requested to perform the study audit.

87. If significant violations of the requirements for the work quality of laboratory work that can affect the study results are detected during assessment or study audits, the Latvian National Accreditation Bureau shall:

87.1. indicate incompatibility details or errors that could affect the credibility of the studies conducted at the laboratory in the inspection protocol;

87.2. notify the competent authority, which requested to perform an inspection of the laboratory, that the studies are invalid;

87.3. annul certification that the laboratory has been assessed in accordance with the requirements of this Regulation;

87.4. indicate that a report characterising the violations of the requirements for the work quality of laboratory must be added to the final review.

88. If the study audit has been performed upon request of another institution, the responsible specialist of the Latvian National Accreditation Bureau shall draw up an opinion and send it to the competent authority that ordered the study.

88.[1] The Latvian National Accreditation Bureau shall submit a report on implementation of the requirements for work quality of laboratory in the state to the European Commission regarding each current year until 31 March of the next year. The report shall include a list of the inspected laboratories, indicating the dates when inspection was performed at the respective laboratory and provide a summary on the conclusions drawn during inspections.
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IV. Closing Provisions

89. Paragraph 4 of this Regulation shall come into force with a special Cabinet Regulation.

90. This Regulation shall come into force from 1 January 2004.

Informative Reference to European Union Directives

[18 October 2005]

This Regulation contains legal norms arising from:

1) Directive 2004/9/EC of the European Parliament and of the Council of 11 February 2004 on the inspection and verification of good laboratory practice (GLP) (codified version);

2) 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 their applications for tests on chemical substances (codified version).

Prime Minister A. Bērziņš

Acting for the Minister for Environmental Protection and Regional Development –
Minister for Transport A. Gorbunovs