Standard to be satisfied by test facilities. etc. conducting toxicity investigation (Industrial Safety and Health Law GLP)

(Notification that prescribes the standard to be satisfied bv test facilities, etc. pursuant to provisions of Paragraph 2. Article 34-3 of Ordinance on Industrial Safety and Health)

Notice of the Ministry of Labour No.76, Sept., 1, 1988
Partially revised: Notice of the Ministry of Labour No.13, March, 29, 2000
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Partially revised: Notice of the Ministry of Health, Labour and Welfare No.208, Apr., 18, 2016

(Application)

Article 1. (1) This notification shall apply to test facilities, etc. in which mutagenicity studies or carcinogenicity studies are carried out in the toxicity investigations as provided by Paragraph 1, Article 57-4 of Industrial Safety and Health Law (Law No. 57, 1972, hereinafter called the "Law").

(2) Of the toxicity investigations as provided by Paragraph 1, Article 57-4 of the Law, the standard to be satisfied by test facilities, etc. in which studies other than mutagenicity studies or carcinogenicity studies are carried out shall conform to the provisions as set forth by Director-General, Labour Standards Bureau, Ministry of Health, Labour, and Welfare.

(Definition)

Article 2. As used in this notification, the following terms shall be defined as set forth in the relevant items.

1) "Study sponsor, etc." means a person who entrusts test facilities, etc. with a study to be performed (hereinafter simply called the "study") or a person who submits the study results to Minister of Health, Labour, and Welfare.

2) "Master schedule sheet" means a document that states for all tests conducted in the test facilities, etc. throughout the year, the test system, kind of studies, date when the study begins, state of study progress , name of the study director, and state of final report preparation, for each of the test substances, etc.

3)"Test system" means a system of measurement apparatus tor physical and chemical data and systems of microorganisms, cultured cells, and animals used in the study.

4) "Specimens" mean those collected from the test system for examination or analysis.

5) "Raw data" mean original observation results, etc. such as worksheets, laboratory notes, memoranda, recording charts, magnetic tapes obtained with respect to the study and those necessary for reconstruction and evaluation of the study concerned.

6) "Test substance" means a chemical substance submitted for the study.

7) "Control substance" means a chemical substance used for investigating the standard conditions of the test system.

(Management)

Article 3. (1) For the test facilities, etc., management shall be stationed to carry out the following matters.

1) For each study and before starting the study concerned, to nominate a study director among people with sufficient knowledge and experience on the study concerned.

2) For each study, to allocate sufficient number of people engaged in the study (hereinafter called the "personnel") for performing the study concerned properly and opportunely among people who have received necessary education or training for pursuing the study concerned or who have sufficient job experience.

3) To make sure that the personnel clearly understand the duties and if necessary; to provide education or training to the personnel.

4) To prepare records concerning education, training and job experience and documents to clearly indicate division of duties of the personnel.

5) For each study and before starting the study concerned, to nominate a person responsible for quality assurance among people who have sufficient knowledge and experience on the study concerned (excluding the personnel engaged in the study concerned). However, when the matters provided in Article 5 are carried out by the person responsible for quality assurance nominated by the study sponsor, etc. with respect to the study concerned, the relevant nomination may be substituted by confirming that person responsible for quality assurance.

6) To make sure that all deviations from the standard provided in this notification notified by the person responsible for quality assurance are transmitted to the study director and corrective actions are taken against the relevant deviations by the study director, and the results are recorded.

7) To prepare a quality assurance program.

8) To nominate a person responsible for the archives.

9) To prepare and distribute the standard operating procedures.

10) To prepare the master schedule sheet.

11) To approve the study protocol.

12) To take measures for safety and health of the personnel.

13) Matters necessary for proper conduct of the study in addition to those set forth in the preceding items.

(2) The management shall be the person who supervises and controls the operation in the

relevant test facility, etc.

(Study Director)

Article 4. The study director shall carry out the following with respect to the study related to the nomination.

1) Before starting the study, to prepare the study protocol, to sign and seal or affix signature, and to receive the approval of the management (in the case the study is carried out by commissioning, the sponsor, etc. is included. This applies hereinafter in this article.), to state the date of approval, and to submit the copy of the study protocol related to the approval to the person responsible for quality assurance.

2) When the study protocol is amended, to obtain approval of the management as well as to prepare a document that carries the date of the amendment and the contents of and the reasons for the amendment, and to submit the copy of the relevant document to the person responsible for quality assurance.

3) To carry out the study in conformity to the study protocol and standard operating procedures.

4) When a computer system is used for the study, to make sure that the relevant computer system operates properly in advance.

5) To record all the data obtained with respect to the study and the progress of the study.

6) To prepare the final report and to sign and seal or to affix signature to the report.

7) If the final report must be corrected, prepare the document in which the date of the correction and the contents of and reasons for the correction are stated, and to sign and seal or to affix signature to the document.

8) To give instructions to the personnel with respect to safety and health, to grasp the personnel's health condition, and to take necessary measures as required.

9) To take necessary corrective actions against the deviations from the study protocol or standard operating procedures, and to record the results.

10) Upon completion of the study, to transfer the study protocol, final report, specimens, raw data, and other necessary records, samples, and materials to the archives.

11) In addition to the matters recited in each of the preceding items, matters necessary for proper conduct of the study.

(Person Responsible for Quality Assurance)

Article 5. The person responsible for quality assurance shall carry out the following with respect to the study related to the nomination.

1) To retain copies of the master schedule sheet, study protocols, and standard operating procedures.

2) To make sure that the matters set forth in each of the items of Paragraph 2 of Article 11 are included in the study protocol.
3) To carry out audits and inspections periodically or whenever necessary according to the nature of the study, in accordance with the quality assurance program, in order to make sure that the study is being carried out in compliance with the study protocol and the standard operating procedures and the study results precisely reflect the raw data.
4) When audits or inspections were carried out, to prepare a report that states the date of audit or inspection executed as well as the findings and submit the copy to the management and the study director each time.
5) If any deviation from the study protocol or any deviation from the standard operating procedures are found as a result of the audit or the inspection, to immediately report to the management and the study director and at the same time to record the contents.
6) To make sure that the corrective actions by the study director as provided in Item 9 of preceding Article are properly implemented.
7) To audit the final report. In such event, to make sure that the study method is accurately stated, and the contents of the final report precisely reflect the raw data.
8) To prepare a document that states the date of audit or inspection executed, and the date when the contents and the findings are reported to the management and the study director, and to sign and seal or to affix the signature.

(Personnel)

Article 6. The personnel shall abide by the following.
1) To take necessary care to prevent contamination of the test substance, control substance, and the test system.
2) To quickly and accurately record the raw data.
3) When any deviation from the study protocol or standard operating procedures is found, to report to the study director and to record the contents.
4) To take sufficient care to the safety and health.
5) The personnel who contracts a disease that would influence the execution of the study shall report to the study director of this and receive his/her directions.

(Person responsible for the archives)

Article 7. The person responsible for the archives shall execute the duty to store the following items.
1) Master schedule sheet
2) Study protocol
3) Final report

4) Raw data
5) Reports or records prepared by the person responsible for quality assurance pursuant to the provisions of Item 4 or Item 5 of Article 5
6) Standard operating procedures
7) Records and documents prepared by the management pursuant to the provisions of Item 4, Paragraph 1, Article 3
8) Records prepared pursuant to the provisions of Item 2, Paragraph 4, Article 9
9) Samples of test substance, etc.
10) Specimens
11) In addition to those set forth in each of the preceding items, records, etc. necessary for evaluation of the study

(Facilities)

Article.8. (1) Test facilities, etc. shall be equipped with the following facilities,
1) Facilities for carrying out the studies
2) Facilities for managing the studies
3) Sample and material storage facilities (Archives)
4) Facilities for treating hygienically wastes generated as a result of execution of the study or facilities for storing safely and hygienically the relevant wastes before they are carried out from the test facilities, etc.

(2) The facilities described in the preceding paragraph shall satisfy the following conditions in order to secure appropriate execution of the study
1) The facilities shall have suitable size and construction and are in a suitable location.
2) For each study, the duties related to the study concerned are properly separated for each facilities.

(Equipment)

Article 9. (1) Test facilities, etc. shall be equipped with the machines, apparatus, and other equipment (hereinafter simply called the "equipment") necessary for securing the appropriate conduct of the study.

(2) The equipment shall provide satisfactory performance and shall be given thoroughgoing consideration for securing safety and health.

(3) The equipment shall be properly located so that the operation, inspection, and maintenance are easily carried out.

(4) The equipment shall be managed as provided below.
1) To inspect and maintain periodically and as required in conformity to the standard operating procedures.

2) To record the results each time the inspection or maintenance of the preceding item has been carried out.

(Standard operating procedures)

Article 10. (1) The following shall be included in the standard operating procedure:

1) Matters related to receipt, storage, and handling of the test substance and control substance.
2) Matters related to operation, inspection, and maintenance of the equipment.
3) Matters related to handling of the test system.
4) Matters related to care and management of experimental animals.
5) Matters related to preparation, storage, and identification of reagents.
6) Matters related to observation, measurement, inspection, and analysis.
7) Matters related to data handling, storage, and retrieval.
8) Matters related to confirmation of performance of the computer system.
9) Matters related to safety and health.
10) Matters related to wastes disposal.
11) Matters necessary for execution of the study in addition to those mentioned in each of the preceding items.

(2) The standard operating procedures shall be made available in each area where the study related to the standard operating procedures is implemented.

(Study Protocol)

Article 11. (1) The study protocol shall be prepared for each study before starting the study concerned.

(2) The following shall be included in the study protocol:

1) Title and purpose of the study
2) Name and address of the test facility, etc.
3) Name and address of the sponsor for studies performed under contact
4) Name and post of the study director
5) Date scheduled to start the study and the study period
6) Name, purity, composition, and physicochemical properties of the test substance and the control substance
7) Test methods adopted
8) Environmental conditions of the test system
9) Observation, measurement, inspection, and analysis methods and frequency
10) Solvent or emulsifier used for dissolving or suspending the test and control substances (if the test substance is gas, the gas used for diluting)

11) Statistical technique used for data analysis
12) Method for storing records, samples, and materials
13) Matters necessary for implementing the study in addition to those mentioned in each of the preceding items

(Quality Assurance Program)

Article 12. The matters to be stated in the quality assurance program shall include the following:

1) Matters related to the study audit and inspection.
2) Matters related to the inspection of facilities for implementing the study
3) Matters related to the audit of the final report.
4) Matters necessary for implementing duties related to quality assurance in addition to those mentioned in each of the preceding items

(Conduct of the Study)

Article 13. In conducting the study, the following matters shall be strictly observed.

1) The study shall be carried out in compliance with the study protocol and standard operating procedures under the guidance and supervision of the study director.
2) The data shall be recorded with accurately legible and hardly erasable method, unless otherwise directly entered into the computer. In such event, the personnel who records the data shall state the date of recording the data, and sign and seal or affix signature to the record.
3) When the data is directly entered into a computer, the date of data entry and the personnel responsible for the entry shall be recorded.
4) The data shall be corrected in such a manner that enables the identification of the data prior to the correction, unless the data directly entered in a computer is corrected. In such event, the personnel who corrects the data shall state the date and reasons of correcting the data, and sign and seal or affix signature to the record.
5) When the data directly entered into a computer is corrected, the data shall be corrected in such a manner that enables the identification of data prior to the correction, and the reasons of the correction, the date, and the personnel responsible for the data entry shall be recorded.
6) On the specimens the symbol or No. that can identify the kind of studies and the test system by an appropriate method as well as the sampling date shall be indicated.
7) On containers containing reagents necessary for carrying out studies (including test and control substances. Hereinafter in this paragraph, this same principle applies) and reagents treated for studies, such as being dissolved in a suitable solvent, etc.

(hereinafter in this article, called the "reagents, etc."), the name of the reagent shall be indicated and as required concentration, storage conditions, and expiration date, in order to prevent misuse.

8) Deteriorated or outdated reagents etc. shall not be used.

9) Should any abnormality occur during studies or any unforeseeable phenomenon occur, this shall immediately be reported to the study director and be recorded in detail.

10) When studies are carried out using animals, animals that contract or exhibit symptoms of diseases that would influence execution of the study shall be isolated from other animals and shall not be used in the studies.

(Final Report)

Article 14. (1) The final report shall be prepared for each study.

(2) The final report shall include the following matters.

1) Title and purpose of the study

2) Name and address of the sponsor for studies performed under contract

3) Name and address of the test facility, etc.

4) Name and post of the study director and the personnel

5) Date of starting the study and the date of finishing the study

6) Name, purity, composition, and physicochemical properties of the test substance and control substance

7) Test method adopted

8) Methods and frequency of observation, measurement, examination, and analysis

9) Statistical technique used for data analysis

10) Test results and discussions on the relevant results, and summary of these

11) Factors assumed to have influenced the quality of the study

12) Information on storage of records, samples, and materials

13) Date of preparing the final report

14) Matters necessary for properly evaluating the study results in addition to those mentioned in each of the preceding item

(3) To the final report, the document prepared by the person responsible for the quality assurance pursuant to the provisions of Item 8 of Article 5 shall be attached.

(Storage)

Article 15. (1) The data and materials as set forth in each item of Article 7 (hereinafter called the "records, etc.") shall be stored in the archives.

(2) The records, etc. shall be stored in conformity to the following:

1) Any other persons than the person responsible for the archives or persons authorized

by him/her shall have no access to the archives.

2) When samples and materials are taken in and out or transferred from the archives, this shall be recorded.

3) Consideration shall be given to minimize damage to records, etc. and deterioration.

4) Records, etc shall be put in order by a method convenient for retrieval such as providing them with indices, etc.

(3) When test facilities, etc. suspend or discontinue their services, the records, etc. shall be transferred to the archives of the successor of the operation or the sponsor.

(Retention Period)

Article 16. (1) Retention period of the records, etc. shall be 10 years from the date of notification made pursuant to the provisions of Paragraph 1 of Article 57-3 of the Law for the test substance.

(2) Notwithstanding the foregoing, the retention period shall be the period during which the specimens, test substances, etc. may be retained in a stable condition, for those which are unable to be retained for 10 years.

(Details)

Article 17. In addition to those prescribed from Article 3 to the preceding article, the matters necessary for securing the test quality shall be provided by Director-General of Labour Standards Bureau of Ministry of Health, Labour, and Welfare.