Kiankahatsu 0729 No. 2
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To Prefectural Labour Standards Bureau, Labour Standards Department
Health Chief Officer

Labour Standards Bureau, Ministry of Health, Labour and Welfare
Director, Chemical Hazards Control Division, Industrial Safety and Health Department

Revision of Checklist of the Industrial Safety and Health Act GLP

In order to properly conduct the hazardousness investigation of chemical substances, the Ministry of Health, Labour and Welfare has established a system of certification for GLP compliance. Based on the "Guidelines for Certification of Compliance with Industrial Safety and Health Act GLP concerning Test Facilities, etc. (Notification of the Director-General, Kihatsu No. 123 of March 17, 1989)," the Ministry provides inspections or other measures. Also, we decided to issue the checklist (hereinafter referred to as the “1989 Checklist”) under the “Establishment of the Checklist under the Industrial Safety and Health Act GLP” (Office Communication of Chemical Substance Investigation Division, Industrial Safety and Health Department, Labour Standards Bureau, Ministry of Labour dated June 2, 1989), with an aim of facilitating the implementation of inspections.

Please note that we revised the checklist, abolish the checklist of 1989, and decided on a new checklist as shown in Appendix 1, based on the guidance concerned with GLP inspection for OECD, No. 3 Guidance for GLP Monitoring Authorities Revised Guidance for Conduct of Laboratory Inspections and Study Audits (1995).

We would like to add that, with regard to the test facility which is included in a separate sheet that is currently receiving the GLP compliance certificate, we have notified thereof as shown in Appendix 2.

Attachment 1

Industrial Safety and Health Law GLP check list

(1) Organization and Personnel

a. Purpose of the inspection

To evaluate the following items:

(i) Whether the test facility, etc. is equipped with human resources such as qualified personnel and Study Personnel commensurate with the type and number of tests to be conducted, as well as a support department.

(ii) Whether the organization is appropriate.

(iii) Whether the manager has established policies on the training and health survey of personnel suitable for the tests to be conducted at the facility.

b. Inspection results

Whether the Test Facility Manager creates the following documents: Test facility etc.; building layout; layout Operation management and systematic organization chart of the test facility, etc. Resume of personnel in charge of the test pertaining to the application for compliance certificate of the Industrial Safety and Health Law GLP List of ongoing and completed tests (Special note; (ex.) minor case which will not affect the evaluation result)	APT / IR / INAPT
Whether the list includes the following information for each test; the test type, the dates of study initiation/completion, the test systems, the method of applying test substances and the name of the Study Director.	APT / IR / INAPT
Policy for personnel health management.	APT / IR / INAPT
Duties of the personnel, training program and training records.	APT / IR / INAPT
Inventory of Standard Operating Procedures (SOPs) of the facility.	APT / IR / INAPT
Specific SOPs pertaining to inspections or test subjects or procedures.	APT / IR / INAPT
List of the Study Directors and the sponsors related to a test to be inspected.	APT / IR / INAPT
Whether the workload carried out at the test facility, etc. is appropriate in terms of the number of personnel and layout.	APT / IR / INAPT
Name, title and qualification of the Study Director, the head of the Quality Assurance Unit and other personnel.	APT / IR / INAPT
Whether the SOPs are placed in all relevant areas of testing.	APT / IR / INAPT

(2) Quality Assurance Programme

a. Purpose

To evaluate whether the management mechanism is appropriate for ensuring that the test is conducted complying with the Industrial Safety and Health Law GLP.

b. Inspection results

Qualification of the head of the QA (Reliability Assurance) unit and all QA personnel .	APT / IR / INAPT
Whether the QA Department function independently from other units.	APT / IR / INAPT
Procedures and methods for the QA unit to plan and implement inspections, method of inspection (monitoring) during a key test phase, tools used for inspection/investigation activities by the QA unit .	APT / IR / INAPT
The extent and depth of the QA inspection during the test period.	APT / IR / INAPT
The QA procedures for checking the Final Report to ensure its agreement with the raw data .	APT / IR / INAPT
Whether the Test Facility Manager receives reports from QA concerning problems likely to affect the quality or integrity of a study.	APT / IR / INAPT
The actions taken by QA when any deviations from the Industrial Safety and Health Law GLP are found.	APT / IR / INAPT
The duties taken by QA when any reconfirmation, revision and updating of SOPs is performed.	APT / IR / INAPT

(3) Test facility, etc.

a. Purpose of the inspection

To determine if the test facility, etc. whether indoor or outdoor, is of suitable size, design and location to meet the requirements of the studies being undertaken.

b. Inspection results

Whether the design enables an adequate degree of separation so that, e.g., test substances, pathological specimens, etc. of one study cannot be confused with those of another.	APT / IR / INAPT
Whether environmental management and monitoring procedures on areas (animal and other biological test systems rooms, test substance storage areas, laboratory areas etc.) are prepared and functioning properly. (Special note; minor case which will not affect the evaluation result)	APT / IR / INAPT
Whether the general housekeeping is adequate for the various facilities and that there are, if necessary, pest control procedures.	APT / IR / INAPT

(4) Care, Housing and Containment of Biological Test Systems

a. Purpose of the inspection

To determine whether the test facility, if engaged in studies using animals or other biological test systems, has support facilities and conditions for their care, housing and containment, adequate to prevent stress and other problems which could affect the test system and hence the quality of data.

b. Inspection results

Whether there are facilities adequate for the test systems used and for testing needs.	APT / IR / INAPT
Whether there are arrangements to quarantine animals and plants being introduced into the facility and that these arrangements are working satisfactorily.	APT / IR / INAPT
Whether there are arrangements to isolate animals (or other elements of a test system, if necessary) known to be, or suspected of being, diseased or carriers of disease.	APT / IR / INAPT
Whether there is adequate monitoring and record-keeping of health, behavior or other aspects, as appropriate to the test system.	APT / IR / INAPT
Whether the equipment for maintaining the environmental conditions required for each test system is adequate, well maintained, and effective.	APT / IR / INAPT
Whether animal cages, racks, tanks and other containers, as well as accessory equipment, are kept sufficiently clean.	APT / IR / INAPT
Whether analyses to check environmental conditions and support systems are carried out as required.	APT / IR / INAPT
Whether facilities exist for removal and disposal of waste (animal carcasses, etc.) and refuse from the test systems and that these are operated so as to minimize invasion of parasitic animals, odors, disease hazards and environmental contamination.	APT / IR / INAPT
Whether storage areas are provided for animal feed or equivalent materials for all test systems; that these areas are not used for the storage of other materials such as test substances, pest control chemicals or disinfectants, and that they are separate from areas in which animals are housed or other biological test systems are kept.	APT / IR / INAPT
Whether stored feed and bedding are protected from deterioration by adverse environmental conditions, infestation or contamination.	APT / IR / INAPT

(5) Apparatus, Materials, Reagents and Specimens

a. Purpose of the inspection

To determine whether the test facility has suitably located, operational apparatus in sufficient quantity and of adequate capacity to meet the requirements of the tests being conducted in the facility and that the materials, reagents and specimens are

properly labelled, used and stored.

b. Inspection results

Whether the apparatus is clean and in good working order.	APT / IR / INAPT
Whether records have been kept of operation, maintenance, verification, calibration and validation of measuring equipment and apparatus (including computerized systems).	APT / IR / INAPT
Whether materials and chemical reagents are properly labelled and stored at appropriate temperatures.	APT / IR / INAPT
Whether expiry dates are not being ignored.	APT / IR / INAPT
Whether labels for reagents should indicate their source, identity and concentration and/or other pertinent information.	APT / IR / INAPT
Whether specimens are well identified by correctly labeling the test system, study, nature and date of collection.	APT / IR / INAPT

(6) Test Systems

a. Purpose of the inspection

To determine whether adequate procedures exist for the handling and control of the variety of test systems required by the studies undertaken in the facility, etc. (e.g. biological test systems: cellular and microbic systems, animals, etc.).

b. Inspection results

Whether test systems are as specified in study plans.	APT / IR / INAPT
Whether test systems are adequately and uniquely identified throughout the study; and that records exist regarding receipt of the test systems (test subjects to be used) and document fully the number of test systems received, used, replaced or discarded.	APT / IR / INAPT
Whether housing or containers of test systems (test subjects to be used) are properly identified with all the necessary information.	APT / IR / INAPT
Whether there is adequate separation of each study being conducted on different substances with the biological test systems.	APT / IR / INAPT
Whether there is an adequate separation of studies being conducted on the same animal species (or the same biological test systems) but with different substances.	APT / IR / INAPT
Whether the biological test system environment is as specified in the study plan or in SOPs for aspects such as temperature, or light/dark cycles.	APT / IR / INAPT
Whether the recording of the receipt, handling, or care of the test systems (test subjects to be used) is appropriate to the test systems.	APT / IR / INAPT

Whether written records are created examination, quarantine, morbidity, mortality, behavior, diagnosis and treatment of, if any, animal test systems.	APT / IR / INAPT
Whether there are provisions for the appropriate disposal of test systems (subjects to be used) at the end of tests.	APT / IR / INAPT

(7) Test and Reference Substances

a. Purpose of the inspection

To determine whether the test facility, etc. has procedures prepared to check the following items:

(i) To ensure that the identify, potency, quantity and composition, etc. of test and reference substances are in accordance with their specifications;

(ii) To properly receive and store test and reference substances.

b. Inspection results

Whether there are written records on the receipt (including identification of the person responsible) of the test and reference substances, and for the handling, sampling, usage and storage of both substances .	APT / IR / INAPT
Whether test and reference substances containers are properly labelled.	APT / IR / INAPT
Whether storage conditions are appropriate to preserve the concentration, purity and stability of the test and reference substances.	APT / IR / INAPT
Whether there are written records on the determination of identity, purity, composition, stability, and for the prevention of contamination of test and reference substances.	APT / IR / INAPT
Whether there are procedures for the determination of the homogeneity and stability of mixtures containing test and reference substances.	APT / IR / INAPT
Whether containers holding mixtures (or dilutions) of the test and reference substances are appropriately labelled and that records are kept of the homogeneity and stability of their contents.	APT / IR / INAPT
When the test is of longer than four weeks' duration, whether samples (specimens) from each batch of test and reference substances have been taken for analytical purposes and that they have been retained for an appropriate time.	APT / IR / INAPT
Whether procedures for mixing substances are designed to prevent errors in identification or cross-contamination.	APT / IR / INAPT

(8) Standard Operating Procedures

a. Purpose of the inspection

To determine whether the test facility has written SOPs relating to all the important aspects of the its operations, considering that one of the most important

management techniques for controlling facility operations is the use of written SOPs. These relate directly to the routine elements of tests conducted by the test facility.

b. Inspection results

Whether each test facility area has immediately available relevant, authorized copies of SOPs.	APT / IR / INAPT
Whether procedures exist for revision and updating of SOPs.	APT / IR / INAPT
Whether any amendments or changes to SOPs have been authorized and dated.	APT / IR / INAPT
Whether historical files of SOPs are maintained.	APT / IR / INAPT
Whether SOPs are available for the following test activities : i) receipt; determination of identity, purity, composition and stability; labelling; handling; sampling; usage; and storage of test and reference substances; ii) use, maintenance, cleaning, calibration and validation of measuring apparatus, computerized systems and environmental control equipment; iii) preparation of reagents and dosing formulations; iv) record-keeping, reporting, storage and retrieval of records and reports; v) preparation and environmental control of areas containing the test systems; vi) receipt, transfer, location, characterization, identification and care of test systems; vii) handling of the test systems before, during and at the termination of the study; viii) treatment and disposal of test systems; ix) use of pest control and cleaning agents; x) Quality Assurance Program operations.	APT / IR / INAPT

(9) Performance of the Study

a. Purpose of the inspection

To verify that written study plans exist and that the plans and the conduct of the study are in accordance with the Industrial Safety and Health Law GLP.

b. Inspection results

Whether the study plan was signed by the Study Director.	APT / IR / INAPT
Whether any amendments to the study plan were signed and dated by the Study Director.	APT / IR / INAPT
Whether the date of the agreement to the study plan by the sponsor was recorded (where applicable).	APT / IR / INAPT
Whether measurements, observations and examinations were in accordance with the study plan and relevant SOPs .	APT / IR / INAPT

Whether the results of these measurements, observations and examinations were recorded directly, promptly, accurately and legibly and were signed (or initialed) and dated.	APT / IR / INAPT
Whether any changes in the raw data did not obscure previous entries.	APT / IR / INAPT
Whether the reason for the change in the raw data and identified the person responsible for the change and the date such change was made was specified.	APT / IR / INAPT
Whether computer-generated or stored data have been identified.	APT / IR / INAPT
Whether the procedures to protect them against unauthorized amendments or loss are adequate.	APT / IR / INAPT
Whether the computerized systems used within the study are reliable, accurate and have been validated.	APT / IR / INAPT
Whether any unforeseen events recorded in the raw data have been investigated and evaluated.	APT / IR / INAPT
Whether the results presented in the reports of the study (interim or final) are consistent and complete and that they correctly reflect the raw data.	APT / IR / INAPT

(10) Reporting of Study Results

a. Purpose of the inspection

To determine whether final reports are prepared in accordance with the Industrial Safety and Health Law GLP.

b. Inspection results

Whether it is signed and dated by the Study Director, under the responsibility of such Study Director, to indicate acceptance of responsibility for the validity of the study and confirming that the study was conducted in accordance with the Industrial Safety and Health Law GLP.	APT / IR / INAPT
If reports from co-operating studies are included in the final report, whether it is signed and dated by the principal scientists who oversaw such studies.	APT / IR / INAPT
Whether a statement of Quality Assurance unit is included in the report and signed and dated.	APT / IR / INAPT
Whether any amendments in the final report were made by the responsible personnel.	APT / IR / INAPT
Whether the final report include a list the archive location of all samples, specimens and raw data.	APT / IR / INAPT

(11) Storage and Retention of Records

a. Purpose of the inspection

To determine whether the facility has generated adequate records and reports in compliance with the Industrial Safety and Health Law GLP, and whether adequate

provision has been made for the safe storage and retention of records and materials.

b. Inspection results

Whether a person has been identified as responsible for the archive.	APT / IR / INAPT
The archive facilities to store study plans, raw data (including that from discontinued studies under the Industrial Safety and Health Law GLP), final reports, samples and specimens and records of education and training of personnel.	APT / IR / INAPT
Whether the procedures for retrieval of archived materials are appropriate.	APT / IR / INAPT
Whether the procedures whereby access to the archives is limited to authorized personnel and records are kept of personnel given access to raw data, slides, etc. are given.	APT / IR / INAPT
Whether a list is maintained of materials removed from and returned to, the archive facilities for the storage.	APT / IR / INAPT
Whether records and materials are retained for the required or appropriate period of time and are protected from loss or damage by fire, adverse environmental conditions, etc.	APT / IR / INAPT