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To: Director-General of Prefectural Labour Standards Bureau

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare

Development of Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc.

The “Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc.” were stipulated as shown in the Appendix, subject to the provisions to be developed subject to Kihatsu No. 602, I, 2.7 (3) and (4) dated September 16, 1988. We hereby decided to carry out a GLP certification of compliance for the test facility, etc. on April 1 and thereafter.

Appendix

Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc.

No. 1. Purpose

To implement the provisions of Articles 34-3 and 34-4 of the Ordinance on Industrial Safety and Health (Ordinance of the Ministry of Labour No. 32 of 1972, hereinafter referred to as the "Ordinance"), this Guidance aims to determine relevant matters for toxicity tests (hereinafter simply referred to as "toxicity inspection" that are judged "acceptable" in No. 3, 3. (1) hereunder as conforming to the Industrial Safety and Health Law GLP; hereinafter the same) under the provisions of Article 57-4, Paragraph 1 of the Industrial Safety and Health Law (Act No. 57 of 1972; hereinafter simply referred to as "toxicity inspection") by certifying compliance (refers to the conformity inspection as provided in No. 3, 2. (1); inspection or judgement certifying compliance with the Industrial Safety and Health Law GLP; hereinafter the same) with the Industrial Safety and Health Law GLP (refers to the standards (Notification of the Ministry of Labour No. 76 of 1988; hereinafter the same) to be applied to test facilities, etc. based on the provisions of Article 34-3, Paragraph 2 of the Ordinance on Industrial Safety and Health; hereinafter the same).

No. 2. Tests for inspection

The tests to certify conformity under the Guidelines shall be mutagenicity and carcinogenicity studies, as specified under Article 1, Paragraph 1 of the Industrial Safety and Health Law GLP.

No. 3. Procedures to monitor compliance

1. Procedures for the application

(1) The person who intends to receive compliance monitoring applies to Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare by submitting the application by Form 1 (hereinafter referred to as "application form"), together with the documents shown in (2) below, for each facility of mutagenicity studies and carcinogenicity studies. In this case, the person who intends to receive the certification of compliance by, and before a designated date shall apply at least 6 months before the relevant dates.

(2) It is necessary for the documents attached to the application form (hereinafter referred to as "document attached") to contain the following contents:

a. Date of establishment of the test facilities, etc., main body of establishments, site areas, stories and the total floor area of the building in which the facilities, etc. occupied for investigation of toxicity are located and articles of incorporation or acts of endowment for a corporation

b. Plan view of the test facilities, etc. and layout of main facilities and equipment

c. Name, quantities, type number of the main equipment and apparatus to be used for the tests on the application.

d. Organizations (including personnel composition) of the test facilities, etc. names, responsibilities of the management and other main persons, and their curriculum vitae, research

careers, name of academic societies, or learned societies where they belong to.

e. Rules related to internal inspections and implementation states of the internal inspection for the last three years

f. Implementation states of education and training of the personnel for the last three years

g. Execution states of the tests on the application for which certification of compliance is intended to receive for the last ten years

h. A copy of standard operating procedures used for the tests on the application, procedures of making, revising and scraping standard operating procedures and a catalog of titles of standard operating procedures

i. Stream of tested substances, positive controls, and wastes (including drainage), etc.

(3) The application form and the original and copy documents attached above are submitted in duplicate.

2. Conformity inspection

(1) The compliance monitoring is carried out, in principle, by the examination of the application form and documents attached (if additional documents are requested in (2) below, relevant documents are also included) and by inspection of test facilities, etc. related to the relevant applications.

(2) If additional documents come to be in need when implementing inspection, these relevant documents shall be requested to submit.

(3) Inspections associated with certification of compliance shall be carried out pursuant to the provisions set forth in Appendix “Guidelines for Inspection on Industrial Safety and Health Law GLP (hereinafter referred to as “inspection guidelines”).

(4) Submission of Explanation Papers, etc. and Advice from Scholars and Experts

a. Submission of Explanation Papers, etc.

As a result of compliance monitoring, Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare shall request the applicants to submit explanation papers or evidence or shall request measures for improvement, before performing the evaluation of 3. (1) below, with noticing relevant points to be improved (in case immediate improvement is difficult, submit a plan for improvement; hereinafter the same) to the test facilities, etc. and with full consideration of giving enough time for the applicants to respond to it, with designated deadline less than 30 days, provided that items are found that are deviated from or can be deviated from the Industrial Safety and Health Law GLP (excluding minor particulars where the credibility of the investigation of toxicity performed in the test facilities, etc. is not judged to be spoiled).

b. Asking Advice to Scholars and Experts

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare shall ask advice to inspection experts or other scholars before performing the evaluation of 3. (1) below, if it is recognized necessary.

3. Judgment

(1) Based on the result of compliance monitoring, the Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare shall (if explanation documents or evidence was requested to be submitted or measures for improvement or the report of the result was requested be submitted on 2 (4) a above; or if hearing was implemented on 2(4)b above; those results are also included) comprehensively evaluate the compliance of the test facilities, etc. with the Industrial

Safety and Health Law GLP and determine which of the following categories applies. However, if the judgment is not appropriate because measures for improvement based on the improvement plan are not completed in the test facilities, etc., judgment can be suspended and also necessary action shall be taken on 2(4) above with notifying it to the applicant.

a. In compliance (refer to being complied with the Industrial Safety and Health Law GLP)

b. Not in compliance (refers to all or part of the facilities, etc. being not complied with the Industrial Safety and Health Law GLP and the credibility of the investigation of toxicity performed in the facilities, etc. is judged to be spoiled.)

(2) Director-General of Labour Standards Bureau of Ministry of Health, Labour, and Welfare judges "Not in compliance" in (1) above in the following cases:

a. When refusing inspection, interfering with it, or not responding or making false replies to the inquiries on inspection.

b. When refusing, not submitting by designated dates, not reporting, submitting false explanation papers, or reporting falsely, despite that explanation papers or evidence are requested to submit or measures for improvement and reports of the result are requested to submit on 2 (4) a.

c. In case where judgment is suspended due to the proviso of (1) and where the suspension of judgment lasted approximately six months. This case does not apply when inevitable reasons exist, for which applicants cannot be blamed.

4. Notification

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare shall, in principle, notify the applicant to certify compliance of the results as prescribed in the above paragraph 3 using Form 2 within six months of the application. The date of certification of compliance of the test facilities, etc. (refers to the date of receiving certification of compliance) shall be the date of inspection (the last date of the inspection when inspection had been performed for more than 2 days), in case the test facilities, etc. are judged to be complied with the Industrial Safety and Health Law GLP and received certification of compliance.

No. 4. Effect of certification of compliance

1. Effect of certification of compliance arises from the date of certification of compliance and it shall lose effect when three years has passed since the relevant date of certification of compliance.
2. When the facilities, etc. receive a new certification of compliance within three years having elapsed since the date of certification of compliance, the former certification of compliance shall only be superseded by the new certification of compliance the previous day before the compliance date of the latter.

No. 5. Notification on change

The person who received the certification of compliance with the Industrial Safety and Health Law GLP (hereinafter referred to as "complied institution") notifies any change in the following items to Director-General of Labour Standards Bureau of Ministry of Health, Labour, and Welfare without delay by Form 3.

1. Name and the address of the complied institution; in the case of a corporation, the name the

representative;

2. Name and address of test facilities, etc. receiving certification of compliance;
3. Among the organization, personnel, facilities, equipment, apparatus, administration, management, etc. of the test facilities, etc., those items which may influence the credibility of test items for which certification of compliance has been received, if changed.

No. 6. Notification of Discontinuation

Complied institutions shall notify to Director-General of Labour Standards Bureau of Ministry of Health, Labour, and Welfare without delay by Form 4 of discontinuation of a part or whole of the services related to the test items for which the certification of compliance has been received.

No. 7. Cancellation of Certification of Compliance

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare cancels the certification of compliance when the complied institution would apply to any of the following cases. In case of cancellation, explanation papers are requested to submit in advance on No.3, 2 (4) a.

1. When test facilities, etc. of complied institutions are found to be deviated from the Industrial Safety and Health Law GLP and the credibility of the investigation of toxicity performed in the facilities, etc. has come out to be spoiled.
2. Based on No. 8 hereunder, when not reporting or reporting falsely, despite requesting reports, or when refusing to give consent for on-site inspections unreasonably, or interfering with said inspection, despite accepting the same.
3. When the test facilities, etc. were awarded a certification of compliance unfairly.

No. 8. Reporting and on-site inspection

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare shall, when deemed necessary to implement an inspection of toxicity adequately, request that a compliant institution report necessary matters, or have the personnel conduct an on-site inspection of the test facility, etc. subject to the consent of said compliant institution and perform necessary inspections. In this case, the on-site inspection shall be performed on the inspection guidelines.

No. 9. Reporting to the OECD Secretariat, etc.

Reporting to the OECD secretariat and other necessary measures are made when certification of compliance is canceled or when test facilities, etc. of complied institutions are found to be deviated from the Industrial Safety and Health Law GLP and the credibility of the investigation of toxicity performed in the facilities, etc. has come out to be spoiled on No. 7 above.

No. 10. Others

Clerical works related to certification of compliance with the Industrial Safety and Health Law GLP pursuant to these guidelines shall be carried out at Chemical Hazards Control Division, Industrial Safety and Health Department, Labour Standards Bureau, Ministry of Health, Labour and Welfare.

Appendix

Guidelines for Inspection on Industrial Safety and Health Law GLP

The inspection specified under No. 3, 2. (1) of the Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc. shall be conducted as set forth below:

1. Inspection team

In principle, an inspection shall be carried out by personnel from the Labour Standards Bureau, Ministry of Health, Labour and Welfare (inspectors of institutions providing toxicity testing services and, if necessary, those with expert knowledge on the test related to the application and the inspection team comprising personnel commissioned under the "Rules on Inspection Experts under the Industrial Safety and Health Law GLP" (hereinafter simply referred to as the "inspection team")).

2. Consent of inspection

The inspection shall be carried out subject to the consent of the applicant.

3. Implementation of inspection

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare shall inform the applicant in advance of the date of inspection and have the inspection team conduct an inspection to certify compliance at the test facility, etc. to be inspected.

4. Procedures of inspection

(1) In principle, inspection is carried out according to the following procedures:

a. Understanding the overall management status of the test facility, etc.;

b. Inspection of the test facility, etc., check of the maintenance status of facility equipment, etc.;

c. On-site inspection related to the tests on the application;

d. Confirmation of maintenance status of SOPs, test plan, quality assessment program and final report, storage;

e. Confirmation of activity status of the units overseeing quality assurance work;

f. Check and reference of the tests on application procedures, such as raw data, test items such as subject substances, specimen and others necessary to certify compliance; provided, however, that if it is deemed difficult to prepare during the inspection, they shall be submitted promptly after the inspection.

(2) When determining a need for the test facility, etc. to comply with the Industrial Safety and Health Law GLP during the inspection, the inspection team shall have it corrected on the spot or give instructions for improvement and request a report thereof.

Form 1

Application for Compliance Certificate on the Test Facility
(Application for Inspection on Safety Studies)

Date:

To: (Note 1)

Address (Location of the head office, in case of a corporation)
Name (Company name and representative's name, in case of a corporation,)
Contact (Phone/fax number, email address, affiliated department/name)

We hereby apply for the certificate of the test facility (field investigation) with the attached documents as shown below:

1. Legal basis (Note 2)
2. Name of the test facility
3. Location of the test facility
4. Test field or items (Note 3)
5. In the case where certification of compliance was received previously, the certification date, test field or items (Note 4)

(Note 1) Please select from the following depending on the law based on the application:
Act on Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA Act"): Chief Executive of the Pharmaceuticals and Medical Devices Agency;
Agricultural Chemicals Control Act: Director-General of the Food Safety and Consumer Affairs Bureau. Ministry of Agriculture, Forestry and Fisheries;
Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (hereinafter referred to as "Chemical Substances Control Act"): Director-General of Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry for degradation and bioconcentration tests, Director-General of the Labour Standards Bureau of the Ministry of Health, Labour and Welfare for toxicity tests, Director-General of the Environmental Policy Bureau Ministry of the Environment for animal and plant toxicity tests;
Industrial Safety and Health Law (hereinafter referred to as the "Industrial Safety and Health Law"): Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare.

(Note 2) Please select from the following depending on the law based on the application:
PMDA Act: Please specify "pharmaceuticals or medical devices" and then "4 (1) Guidelines for Inspection of Pharmaceutical GLP or Medical Device GLP under the Industrial Safety and Health Law." When submitting applications at the same time, applications for pharmaceutical and medical devices must each be in writing, respectively;
Agricultural Chemicals Control Act: "Appropriate implementation of tests on toxicity and persistence

of agricultural chemicals" 4.;

Chemical Substances Control Act: "Guidelines to certify Compliance of Test Facilities, etc." 2.;

Industrial Safety and Health Law: "Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc." No. 3

(Note 3) (1) When it is based on the Agricultural Chemicals Control Act, please specify "4. Test field" and when it is based on the PMDA Act, the Chemical Substances Control Act, or the Industrial Safety and Health Law, please specify "4. Test items."

In case it is based on the Chemical Substances Control Act (excluding the degradation test) and when applying for a certificate of compliance targeting part of the tests to determine bioconcentration, toxicity, etc. or animal and plant toxicity, please specify the tests on the application procedures such as "bioconcentration test (distribution coefficient test of chemical between 1-octanol and water)," "toxicity test (28-day repeated dose toxicity test)" and "animal and plant toxicity test (algae growth inhibition test)".

(2) When it is based on the PMDA Act, please specify the possible test items.

(3) Examples of test items to be specified:

Toxicity test (single dose toxicity test (acute), repeated dose toxicity test)

(Note 4) When it is based on the PMDA Act, please state the date of the past GLP conformity investigation (or GLP inspection by the Ministry of Health, Labour and Welfare) and the date of issue of the written certificate of compliance (or evaluation result notification).

(Note) The form shall be JIS A4 in size.

Form 2

No.
Date:

To: Applicant for Compliance Certificate

Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare

Certification of Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc.

We hereby notify the conclusion of the subject pursuant to the application dated (dd/mm/yy).

1. Name of the test facility for certification of compliance

2. Name of the test items for certification of compliance

3. Date of Inspection (dd/mm/yy- dd/mm/yy)

4. Evaluation result

5. Remarks

Note: The date of certification of compliance of the test facilities, etc. shall be the date of inspection (the last date of the inspection when inspection had been performed for more than two days).

Form 3

Report on Changes in the Test Facilities

Date:

To: Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare

Address:
Name Seal

Based on the provision of No. 5 of the Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc., we hereby report the following:

1. Name and location of the test facility, etc.

2. The latest date of certification of compliance and its number

3. Details of the changes

4. Reason for the changes

5. Date of the changes

Note 1: The form shall be JIS A4 in size.
Note 2: Please specify the location of the principal office, in case of a corporation
Note 3: Please specify the names of the corporation and its representative, in case of a corporation.

Form 4

Report on Abolishment of the Test Facilities

Date

To: Director-General of Labour Standards Bureau of Ministry of Health, Labour and Welfare

Address:
Name: Seal

Based on provision No. 6 of the Guidelines to certify Compliance with Industrial Safety and Health Law GLP concerning Test Facilities, etc., we hereby report the following:

1. Name and location of the test facility, etc.

2. The latest date of certification of compliance and its number

3. Scope of the services to be abolished

4. Reasons for the abolishment

5. Date of the abolishment

Note 1: The form shall be JIS A4 in size.
Note 2: Please specify the location of the principal office, in case of a corporation.
Note 3: Please specify the names of the corporation and its representative, in case of a corporation.