On the Handling of Test Results to be used as Judgment Data in Evaluation, etc. of New Chemical Substances

(November 21, 2003;
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When handling test results to be used as evaluation data under article 4 and article 4-2 of the "Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Act No. 117, of 1973)" (hereinafter referred to as the "Act") (including a case where it is applied mutatis mutandis to article 5-2 of the Act; the same shall apply hereinafter) and when handling test results generated by studies of hazardous properties under paragraph (1) of article 5-4, paragraph (1) of article 24, and paragraph (1) of article 25-3 of the Act, the following handling points shall apply from April 1, 2004.

In addition, for a test facility where flora-and-fauna toxicity tests prescribed in 1(1)(iv) of the separate attachment, "Implementation Points for Confirming Standard Compliance of Test Facility" (hereinafter referred to as the "Implementation Points for Confirming Standard Compliance") are conducted, it shall be possible to conduct application from the test facility in accordance with examples of paragraph (2) of the Implementation Points for Confirming Standard Compliance and inspection in accordance with examples of paragraph (3) of the Implementation Points for Confirming Standard Compliance even before April 1, 2004. In these cases, the application or inspection shall be deemed to be conducted on April 1, 2004 under the same provisions.

Also, "On the handling of test results to be used as judgment data in evaluation, etc. of new chemical substances (dated November 18, 1988) (Notification of Director General, Public Health Bureau, No. 39, November 18, 1988; Notification of Director General, Basic Industries Bureau, Ministry of Ministry of Economy, Trade and Industry, No. 822, 1988)" (hereinafter referred to as the "former handling points") was abolished on March 31, 2004.

Account

Handling Points of Test Results

1. General Provisions

(1) Among test results to be used as judgment data under article 4 and article 4-2 of the Act and those generated by tests for study of hazardous properties under paragraph (1) of article 5-4, paragraph (1) of article 24, and paragraph (1) of article 25-3 of the Act, the test results (hereinafter referred to as the "Standards (Chemical Substances GLP) application test results") generated by conducting tests performed for obtaining information for article 1 of the "Ministerial Ordinance Specifying Items Concerning the Testing of New Chemical Substances and the Study of the Hazardous Properties of Type I Monitoring Chemical Substances and Type II Monitoring Chemical Substances (Prime Minister's Office; Ministry of Health and Welfare, and Ministry of International Trade and Industry, No. 1 of 1974)" (limited to tests prescribed in paragraph 1(1) of the separate attachment, "Implementation Points for Confirming Standard Compliance of Test Facility"), tests under

article 2, article 2-2, or article 2-3 of the Ordinance, tests for study under article 2-4 or article 3 of the Ordinance, and tests for study under article 1 of the "Ministerial Ordinance Specifying Items Concerning the Study of the Hazardous Properties of Type III Monitoring Chemical Substances (Ministry of Economy, Trade and Industry, Ministry of the Environment, No. 10 of 2003)" must be the test results (hereinafter referred to as the "standard compliance test results") generated and compiled by a test facility that complies, in principle, with the "Standard for the test facility conducting tests concerning new chemical substances, etc." (hereinafter referred to as "the Standards") prescribed in “On the standard for the test facility conducting tests concerning new chemical substances, etc. (Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, No. 1121003, November 21, 2003; Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry, No. 3, November 17, 2003; Environmental Policy Bureau, Ministry of the Environment, No. 031121004)” from April 1, 2004.

In addition, test results generated by tests (except for flora-and-fauna toxicity tests prescribed in 1(1) <4> of the Implementation Points for Confirming Standard Compliance) conducted before March 31, 2004 shall be handled according to the former handling points.

(2) In the case where standard application test results are attached to a notification of manufacture, import, or export of new chemical substances pursuant to article 3 or article 5-2 of the Act or to a report of a study result on hazardous properties under paragraph (1) of article 5-4, paragraph (1) of article 24, or paragraph (1) of article 25-3 of the Act, information on the following matter shall be also attached.
However, in the case where the standard application test results are handled as standard compliance test results pursuant to the provision of 2(2) or (3) of this paper, it is not necessary to attach the information (i) or (ii) below:

(i) a summary of the test facility including the name, location, establishment date, the articles of incorporation or articles of endowment, organization, personnel structure, area of the site, the number of the story and the gross floor area of the building that houses equipment etc., and the layout, type and details, etc. of the equipment and instrument, etc. In addition, a booklet describing general appearance of the building, major equipment, etc., in the case where the booklet exists;

(ii) the name of persons (including the study director) who were engaged in the said test and their work responsibility, personal histories, research careers, and the name of academic societies or academic organizations they belong to;

(iii) the name of the quality assurance personnel of the said test and the name of division they belong to; and

(iv) a statement, authorized by the test facility management or study director, ensuring that the said test results have been generated and finalized in compliance with the Standards (Chemical Substances GLP Standards). (In the case where the said test results have been generated in a foreign state, GLP standards of the said state will be acceptable if the GLP standards are recognized as compliant with the principles of OECD-GLP.)

2. On the Inspection, etc.

(1) The Director-General, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare; the Director-General, Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry; or the Director-General, Environmental Policy Bureau, Ministry of the

Environment shall conduct an inspection to the test facilities or Study Audit for the Standards (Chemical Substances GLP Standards) application study results, or shall require reports from the test facility management of test facilities (hereinafter referred to as the "inspections") in order to confirm the reliability of the Standards (Chemical Substances GLP Standards) application on study results.

(2) For standard application test results, those generated by a test facility which has received a confirmation compliance with the Standards pursuant to the separate attachment, "Implementation Points for Confirming Standard Compliance of Test Facility" before the beginning of the said study, has received confirmations continuously at intervals of under 3 years within the last 3 years, and has submitted necessary notifications during the term, shall be handled in principle as the standard compliance test results.

Moreover, test results generated by a test facility whose compliance with the Standard was already confirmed pursuant to the separate attachment, "Implementation Points for Confirming Standard Compliance of Test Facility", and were subject to the Study Audit that accompanies an inspection for the said confirmation of the compliance shall be similarly handled as the standard compliance test results.

(3) In the case where test results generated by a test facility in a foreign state are accompanied by document (hereinafter referred to as a "certificate of confirmation") certifying that a government organization or an equivalent organization thereof the said state has already confirmed the compliance of the said test facility with the GLP standards (that is recognized as compliant with the principles of OECD-GLP) of the said state within 3 years before the beginning of the said test, the said test results shall be handled in principle as the standard compliance test results.

However, in the case where test results have been generated by a test facility whose compliance with the Standard was already confirmed by a competent authority in the European Community listed in Section II, Part B of the "Sectoral Annex on Good Laboratory Practices (GLP) for Chemicals" of the "Agreement on Mutual Recognition between Japan and the European Community", the test results shall be handled in principle as the standard compliance test results irrespective of the presence or absence of an attachment.

(4) Note, however, that both (2) and (3) above are not intended to prohibit inspection, etc. to confirm reliability of test results. Hence, in the case where the test results are recognized as noncompliant with the Standard by inspections, the test results cannot in principle make the standard compliance test results.

3. On the handling, etc. of standard application test results that do not partly comply with the Standards

(1) In the case where standard application test results that do not partly comply with the Standards are submitted as data, a person (hereinafter referred to as "notification person, etc.") who submits the concerned notification of manufacture, import, or export of new chemical substances or the concerned study report on hazardous properties shall be asked to submit data demonstrating that the noncompliance portion with the Standards does not influence the reliability of the test results or that the influence is within the allowable range. Moreover, inspections shall be conducted if needed. In the case where the said test results are recognized as reliable by the inspection, etc., the said test results shall be handled as data for evaluation, etc.

In this case, if the test results have been generated by a test facility in a foreign state, and if a government organization or an equivalent organization thereof the said state submits results of inspection, etc. that recognize the said test results as reliable, the said test results shall be handled similarly as data for evaluation, etc.

(2) Test results generated by a test facility in a foreign state, for which it is impossible or extremely difficult to attach a certificate of confirmation prescribed in 2(3) above or either data prescribed in 3(1) above or results of inspections because of the absence of GLP standards in the state or for other proper reasons, shall be handled according to the examples described previously.

4. Exclusion from Data of Evaluation, etc.

In the case where it is judged that reliability of test results cannot be confirmed or is reduced, the said test results may be excluded from evaluation data of notification of manufacture, import, or export of new chemical substances concerning the said test, or from judgment data of study results of hazardous properties concerning the said test, because the case falls under either (a) or (b) below:

(a) in the case where the data prescribed in 3 (1) above is not submitted by the notification person, or where the data is recognized as inadequate if submitted; or

(b) in the case where the concerned test facility, etc. refuses to undergo an inspections pursuant to the provision of 2 or 3 (1) above, or where reliability of the said test results is recognized as reduced by judgment on the results of inspections (in the case where the said test was conducted by a test facility in a foreign state, results of inspections, conducted by a government organization or an equivalent organization thereof the said state.)

5. On the relationship between data on attached test results and the final report prescribed in the Standards in the case of a notification of a new chemical substance or a study report of hazardous properties

The Standards (Chemical Substances GLP) application test results are attached on the occasion of submitting a notification of a new chemical substance or a study report of hazardous properties shall not differ in content from what is summarized as the final report.

Separate Attachment

Implementation Points for Confirming Standard Compliance of Test Facility

When confirming whether a test facility is at a level that complies with the Standard (hereinafter referred to as "confirmation"), the Director-General, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare; the Director-General, Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry (METI); or the Director-General, Environmental Policy Bureau, Ministry of the Environment shall follow the procedure below.

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1. Test Items being subject to confirmation

(1) Confirmation shall be conducted for each test item of the tests (i) to (iv) below. As for tests (ii) to (iv), it shall be possible that only part of the test items is subject to the confirmation, as appropriate:

(i) biodegradation test of a chemical substance by using microorganisms, etc. (hereinafter referred to as "biodegradation test");

(ii) bioconcentration test in fish and shellfish and 1-octanol/water partition coefficient determination test of a chemical substance, (hereinafter referred to as "bioconcentration, etc. test");

(iii) chronic toxicity study, reproduction/developmental toxicity test, prenatal developmental toxicity study, mutagenicity test, carcinogenicity study, toxicokinetics, pharmacology study, and repeated dose toxicity study in rodents concerning a chemical substance (hereinafter referred to as "toxicity, etc. test"); and

(iv) avian reproduction test, alga, growth inhibition test, daphnia acute immobilization test, fish, acute toxicity test, daphnia reproduction test, fish, early-life stage toxicity test and other tests to examine the effect on the inhabitation and/or growth of flora and fauna in the human living environment deemed especially necessary by the Minister of Economy, Trade and Industry and the Minister of the Environment, from the perspective of the state of persistence in the environment of Type III Monitoring Chemical Substances(hereinafter referred to as "flora-and-fauna toxicity test").

2. Application Procedure

(1) Those who intend to receive a confirmation shall submit an application document on the test facility and each test item, separately, and one of its copy to the following competent director-general by using the Form 1. However, in the case where biodegradation test and bioconcentration, etc. test are conducted in the same test facility, the same application document can be used:

(i) for application concerning biodegradation test and bioconcentration, etc test : the Director-General, Manufacturing Industries Bureau, Ministry of Economy, Trade and Industry (METI);

(ii) for application concerning toxicity, etc test : the Director-General, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare; and

(iii) for application concerning flora-and-fauna toxicity test: the Director-General, Environmental Policy Bureau, Ministry of the Environment.

In addition, those who intend to receive the confirmation by a specific date shall submit these application documents 6 months before the said specific date.

(2) An application document and its copy described (1) above shall respectively accompany information on the following matter:

A the establishment date, establishment entity, articles of incorporation or articles of endowment, area of the site, and number of the story .and the gross floor area of the building that houses equipment, etc.

B the plane view of the test facility, and the layout of main facility, equipment, instrument, etc.;

C the name, number, model number, etc. of main equipment and instrument used in the test concerning the application;

D the organization and personnel structure of the test facility, name of test facility management and other main staff, their work responsibility, personal histories, research careers, and name of academic societies or academic organizations they belong to;

E the regulation concerning the internal audit, and implementation status of the internal audit during the last three years;

F the implementation status of education and training of the staff during the last three years; and

G the implementation status of tests of test items concerning the application during the last decade.

3. Confirmation

(1) Confirmation shall be conducted by evaluating application document and submitted data described in 2 above and inspection of the test facility concerning the application.

However, as for a test facility that has received confirmation pursuant to this Handling Points, it is possible to entirely or partially omit the inspection concerning tests, excluding already confirmed tests.

Moreover, as for a test facility that complies with the GLP standards complied with other regulations, etc. that are recognized as equivalent to the principles of OECD-GLP, it is possible to entirely or partially omit the inspection in the case where the competent director-general recognizes as appropriate.

(2) Inspection shall be conducted by dispatching a person, who is nominated under the name of the competent director-general, to the said test facility.

(3) In the case where the test facility is recognized as compliant with the Standards by the inspections described (1) above, the competent director-general shall notify the effect of the confirmation to the applicant. In the case where the test facility is recognized as noncompliant with the Standards, the competent director-general shall notify the effect of the confirmation to the applicant.

4. Notification of Change

In the case where there is any change in the following matter, those who have received the notice of confirmation described 3 above shall submit a notification of the change to the competent director-general, without delay, by using Form 2:

(1) the applicant’s name. In the case where the applicant is a corporation, any one of representative's name, test facility’s name, or test facility’s address; and

(2) among organization, personnel, facility, equipment, instrument, maintenance, management, etc, whatever that is recognized to potentially effect reliability of test results concerning an item of the confirmed test upon modification thereof.

5. Notification of Abolition

In the case where a test facility entirely or partially abolish business (including remake, transfer, full-renovation of a building of the test facility, etc.) concerning confirmed test items, those who have received a notice of the confirmation described 3 above shall submit a notification of the abolition to the competent director-general, without delay, by using Form 3.

(Reference) Competent Authorities of the European Community (as of December 27, 2002)

(Extracted from the "Sectoral Annex on Good Laboratory Practices (GLP) for Chemicals" of "Agreement on Mutual Recognition between Japan and the European Community")

Competent authorities of the European Community are the following authorities of the Member States of the European Community or authorities succeeding them.

Belgium	Ministère des Affaires Sociales, de la santé publique et de l'environnement
Denmark	Erhvervsfremme Styrelsen (EFS) Danish Medicines Agency
Germany	Bundesministerium fur Umwelt, Naturschutz und Reaktorsicherheit
Greece	General Chemical State Laboratory (Γενικού Χημείου του Κράτους)
Spain	Agencia Española del Medicamento, Subdirección General de Seguridad de Medicamentos Ministerio de Ciencia y Tecnología, Subdirección General de Calidad y Seguridad Industrial Ministerio de Sanidad y Consumo,Subdirección General de Seguridad Alimentaria Ministerio de Sanidad y Consumo, Subdirección General de Sanidad Ambiental y Salud Laboral
France	Groupe interministériel des produits chimiques Agence Française de Sécurité SAnitaire des Produits de Santé (AFSSAPS) Agence Française de Sécurité Sanitaire des Aliments Agence nationale du medicament vétérinaire
Ireland	National Accreditation Board
Italy	Ministero della Salute
Netherlands	Ministerie van Volksgezondheid, Welzijn en Sport, Inspectie voor de Gezondheidszorg (GLP - afdeling)
Austria	Federal Ministryof agriculture, forestry, environment and water management
Portugal	Instituto Português da Qualidade (IPQ) Ministro da Economia e da Inovação Instituto Nacional da Farmácia e do Medicamento (INFARMED)
Finland	Sosiaali- ja terveydenhuollon tuotevalvontakeskus/Social- och hälsovårdens produkttillsynscentral
Sweden	Medical Products Agency Swedish Board for Accreditation and Conformity Assessment (SWEDAC)
United Kingdom	Department of Health, Good Laboratory Practice Monitoring Authority