Guidance for the Inspection of compliance with the standard provided for in Articles 5 to 19 of the Ministerial Ordinance on Good Laboratory Practice for Agricultural Chemicals

(Notification 30 Shouan No.5999, issued on March 25, 2019 by the Director of Plant Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries)

1. Procedures of conducting Inspection

The Inspection in accordance with Section 5 of “Inspection and confirmation of compliance with the standard provided for in Articles 5 to 19 of the Ministerial Ordinance on Good Laboratory Practice for Agricultural Chemicals" (Notification 30 Shouan No.4215, issued on November 30, 2018 by the Director-General, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries) (hereinafter referred to as "the notification of the Director-General") is to be conducted as follows, utilizing the Inspection Record table (Attachment 1).

(i) Briefly describe the contents and causes of any deviations identified in respect of the “Inspection Items” listed in the Inspection Record table.

(ii) Classify the identified deviations as either “temporary or partial, not immediately affecting the reliability of the test results” or “highly likely to affect the reliability of the test results”, assigning 1 point in case of the former (2 points for deviations on important items) and 5 points in case of the latter.

2. Producing a report of inspection results

The representative of the inspector (hereinafter referred to as "GLP Inspection Manager”) must prepare an inspection report pursuant to Section 6 of the notification of the Director-General, in the form presented in Attachment 2, and submit it, along with the Inspection Record table, to the Director-General, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries.

3. Overall evaluation of inspection results

The conclusion pursuant to Item (ix) of Section 6 of the notification of the Director-General, is to be derived as follows.

(i) Cases in which the conclusion shall be “Not In Compliance”:

(a) Test facility

- Falsification of or tampering with data is taking place throughout the organization.
- Improvement to address the identified deviations is unlikely and therefore the test facility is deemed incapable of ensuring the reliability of study reports.

(b) Study Reports

・The data is falsified or tampered with by the Study Director (the Principal Investigator) or the Study Personnel.
・Study related materials that should be stored in Archive are lost or missing.
・The reliability of the study report cannot be ensured due to the absence of raw data.

(ii) The conclusion shall be "In Compliance" where none of (i) above applies.

(iii) Where a test facility is classified as "In Compliance" with not less than 10 points in the total score of the Inspection Record table and, in the light of overall severity of the deviations, deemed as requiring follow-up inspection immediately after relevant improvements for the sake of securing reliability of studies prepared hereafter, such inspection shall be conducted upon the receipt of the Application for Confirmation of GLP Compliance of Test Facility provided for in Section 3 of the notification of the Director-General, which is to be submitted by the test facility after a study report of the relevant study area is first prepared following the improvements.

Supplementary provision (25 March, 2019)

This notification applies from the instruction of the inspection under Section 4 of the notification of the Director-General after April 1, 2019.

Attachment 1

Inspection Record table

1. Describe the following items:
(i) Name and division of Inspector(s)
(ii) Name of the test facility inspected
(iii) Date(s) of the inspection
(iv) Name of the study audited

2. Instructions for records
(i) For any deviations identified concerning each item of the column of "Inspection Items", describe "(a) Contents of the deviation" and "(b) Cause of the deviation" in the column of the "Inspection results".

(ii) In the column of "Score", enter the following scores depending on the degree of the deviation identified in (i).
If a deviation is "temporary or partial, not immediately affecting the reliability of a study": 1 point (2 points for important items in bold).
If a deviation is "highly likely to affect the reliability of a study": 5 points.

(iii) In the column of "Improvements with respect to the deviation identified during the last inspection", describe" (a): Previous findings and instructions" and "(b): Solution and improvement of (a)."

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
1. Test Facility Management (Test Site Management)			
(designation of personnel) **have in place a document attesting to the status of test facility management in the test facility (Article 5 (i))** **designate Study Director, personnel of Quality Assurance Unit, Archivist, Test item management, and Apparatus management (Test site management and Principal Investigator, if needed)** **(Article 5 (ii)〜(iv))** **(Article 6 (i)〜(iii), for TSM)** **If these personnel are replaced, records of the replacement and the reasons for the replacement are retained**			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
(sufficient personnel) ensure that sufficient personnel are available to appropriately conduct studies (Article 5 (vi)) (Article 6 (v), for TSM)			
(education and training) provide the necessary education and training for personnel (Article 5 (vii)) (Article 6 (vi), for TSM) prepare and maintain documents on education and training programs provided for personnel and their work experience, and documents that clearly describe specific job assignments (Article 5 (viii)) (Article 6 (vii), for TSM)			
(Preparation and management of master schedule) **ensure and retain that the master schedule has been properly prepared** **(Article 5 (xi))** **(Article 6 (ix), for TSM)**			
(cooperation with the test site) establish a communication scheme in order to ensure that the Study Director, Principal Investigator(s) and study personnel and the Quality Assurance Unit(s) are closely coordinating if the study is conducted in a test site (Article 5 (xii))			
(other) perform other activities for operating and managing the test facility (Article 5 (xv)) (Article 6 (xii), for TSM)			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
2. Study Director (Principal Investigator)			
(management of study) **ensure that each study is conducted in accordance with the Standard Operating Procedures and study plan; when there has been any deviation from the matter of specified by the Standard Operating Procedures or study plan, to take appropriately improvement measures if necessary, after evaluating potential consequences of any deviations from the Standard Operating Procedures or study plan; and also to prepare and retain the documents on the ensuring, deviations and corrective actions** **(Article 7 (iii))** **(Article 8, for PI)**			
(confirmation of raw data) **ensure that raw data are recorded accurately, write the dates, and sign or affix the name and seal on the related documents** **(Article 7 (iv) and 17 (v))** **(Article 8, for PI)**			
(transferr study-specific records and materials to archive) retain the study plan, final report, raw data and other materials related to the study in archives after the completion of the study (Article 7 (vi)) (Article 8, for PI)			
(other) perform other activities pertaining to the management of conducting, recording and reporting the study (Article 7 (vii)) (Article 8, for PI)			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
3. Study Personnel			
(conduct of study) **conduct studies in accordance with the Standard Operating Procedures and study plan; when there has been any deviation from the provisions of procedures and study plan, to record the details of any deviations and reasons for their occurrence, and to report them to the Study Director (or the Principal Investigator)** **(Article 9 (i) and 17 (ii))** **record raw data promptly and accurately, write the dates, and sign or affix the name and seal on the related documents** **(Article 9 (ii) and 17 (iii))** **If change the raw data, the change shall be given so that the data before the change is not obscured, write the reason for the changes and the date when the changes are given, and sign or affix the name and seal on the related documents** **(Article 17 (iv))** **the indication to identify each study shall be done, and specimens shall be indicated to confirm their origin** **(Article 17 (i))**			
(safety and health) report any health problem that may affect the performance of the study to the Study Director (Article 9 (iii))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
4. Quality Assurance Unit			
(Study-based inspections) **retain copies of the Standard Operating Procedures, master schedule and study plans** **(Article 10(2)(i))** **inspect that the study plan is prepared in accordance with the provisions of Agricultural Chemicals GLP Standards, and retain the inspection records** **(Article 10(2)(ii))** **inspect that the studies have been conducted in accordance with the provisions of Agricultural Chemicals GLP Standards, the Standard Operating Procedures, and the study plans, and retain the inspection records** **(Article 10(2)(iii))** **inspect that the study methods used are accurately described in the final report and that the raw data are accurately reflected** **(Article 10(2)(iv))**			
(Facility-based inspections) **regularly inspect the equipment and management of the test facility, and retain the inspection records** **(Article 10(2)(v))**			
(report of inspection results) **report the inspection results to the test facility management and the Study Director (or TSM and PI, if needed)** **(Article 10(2)(vi) and (viii))**			
(personnel of Quality Assurance Unit) **personnel of the Quality Assurance Unit who are designated to be responsible for each study, shall not be engaged in the conduct of such study** **(Article 10(3))**			
(other) perform any other activities necessary to assure that the studies are conducted in accordance with the provisions of Agricultural Chemicals GLP Standards (Article 10(2)(viii))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
5. Test Facility			
(i) have the necessary areas and construction for conducting the study (ii) have a structure that allows distinct operations to be separately performed and a sufficient number of rooms or areas (iii) have rooms or areas for the diagnosis, treatment and control of diseases (iv) separately maintain the rooms or areas where studies are conducted, and the rooms or areas where the apparatus are stored (v) separately maintain the rooms or areas where the test or reference items are received and stored, and the rooms or areas where the vehicle are mixed with the test item (vi) the rooms or areas where the test or reference items are stored shall be capable of maintaining the identity, concentration, purity and stability of those items and ensuring their safe storage, and also be separated from the rooms or areas where the studies are conducted (vii) have archives capable of appropriately retaining study plans, final reports, raw data, specimens and other materials related to the studies (viii) be properly collected, stored and disposed waste so as not to affect the studies. (Article 11(i)～(viii))			
6. Apparatus, Materials and Reagents			
(1) The apparatus used to prepare study reports, apparatus used to maintain the environment of the facility and other apparatus necessary for conducting the studies (hereinafter referred to simply as the “apparatus”) shall be properly designed, have sufficient processing capacity, and be properly placed. (2) The Apparatus management shall ensure that the apparatus is regularly maintained, inspected, cleaned and calibrated according to the Standard Operating Procedures, and prepare and retain the records of the results thereof. (3) Apparatus and materials used in a study shall not adversely affect the test systems. (4) Reagents and solutions (hereinafter referred to as the “reagents, etc.” in this paragraph) shall be appropriately labeled to indicate name, storage conditions, expiry date and other information necessary to identify the reagents, etc. (Article 12(1)～(4))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
7. Test Systems			
(1) Apparatus used for obtaining physical chemical data as a part of the physical chemical test systems are appropriately arranged or designed and provided with sufficient data processing capability, and their functions shall be maintained. (Article 13(1)) (2) The biological test systems satisfy the following requirements: (i) the appropriate conditions for the storage, containment, handling and management of the test systems shall be defined properly in order to ensure the reliability of data; (ii) newly received test systems shall be isolated until their health status has been evaluated; (iii) if any unusual mortality or disease occurs in the test systems, this lot shall not be used in studies; (iv) at the experimental starting date (the day when raw data was first obtained in the study. The same applies in Article 16, paragraph (1), item (vii) and Article 18, paragraph (1), item (viii)), test systems shall be free from any disease or pathological condition that may interfere with the purpose or performance of the study; (v) if test systems are affected by a disease or injured during the course of a study, it shall be isolated and treated if it is necessary to maintain the integrity of the study; (vi) any diagnosis and treatment of any disease before or during a study shall be recorded; (vii) records of source, date of arrival, and arrival condition of test systems shall be maintained; (viii) test systems shall be acclimated to the study environment for a period of time before the first administration or application of the test or reference item; (ix) all information for identifying the test systems shall be indicated in its housing or containers (limited to housing or containers sufficiently cleaned at appropriate intervals to maintain hygienic conditions), and individual test systems shall be identified by additional appropriate indications, if necessary; and (x) test systems used in field studies shall not be affected by spray drift or past usage of agricultural chemicals. (Article 13(2)(i)～(x))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
8.Test and Reference Items			
(i) records including test and reference item characterization, date of receipt, expiry date, quantities received and used in studies shall be maintained (ii) test and reference items shall be checked for homogeneity and stability when they are handled, sampled and stored, and procedures for preventing contamination or mix-up shall be provided (iii) identification information, expiry date and storage instructions of the test and reference item shall be indicated on storage container(s) of these (iv) test and reference items shall be identified necessary to allow for distinction of their lot (v) in case where the test item is supplied by the Sponsor (the entity who commissioned the study to the test facility; the same applies hereinafter), a collaborative scheme shall be established between the Sponsor and the test facility to verify the identity of test item to be used in study (vi) when the test item is administered or applied in a mixture with a vehicle, the homogeneity, concentration and stability of the test item in that vehicle shall be determined (vii) a sample for analysis shall be retained from the lot of test item to be used in study (excluding those whose experimental period is less than 4 weeks). (Article 14(i)～(vii))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
9. Standard Operating Procedures			
(Establish of Standard Operating Procedures) The Standard Operating Procedures shall describe the operational methods and procedures for the following tasks: (i) management of test and reference items; (ii) use, maintenance, cleaning and calibration of apparatus; (iii) management of electronic data processing system; (iv) preparation and labeling of materials, reagents and solutions; (v) recording, reporting, storage and search of records; (vi) management of the test systems; (vii) inspection activities related to the studies and facilities to be performed by the Quality Assurance Unit; and (viii) other necessary matters. (Article 15(1))			
(Approval of Standard Operating Procedures) **Test Facility Management approve and maintain the Standard Operating Procedures.** **(Article 5(x))** **(Article 6 (viii), for TSM)** **The test facility management have the Standard Operating Procedures in place in all the rooms or areas where the tasks listed in theStandard Operating Procedures are undertaken.** **(Article 15(2))**			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
10 Study Plan			
(Content of the study plan) the study plan is prepared for every study containing the following information and make the study plan be verified by the Quality Assurance Unit: (i) a title, type and purpose of the study; (ii) information concerning the test and reference item; (iii) name and address of the Sponsor; (iv) name and address of the test facility; (v) name and affiliation of the Study Director; (vi) name and affiliation of the Principal Investigator(s), and the phase(s) of the study delegated to the Principal Investigator(s) by the Study Director if the study is to be conducted at test site(s); (vii) the date scheduled for the study initiation date (the date when the signature or affixation of the name and seal are given as provided in item (xii). The same applies in Article 18, paragraph (1), item (viii)) and the proposed experimental starting date and completion date (the last date when raw data is obtained from the study. The same applies in the said item); (viii) information on the study guidelines to be referred to; (ix) information on the test system; (x) information on the study methods; (xi) information on the records to be retained; (xii) signature or affixation of the name and seal of the Study Director with the date; and (xiii) other necessary matters. (Article 16(1))			
(Preparation and management of the study plan) **The Study Director prepare the study plan and sign or affix the name and seal.** **(Article 5(ix))** **The Study Director send a copy of the study plan, when it was prepared or amended, to the Quality Assurance Unit** **(Article 7(i), 16(1))** **If the the Study Director make changes to study plano, the Study Director record the date, the part, and the reason for the change in writing, sign or affix the name and seal, and retain the document with the study plan** **(Article 16(2))** **The Study Director make Standard Operating Procedures and study plans available to study personnel** **(Article 7(ii))**			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
11. Electronic data processing system			
(designe of the electronic data processing system) electronic data processing system shall be designed so that the data can be changed without obscuring the data before the changes (Article 17(6)(i))			
(management of the electronic data processing system) The Study Director ensure in advance that the electronic data processing system appropriately operate, if the electronic data processing system are to be used (Article 7 (v)) (Article 8, for PI) when the data is input into the electronic data processing system, the individual(s) responsible for the data input shall verify the data at the time of input (Article 17(6)(ii))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
12. Final Report			
(Content of the final report) The final report prepared for every study that contains the following information: (i) a title, date of preparation of final report and type and purpose of the study; (ii) information concerning the test and reference item; (iii) name and address of the Sponsor, if the study is conducted at its request; (iv) name and address of the test facility; (v) name and affiliation of the Study Director; (vi) name and affiliation of the Principal Investigator(s) and the phase(s) of the study delegated to the Principal Investigator(s) by the Study Director if the studies are conducted at the test site(s); (vii) name and affiliation of Experts (referred to as the “Expert” in the following paragraph) having contributed reports to the final report, if applicable; (viii) study initiation date, experimental starting date and experimental completion date; (ix) description of materials and test methods used in the study; (x) information on study guidelines consulted (xi) a summary, evaluation and discussion of the study results, and other matters related to the study results; (xii) information on archiving the study plan, samples of the test and reference item, specimens, raw data and final report; (xiii) statement that the study was conducted in accordance with this Ministerial Ordinance; (xiv) signature, or affixation of the name and seal of the Study Director with the date; and (xv) other necessary matters (Article 18(1))			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
(Preparation of the final report) **The Study Director prepare a final report for every study** **(Article 18(1))** **Any reports prepared by the Principal Investigator or Expert shall contain the date when they were prepared, be signed or affixed the name and seal by those persons, and be attached to the final report** **(Article 18(2))** **The Quality Assurance Unit prepare Quality Assurance Statement that contains the dates and results of the inspections and the dates when these results were reported to the Test facility management and the Study Director (Test site management and Principal Investigator, if needed)** **(Article 10(2)(vii))** **The Study Director attach the Quality Assurance Statement prepared by the Quality Assurance Unit to the final report** **(Article 18(3))** **If the final report is to be amended, the Study Director shall record the date, the specific part and the reason for the amendment in writing, sign or affix the name and seal, and retain the document with the final report** **(Article 18(4))**			

Inspection items	Inspection results	Score	Improvement with respect to the deviation identified during the last inspection
13. Storage and Retention of Records and Materials			
(Records and Materials to be stored and storage period) The test facility management shall appropriately retain the following materials for 10 years (for the matters set forth in item (i), the shorter period of either 10 years or the period from the study completion date until the date when the evaluation of the samples or specimens becomes difficult) starting from the study completion date in the archives (i) samples of test and reference items, and specimens (ii) the study plan, raw data and the final report of each study (iii) the master schedules and records of all inspections performed by the Quality Assurance Unit (iv) records of qualifications, training, experience, and job descriptions of personnel (v) records of the maintenance and calibration of apparatus (vi) documents on the validation of electronic data processing system (vii) Standard Operating Procedures (viii) environmental monitoring records (Article 19(1))			
（Organizing materials） The Archivist shall make an index on the materials to be retained in the archives so that the materials can be easily retrieved. (Article 19(3))			
(Access to the archives) **Only the Archivist and persons who are authorized by the Archivist have access to the archives (Article 19(4))** **The Archivist shall record the access of the persons specified in the preceding paragraph and movement of material in and out of the archives** **(Article 19(5))**			
(Disposal of the materials) When materials are disposed of before required retention period for any reason, this should be justified and documented. (Article 19(2))			
	Total score		

Attachment 2

Form (Writing example)

Inspection Report

Date (YY/MM/DD)

To: The Director-General,
Food Safety and Consumers Affairs Bureau,
the Ministry of Agriculture, Forestry and Fisheries.

Name of GLP Inspection Manager (*)

I hereby report the results of inspection as detailed below.

1. Name and division of Inspector(s):
2. Name and Address of the test facility inspected:
3. Date(s) of the Inspection:
4. Purpose of inspections:
   Write any one of the following.
   - For inspection under 2, (1), (a) of the notification of the Director-General;
     Confirmation of 2, (1), (a) of "Inspection and Confirmation of compliance with the standard provided for in Articles 5 to 19 of the Ministerial Ordinance on Good Laboratory Practice for Agricultural Chemicals" (Notification 30 Shouan No.4215, issued on November 30, 2018 by the Director-General, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries) on the test facility which submitted the "Application for Confirmation of GLP Compliance of Test Facility" [yy/mm/dd]

   - For inspections under 2, (2) of the notification of the Director-General;
     Confirmation of 2, (2) of "Inspection and Confirmation of compliance with the standard provided for in Articles 5 to 19 of the Ministerial Ordinance on Good Laboratory Practice for Agricultural Chemicals" (Notification 30 Shouan No.4215, issued on November 30, 2018 by the Director-General, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries) on the test result for which "Application for Confirmation of GLP Compliance of Test result" is submitted on [yy/mm/dd]

5. Outline of the test facility (including past and recent developments):

6. Studies audited (area of study and name of study):
7. Names and affiliations of staff members who participated in the inspection
   (Name and affiliation of Test Facility Management, Study Director, Principal Investigator (if applied.), Quality Assurance Programme, and Archivist.)
8. Compliance of the test facility and the audited studies with "the standard provided for in Articles 5 to 19 of the Ministerial Ordinance on Good Laboratory Practice for Agricultural Chemicals"
   See the attached Inspection Record table:
9. Conclusion
   (Along with the overall evaluation as a result of the inspection, indicate either "In Compliance" or "Not In Compliance".)
10. Other matters
    ・Improvements of the deviations found in the last inspection
    ・Implementable studies

Remark: If the independent administrative agency, Food and Agricultural Materials Inspection Center conducts GLP inspection, the name of the GLP Inspection Manager shall be the President of the Food and Agricultural Materials Inspection Center.