General Accreditation Criteria

Organisation for Economic Co-operation and Development (OECD)

Principles of Good Laboratory Practice (GLP) Recognition

Application Document

July 2018

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OECD Principles of Good Laboratory Practice Recognition Application Document

Section 1: OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring

The general criteria for the conduct of non-clinical health and environmental safety studies are described in the *OECD Principles of Good Laboratory Practice*.

Although NATA is the responsible authority for Australia's Good Laboratory Practice (GLP) compliance monitoring program, the OECD documents are not available from NATA and must be obtained from the OECD Environment Directorate (fax: +33 1 4524 1675) or downloaded from the OECD website: http://www.oecd.org

The following documents are from the OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring:

OECD Principle of GLP

No.1 *The OECD Principles of Good Laboratory Practice*

This is the primary or base criteria document against which all GLP compliant facilities are assessed.

Consensus Documents

No. 4 *Quality Assurance and GLP*

No. 5 *Compliance of Laboratory Suppliers with GLP Principles*

No. 6 *The Application of the GLP Principles to Field Studies*

No. 7 *The Application of the GLP Principles to Short-term Studies*

No. 8 *The Role and Responsibilities of the Study Director in GLP Studies*

No. 13 *The Application of the OECD Principles of GLP to the Organisation and Management of Multi-Site Studies*

Advisory Documents of the Working Group on GLP

No. 11 The Role and Responsibilities of the Sponsor in the Application of the Principles of GLP

No. 14 The Application of the Principles of GLP to in vitro Studies

No. 15 Establishment and Control of Archives that Operate in Compliance with the Principles of GLP

No. 16 Guidance on the GLP Requirements for Peer Review of Histopathology

No. 17 The Application of the Principles of GLP to Computerised Systems

No 19 Advisory Document of the Working Group on Good Laboratory Practice on the Management, Characterisation and Use of Test Items

Section 2: Supplementary criteria for recognition

2.1 Multi-site studies

Note: Refer to Consensus Document Number 13 of the OECD Working Group for Good Laboratory Practice, *The Application of the OECD Principles of GLP to the Organisation and Management of Multi-Site Studies*

GLP studies may cover activities (phases) conducted at more than one location. Such studies are referred to as 'multi-site', which includes the test facility and all test sites e.g. field activities performed at various test sites and laboratory activities performed at a test facility. Even though a study may be multi-site in nature, it is still considered to be a single study which should be covered by a single study plan under the control of one Study Director.

Subcontracting study activities

Wherever possible, it is preferred that study activities are performed by test sites that have been inspected for compliance with the OECD Principles of GLP. However, on some occasions it may be necessary for part of a GLP study to be conducted at a test site that is not part of a national GLP compliance monitoring program. For example, to conduct specific study phases due to a lack of expertise, facilities or equipment.

As detailed in Document No 13 - *The Application of the OECD Principles of GLP to the Organisation and Management of Multi-Site Studies,* if there is a need to sub-contract work to organisationally distinct test sites that are not included in a national GLP compliance monitoring programme, the rationale for selection of these sites must be documented i.e. in the study plan and report and in a documented policy and/or procedure.

Study phase(s) performed at such site(s) may only be included as part of the GLP recognised facility's GLP compliance statement (study report) if:

a) management from the GLP recognised facility maintains responsibility for GLP compliance. Test Facility Management's responsibilities for GLP compliance cannot be delegated to management at the subcontracted test site;

b) the staff conducting the activity adhere to and follow all of the relevant policies, procedures and SOPs of the GLP recognised facility's, unless otherwise defined in the study plan and approved by Test Facility Management;

c) the facilities, staff and processes used for GLP studies are regularly audited as part of the GLP recognised facility's Quality Assurance Program to confirm GLP compliance and;

d) these sites will be inspected as part of routine reassessments. The costs associated with these visits and their frequency will depend on the complexity of the phases conducted.

If the above criteria are met the Mutual Acceptance of Data (MAD) agreement would apply to the data produced by these test sites as the sites have been inspected by the national GLP compliance monitoring authority.

This extension of a Test Facility's NATA GLP Recognition can only be applied to work for specific phase(s) of a study/ies and cannot be used to confer GLP compliance on the non-GLP test site or to any other work undertaken by them. A contracted test site cannot perform GLP compliant phases independently from the test facility. If they wish to do so they must seek separate GLP recognition.

Data from test sites that have not been inspected by a national compliance monitoring authority, including NATA, may also be included in the GLP compliance statement in the report if the Study Director is assured that the work was conducted in accordance with the Principles i.e. a declaration of compliance is made. However;

a) The Mutual Acceptance of Data (MAD) agreement would not apply to the data produced by these test sites;
b) Records must be available to support the Study Director's decision;
c) The Study Director's statement must mention that the test sites have not been inspected by the national GLP compliance monitoring authority and that MAD does not apply;
d) These test sites may also be inspected by NATA and costs for this inspection would be levied. If the work is found to be not in compliance with the Principles, the Study Director's statement would need to be revised accordingly.

Alternatively the work can be excluded from the statement of compliance.

Any subcontracting arrangements will be reviewed during an assessment. The appropriateness of these arrangements will depend on the frequency and the extent of the subcontracted work.

A copy of any contractual arrangement in relation to GLP activities with sub-contractors that are not NATA recognised for GLP compliance must be available to NATA for review. These documents, and the records of audits or meetings undertaken to assess the compliance status of the contracted site prior to use in a GLP study, will be inspected at an assessment.

In addition to the contracting out of study related work, contracting of other GLP activities may also occur (e.g. QA auditing services, computer system support, contract archiving, etc.). In these situations there must be formal contracts and, if appropriate, detailed service level agreements which define the nature and extent of services to be provided.

In all situations, the overall responsibility for the compliance of the facility and/or of studies (i.e. the roles of Test Facility/Test site management) cannot be contracted to external organisations.

2.2 Equipment and traceability of measurement

In accordance with the *OECD Principles on Good Laboratory Practice*, Section II, Clause 4.2, standard operating procedures need to cover the periodic inspection, cleaning, maintenance and calibration (including the need, where appropriate, for traceability to national or international standards of measurements) of apparatus.

Traceability is required where the apparatus contributes directly to the study data. This would include equipment used for the preparation of test items, reference items or where temperature is critical to the study e.g. stability studies.

Where metrological traceability is required, NATA's *Metrological Traceability* must be applied. Where traceability is not essential the facility should consider how to demonstrate the equipment is fit for purpose and functioning as required.

2.3 Retention of records

Unless otherwise prescribed by regulatory or contractual obligation, retention times will not be less than four years or, in the case of equipment records, the maximum recalibration interval of equipment (whichever is the longer period).

Section 3: Interpretative information on the OECD Principles of Good Laboratory Practice

This section provides interpretative information on the application of the Principles.

The clause numbers relate to those covered by Section II of the Principles. As not all clauses require interpretation the numbering may not be consecutive.

1 Test Facility Organisation and Personnel

The name of a test site or a number allocated to a study by a test site can be regarded as test site identifiers.

2 Quality Assurance

The Study Director and/or Principal Investigator and, where relevant, management are responsible for taking corrective action to non-conformities identified by Quality Assurance personnel.

For multi-site studies, the mechanism for reporting the results of quality assurance inspections must be documented. It is recommended that this be in either in a SOP or in the study plan. This would include detailing the responsibilities for reporting results to the appropriate people where this has been delegated.

4 Apparatus, Materials and Reagents

The requirements for computerised systems applies to all systems used regardless of their complexity. These systems may be used for a variety of activities including the direct or indirect capturing of data from automated instruments, operation/control of automated equipment and the processing, reporting and storage of data.

The criteria for when to apply computerised system validation and/or qualification approaches, based on risk, must be developed and documented.

6 Test and Reference Items

If characterisation information is not provided, or is insufficient, the characterisation of the test and reference items cannot be considered compliant with the OECD Principles of GLP.

7 Standard Operating Procedures

The responsibility to approve technical SOPs may be delegated by management.

8 Performance of the Study

The facility should confirm with the relevant regulator whether the sponsor and test facility management are required to sign the study plan.

The documented agreement for Principal Investigators that are part of the same organisation as the Study Director can be demonstrated by the employment contract, position description or similar documents. Principal Investigators from test sites that are organisationally distinct from the test facility will, however, need to document their agreement to conduct the delegated phase in accordance with the Principles (e.g. by signing the study plan prior to the commencement of the delegated phase).

Facilities should use the OECD Test Guidelines as the basis for test methods. These can be obtained free of charge from the OECD website.

9 Reporting of Study Results

Where relevant (e.g. crop studies) the actual amount of test item applied is to be detailed in final reports, not the target volume.

10 Storage & Retention of Records and Materials

Original records should, where possible, be archived. If original data cannot be archived by the facility the copied record is to be certified as the same as the original prior to archiving or transferring to another archive.

Section 4: GLP specific recognition procedures

Recognition of overseas facilities and sites

The Mutual Acceptance of Data (MAD) directives are integral to the OECD Principles of GLP. They state that data generated in a facility that is recognised as GLP compliant by the national GLP compliance monitoring authority must be accepted internationally for purposes of assessment by OECD member countries and non-member countries which are adherents to the MAD decision.

Requests for GLP recognition from test facilities located in countries that are adherents to the MAD directives will be directed to the relevant national GLP compliance monitoring authority. A list of these can be found on the GLP section of the OECD website.

NATA would only assess facilities or sites located overseas if:

- a request was received from an Australian regulator; and
- the facility or site was located in a country that does not have a GLP compliance monitoring authority adhering to the MAD directives.

NATA recognition of these facilities would only apply in the country to which the data was presented. There is no obligation on the part of regulators in other countries to accept NATA recognition. Such facilities will be listed in NATA's annual report to the OECD GLP Working Group; however, they would not be included in the Australian GLP compliance monitoring program and would not be able to claim recognition under the Australian monitoring program.

On some occasions NATA may assess an Australian-based facility that periodically undertakes a component of its GLP study activities outside of Australia, for example, activities carried out at a temporary 'site' such as field plots or paddocks being used in an animal or crop residue study. In such cases, the activities undertaken must be controlled by the Australian-based test facility or test site responsible for the study or phase of the study. Depending upon the activity, NATA may perform an on-site assessment of the overseas 'site'. This may include observing processes such as dosing or spraying, sampling etc. and assessing the suitability of equipment and storage conditions for samples and test items. In addition, records of the GLP activities would be reviewed during study audits. The 'site' assessed would not be included in NATA's list of GLP compliant facilities and cannot itself claim that it was GLP compliant in its own right.

Any permanent test site located overseas such as a laboratory, field contractor’s site or animal house etc. would only be assessed by NATA at the request of the Australian regulator. Where possible, overseas test sites should be assessed by the national compliance monitoring authority in which they are located. If the test site is located in a country that does not adhere to the MAD Agreement, regulators are not obliged to accept this data.

Before an overseas assessment takes place, the national GLP compliance monitoring authority of the country in which the activity is performed would be consulted to determine whether recognition under that authority’s program could be considered (if necessary or relevant).

Fees associated with Australian test sites

Application fees are waived for organisations adding new test sites that are to be used for GLP activities. As for all facilities, any additional costs associated with

assessing the processes and facilities used at these sites would be incorporated into annual fees of the facility commensurate with the scope, location of the sites and complexity of the work undertaken.

Facilities can choose to have any or all of the test sites that are part of the organisation listed separately or incorporated into a facility. If a facility wishes to list test sites separately, an administration fee in accordance with NATA's fee schedule will be charge for each separately listed test site. These sites would receive separate Notification of GLP recognition documents and would be listed separately on the NATA website and in the Annual Overview of GLP Test Facilities provided to the OECD Working Group on GLP.

Facilities may prefer to incorporate the site(s) into the main facility to save administration costs. However, only one Notification of GLP recognition document would be issued and the types of studies undertaken by the facility at these sites would be included in the List of Studies Inspected. There would also be only one listing for the facility on the NATA website and in the Annual Overview of GLP Test Facilities. Overseas compliance monitoring authorities, regulators, sponsors and other interested parties would therefore be unable to see the list of compliant studies undertaken at the separate sites.

Notification of GLP Recognition document

The scope of all GLP recognised facilities i.e. Notification of GLP Recognition, includes reference to the Principles and a list of the types of studies assessed. A copy of the types of studies available under NATA's GLP compliance program is provided in Section 5 of this document. Application for recognition may be made for one or more types of study/ies covering nonclinical health and environmental safety studies.

The scope of recognition is not a reflection of a facility's technical capability or capacity to conduct a particular type of study. It is an indication of the types of studies reviewed and processes adopted or discussed at assessment. The scopes of recognition of all NATA GLP recognised facilities are available on the NATA website.

Additional study types cannot be included in the Notification of GLP Recognition document unless such studies have been assessed by NATA for GLP compliance.

After recognition

Unscheduled reassessments may be conducted to investigate a complaint that casts doubt over a facility's continuing compliance with the recognition criteria or at the request of an Australian regulator or overseas compliance monitoring authority. At such assessments, specific activities may be targeted for review rather than the entire facility's operation.

To ensure currency, the Notification of GLP Recognition document is reviewed and, where necessary, revised at every study audit and reassessment.

Should recognition be reviewed in part or whole (i.e. suspended), the responsibility rests with the facility to notify NATA once studies have been conducted in order for the suspension to be reviewed within the timeframe detailed in the *NATA Rules*.

Study audits

Following the initial assessment, the first study audit visit is performed at 12 months and thereafter as part of scheduled reassessments.

When conducted 12 months after the initial assessment, such a visit will normally be conducted in one day, however, the time required is dependent upon the scope of recognition and the types of studies being performed. Prior to the visit, the facility will be requested to provide its master schedule which details all the studies conducted.

Additions to Notification of GLP Recognition document between scheduled reassessments

A facility may wish to add a study to the List of Studies Inspected in its existing Notification of GLP Recognition document between scheduled reassessments. In such cases a written request must be made to NATA by the facility's Authorised Representative. The proposed addition will then be considered by NATA to determine whether the type of study is already covered by the facility's recognition or whether the request for the addition is within the scope of the OECD Principles of GLP.

Once it is confirmed that the study is not covered by the facility's recognition, the facility will be requested to forward the study plan for review. Upon completion of the review, a decision will be made as to whether an on-site assessment will be necessary. This may be dependent on the availability of information able to be reviewed off-site, the need to visit a test site, etc.

Fees are levied for the conduct of assessments and study audits, between scheduled reassessments, to accommodate additions to the Notification of GLP Recognition document in accordance with NATA's Fee Schedule.

Process to follow if no studies are conducted after recognition

If no studies have been performed for one assessment cycle (i.e. two years) they will be removed from the Notification of GLP Recognition document unless the facility can demonstrate ongoing GLP compliance for these study types. If recognition is continued, the facility must advise NATA as soon as a GLP study has been planned. An on-site review (study audit) of a GLP study will be performed once the study has been completed.

No charges for these visits will be levied as they will be covered by the annual fees. Alternatively, the facility can request that their recognition be withdrawn. It will, however, need to re-apply if it recommences studies and wishes to be recognised again.

Where a study type has not been conducted within two assessment cycles, the recognition status of the facility will be reviewed.

Study reports and use of NATA endorsement

The GLP compliance statement (clause 1.2.2h of the OECD Principles), included in a study report and signed and dated by the Study Director (and, if applicable, the Principal Investigator for a delegated phase), is used by receiving authorities when deciding on the acceptance of data presented in support of an application for registration of a product. This statement is not, however, evidence in itself that the facility issuing the report is in a national GLP compliance monitoring program. To ensure acceptance by an Australian or overseas receiving authority, it is recommended that NATA recognised facilities in the Australian GLP compliance monitoring program apply the NATA GLP endorsement, in conjunction with the facility recognition number (and for corporate recognitions, the site number) on study reports for work that is covered by their scope of recognition.

The NATA endorsement may also need to be applied due to sponsor request or contractual requirements.

The endorsement should not be listed as part of the Study Director's or QA statements.

Provision for information for non-compliant, facilities, studies or phases of studies in the GLP Program

Relevant regulatory authorities in Australia and other national GLP compliance monitoring authorities are advised when a facility is suspended, cancelled or voluntarily withdraws from the program. The following information will be provided:

- Reporting Monitoring Authority.
- Contact at Monitoring Authority.
- Name and address of test facility/test site.
- Study conducted by facility or test sites
- Number of years of recognition by NATA
- Date of the last successful assessment
- Date that the non compliance first occurred or date that compliance issues were first identified.
- Nature of the non compliance
- Areas of the facility (if not all) affected by the non compliance.
- Number of studies affected (if known)
- Type of studies affected

Relevant regulatory authorities in Australia and other national GLP compliance monitoring authorities are also advised of any non-compliant studies conducted by a recognised facility.

The following information will be provided:

- Study Title and Number
- Nature of the non-compliance and impact on the validity of data
- Purpose of study
- Test Item (test material)
- Study Status
- Sponsoring organisation and whether they have been identified
- Whether a report amendment has been issued and, if relevant, the date
- Submission status, if known
- Action taken
- Relevant Comments

This information will be provided to overseas regulators by the national compliance monitoring authority.

Note: It is the responsibility of facilities (where relevant, both Australian and overseas) acting as test sites to ensure that any contractual arrangements take account of the possibility of disclosure of information by NATA.

Provision for information for inspections conducted at the request of an Australian regulatory authority or other national compliance monitoring authority

NATA may receive requests from an Australian regulator or overseas compliance monitoring authority for information concerning the compliance of an Australian facility, or to conduct a reassessment and/or study audit on their behalf. These may be unscheduled or may be conducted as part of a scheduled reassessment. Representatives from the authority requesting the reassessment and/or study audit may be present, and participate in the inspection or audit. NATA is required to facilitate such requests under the OECD Council Decision - Recommendation [C(89)87Final]. The following information may be provided:

- Names and addresses of test facility and test sites;
- Facility and site recognition numbers;
- Study number, study title and compliance status of audited studies;
- Compliance status of facility resulting from the reassessment;
- Summary of findings from reassessment and/or study audit;
- Copy of the report on reassessment and/or study audit;
- Summary of facility's response to findings detailed in the report on reassessment and/or study audit.

Note: It is the responsibility of facilities (where relevant, both Australian and overseas) acting as test sites to ensure that any contractual arrangements take account of the possibility of disclosure of information by NATA.

Confidentiality

In the GLP Program NATA is required to advise relevant Australian regulatory authorities, and overseas compliance monitoring authorities (through the OECD Working Group on GLP) of facilities that are, or have applied to be, in the Australian program including their compliance status. NATA is required to provide this information under the OECD Council Decision - Recommendation [C(89)87Final].

This is done via an Annual Overview which includes the following:

- Trading name;
- Address;
- Facility and site numbers;
- Types of studies inspected;
- Date of recognition;
- Date of last NATA assessment or study audit;
- Compliance status at time of last assessment or study audit;
- If any studies were found to be non-compliant.

Regulators have access to the Annual Overviews via either the OECD website (password protected) or by contacting their national compliance monitoring authority.

Please note that specific information about non-compliant studies and facilities is not listed in the Annual Overview. This information is, however, exchanged between compliance monitoring authorities and regulators (see above).

Authorised Representatives formally consent to NATA disclosing information to facilitate the above requirements by signing the relevant section of the *Application for Accreditation* or *Change of Authorised Representative* form.

References

NATA Fee Schedules

NATA Rules

OECD Principles on Good Laboratory Practice

OECD Principle of GLP Document No.1:*The OECD Principles of Good Laboratory Practice*

OECD Principle of GLP Consensus Document No. 4:*Quality Assurance and GLP*

OECD Principle of GLP Consensus Document No. 5:*Compliance of Laboratory Suppliers with GLP Principles*

OECD Principle of GLP Consensus Document No. 6:*The Application of the GLP Principles to Field Studies*

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OECD Principle of GLP Advisory Documents of the Working Group on GLP *No 19: Advisory Document of the Working Group on Good Laboratory Practice on the Management, Characterisation and Use of Test Items*

Amendment Table

The table below provides a summary of changes made to the document with this issue.

AMENDMENT TABLE	
Section	**Amendment**
Section 1 and References	Addition of Document No 19 - *Management, Characterisation and Use of Test Items*
Section 4	Revision of the information to be provided to OECD Working Group and Regulators regarding non-compliant, facilities, studies or phases of studies in the GLP Program.