General Recognition Criteria

Organisation for Economic Co-operation and Development (OECD)

Principles of Good Laboratory Practice (GLP)

Application Document

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Purpose

This document provides:

- interpretative criteria and recommendations for the application of the *OECD Series on the Principles of Good Laboratory Practice and Compliance Monitoring*;
- additional criteria for NATA GLP recognition;
- additional information on NATA's procedures for GLP recognition.

Facilities must comply with all documents in the *NATA OECD Principles of Good Laboratory Practice Recognition Criteria* package (refer to *NATA Procedures for Accreditation)* available from the NATA website.

OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring

The following documents, available from the OECD website (https://www.oecd.org/chemicalsafety/testing/good-laboratory-practiceglp.htm), form 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. 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 Management, Characterisation and Use of Test Items

No. 22 GLP Data Integrity

No. 23 Quality Assurance and GLP

Interpretative information on the *OECD Principles of Good Laboratory Practice*

This section provides interpretative information on the application of the *OECD Principles of GLP*.

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

1 Test Facility Organisation and Personnel

NATA requires that a copy of the master schedule prior to a study audit be available. To assist the tracking of key information relevant to studies, the following must be included in the master schedule:

- type of study;
- name of Study Director;
- name(s) of the Principal Investigator(s) on the test site(s) master schedule(s);
- critical dates including study and experimental start and finish dates;
- study number and the test site identifier(s);
- test system; and
- test item.

This information may be maintained in various formats and be included in more than one document. GLP compliance can only be claimed for studies that are listed in the master schedule.

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 nonconformities identified by Quality Assurance personnel.

For multi-site studies, the process for reporting the results of quality assurance inspections must be documented. It is recommended that this be in either a Standard Operating Procedure (SOP) or the study plan and detail the responsibilities for reporting results to the appropriate people where this has been delegated.

Process based audits relevant to the conduct of studies to demonstrate QA coverage must be listed in QA statements. Study Directors must ensure that the information maintained on such audits allows for adequate verification of QA coverage to be demonstrated. This includes details of process-based audits conducted at test sites.

6 Test and Reference Items

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

Records of characterisation must be available at the test facility/site and be traceable to the batch of test item and, where relevant, the vehicle used for the study.

7 Standard Operating Procedures (SOPs)

The responsibility to approve technical SOPs may be delegated by management. Where delegation is allowed, the process must be documented.

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, who are part of the same organisation as the Study Director, can be demonstrated by an 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).

Where available, the latest version of the OECD Test Guidelines must be followed. These are available from the OECD website (http://www.oecd.org/env/ehs/testing/oecdguidelinesforthetestingofchemicals.htm) and include:

Section 1: Physical Chemical Properties

Section 2: Effects on Biotic Systems

Section 3: Environmental Fate and Behaviour

Section 4: Health Effects

Section 5: Other Test Guidelines

NATA's review and discussion with facility staff during an assessment of the test studies performed does not confirm the facility's technical competence.

9 Reporting of Study Results

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

10 Storage and 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.

Additional criteria for NATA GLP recognition

Multi-site studies

Refer to *Consensus Document of the Working Group for Good Laboratory Practice, Number 13, 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 must 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.

If there is a need to subcontract 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 in a policy/procedure and included in the specific study plan and the report.

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

- management from the GLP recognised facility maintains responsibility for GLP compliance (i.e. the Test Facility Management's responsibilities for GLP compliance cannot be delegated to management at the subcontracted test site);
- the staff conducting the activity adhere to and follow all of the relevant policies, procedures and SOPs of the GLP recognised facility, unless otherwise defined in the study plan and approved by Test Facility Management;
- 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;
- these sites are inspected by NATA as part of routine reassessments. The costs associated with these visits and their frequency will depend on the complexity of the phases conducted and in accordance with the hourly rate in NATA's current *Fee Schedule*.

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 a specific phase(s) of a study/ies and cannot be used to confer GLP compliance to the subcontracted test site or to any other work undertaken by it. A subcontracted test site cannot perform GLP compliant phases independently from the test facility. If it wishes to do so, it 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 *OECD Principles of GLP* (i.e. a declaration of compliance is made). However:

- the MAD agreement would not apply to the data produced by these test sites;
- records must be available to support the Study Director's decision;
- 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.

If requested by a receiving authority these test sites may also be inspected by NATA and costs for such inspections levied in accordance with the current NATA *Fee Schedule*. If the work is found to be not in compliance with the *OECD Principles of GLP*, 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 subcontractors that are not NATA recognised for GLP compliance must be available to NATA for review. These documents and the records available, demonstrating the compliance status of the contracted site prior to use in a GLP study will be inspected at an assessment.

Subcontracting of GLP activities may also include, for example, QA auditing services, computer system support, archiving, cloud computing services etc. In these situations, there must be formal arrangements and, where necessary, appropriately 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 delegated to external service providers.

Equipment and traceability of measurement

In accordance with the *OECD Principles on GLP*, Section II, Clause 4.2, SOPs 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 *General Accreditation Criteria*: *Metrological Traceability Policy* must be applied. Where traceability is not essential, the facility should consider how to demonstrate that equipment is fit for purpose and functioning as required.

Retention of records

Unless otherwise prescribed by regulatory or contractual obligation, retention times will not be less than 6 years or, in the case of equipment records, the maximum recalibration interval of equipment (whichever is the longer period).

NATA's procedures for GLP recognition

Additional information on fees associated with Australian test sites

Refer to the *NATA Procedures for accreditation* and *Fee Schedule* available from the NATA website.

The annual NATA fee covers the cost of the study audit conducted one year after the initial assessment, two-yearly reassessments, and any site visits associated with reassessments. If additional site visits or study audits are required (e.g. at the request of sponsors or Australian or overseas regulatory/receiving authorities), all costs plus time at the hourly rate will be charged.

If the facility issues reports from more than one address (i.e. site), an application for recognition of such sites will need to be submitted.

Scope of GLP Recognition

The NATA *Scope of Recognition* for compliance with *the OECD Principles of GLP* covers all non-clinical health and environmental safety studies conducted within Australia for regulatory purposes.

The NATA website also details the types of studies that have been inspected. The types of studies available under NATA's GLP compliance program are included in the NATA document *Specific Accreditation Guidance: OECD GLP Program - Types of Studies Inspected,* available from the NATA website.

The *Scope of Recognition* is not a reflection of a facility's technical competence to conduct a particular type of study. Instead, it is an indication of the types of studies reviewed and processes adopted or discussed at assessment.

Additional study types (Services or Determinations) cannot be included in the *Scope of Recognition* document unless such studies have been inspected by NATA for GLP compliance.

After recognition

All sites under the management of the test facility will be inspected during the reassessment (via study audits, reviewing records etc.). In addition, critical phases of GLP studies will be observed. If the same activity occurs at different locations (e.g. field sites) a representative sample of one or more of these sites will be visited as part of a reassessment.

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 *Scope of 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.

Prior to the visit, the facility will be requested to provide its master schedule which details all the studies conducted.

Additions to study types between scheduled reassessments

A facility may wish to add a new phase of a study (or study type) not specifically inspected by NATA and hence not included in its existing *Scope of Recognition* between scheduled reassessments. In such cases, the *Application for changes to the scope of accreditation* form available from the NATA website must be completed.

The additional study will only be added to the *Scope of Recognition* after it has been inspected by NATA.

It is the responsibility of the facility's management to ensure the *OECD Principles of GLP* are complied with when new study types are conducted. If compliance cannot be demonstrated at a NATA assessment, any Study Director's statement previously made, relevant to the noncompliant new studies, will need to be revised and the appropriate authorities advised.

The assessment of compliance of additional study types can occur at a routine visit or as a stand-alone activity. Depending on the extent of the change, this may involve a full assessment of the facility, associated activity and/or study audit. As a minimum, a study audit of a completed study will need be conducted.

An application for recognition is required to be completed if the request involves the addition at a new location. Visits to inspect activities associated with the study and facilities used may also be undertaken. If the request involves an addition at the same location and the work can be added to the *Scope of Recognition* of the existing site, then an application form and fee are not required.

Activities undertaken to inspect the new study type will be charged in accordance with NATA's *Fee Schedule*. If these visits are performed in conjunction with a routine reassessment, some of the associated costs will be reduced, however, any additional time and expenses associated with the new activities will be charged.

Process to follow if no studies are conducted

If no studies have been undertaken since the initial assessment, or within two years of the last on-site reassessment and none are planned, a NATA in-office surveillance activity will be performed. This activity consists of a review of documents including the current master schedule.

If recognition is maintained after this activity, the facility must advise NATA as soon as a GLP study has been planned to enable a reassessment, including an on-site activity and study audit, to be performed. No charges for these activities will be levied as they will be covered by the annual fees.

The in-office surveillance activities will be undertaken at twelve-month intervals until a reassessment that covers both on-site activities and study audits can be performed.

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

Alternatively, the facility can request for GLP recognition to be withdrawn, however, the facility will need to reapply if studies are recommenced and NATA GLP recognition is required.

Study reports and use of NATA endorsement

Facilities recognised by NATA, as part of the Australian GLP compliance monitoring program, for studies covered by the *OECD Principles of GLP* may apply the NATA endorsement to study reports they issue.

The GLP compliance statement (clause 1.2.2h of the *OECD Principles of GLP*) 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 reviewing data presented in support of an application for registration of a product. This statement is not, however, evidence that the facility issuing the report is in a national GLP compliance monitoring program as a facility may make a self-declaration of GLP compliance.

To ensure acceptance by an Australian or overseas receiving authority, it is therefore recommended that facilities recognised as GLP compliant by NATA use the NATA GLP endorsement.

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

Additional details relating to the appropriate forms of endorsement and the reproduction of endorsed reports are provided in the relevant schedule of the *NATA Rules*. Also refer to the NATA *General Accreditation Criteria: Use of the NATA emblem, NATA endorsement and references to accreditation* for further details of the circumstances under which the endorsement may be applied.

Non-compliant studies or facilities

If non-compliant studies or facilities are identified during a visit the facility will be required to:

- issue report amendments to remove the claim of GLP compliance from the Study Director/Principal investigator's statement for any studies identified at the visit. The amended report (or report amendment) must clearly state the reasons for any non-compliance in the Study Director/ Principal Investigator's statement;
- provide a documented plan to investigate all studies that may be affected over a specific time period for review and agreement by NATA;
- in a specified timeframe, provide a summary to NATA detailing the studies reviewed and the issues found.

A follow up visit (STF) will be undertaken to confirm the action taken. Further report amendments or amended reports may be required after this visit.

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

When a facility is found to be non-compliant or non-compliant studies are identified, NATA is obligated (under the OECD Council Decision - Recommendation [C(89)87Final]) to advise regulatory authorities in Australia and other national GLP compliance monitoring authorities through the OECD Working Group on GLP.

When a facility is suspended or cancelled from the program the following information will be provided:

- reporting Monitoring Authority;
- contact at Monitoring Authority;
- name and address of test facility/test site;
- the facility's NATA recognition and site number;
- type of studies conducted by facility or test sites;
- number of years of recognition by NATA;
- date of the last successful assessment;

and, where relevant:

- 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).

The following information will also be provided for non-compliant studies:

- 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;
- whether a report amendment has been issued and, if relevant, the date;
- submission status, if known;
- action taken;
- other relevant comments.

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

It is the responsibility of facilities (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.

Requests for information from NATA by 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, including the provision of information, under the OECD Council Decision - Recommendation [C(89)87Final]. The following information may be provided:

- names and addresses of the test facility and test sites;
- the facility's NATA recognition and site numbers;
- study number, study title and compliance status of audited studies;
- compliance status of the facility resulting from the reassessment;
- summary of findings from the reassessment and/or study audit;
- copy of the report on reassessment and/or study audit;
- summary of the facility's response to findings detailed in the report on reassessment and/or study audit.

It is the responsibility of facilities (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

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 and includes the following:

- trading name;
- the facility's and testing site's addresses;
- the facility's NATA recognition 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.

The name and address that appear on study plans (protocols) and final reports will be the name and address that is listed on the NATA website and in the Annual Overview of GLP Test Facilities.

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

Authorised Representatives formally consent to NATA disclosing information to facilitate the above by signing the relevant section of the *Application for Accreditation* or *Facility Details Update* forms.

References

This section lists publications referenced in this document. The year of publication is not included as it is expected that only current versions of the references shall be used.

OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring

Refer to the relevant sections in this document.

NATA Publications

General Accreditation Criteria	*Measurement traceability policy*
General Accreditation Criteria	*Use of the NATA emblem, NATA endorsement and references to accreditation*

NATA Fee Schedule

NATA Procedures for accreditation

NATA Rules

Amendment Table

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

Section or Clause	Amendment
Page 4	The reference to Document No. 4 *Quality Assurance and GLP* was replaced with a reference to Document No. 23 *Quality Assurance and GLP*.