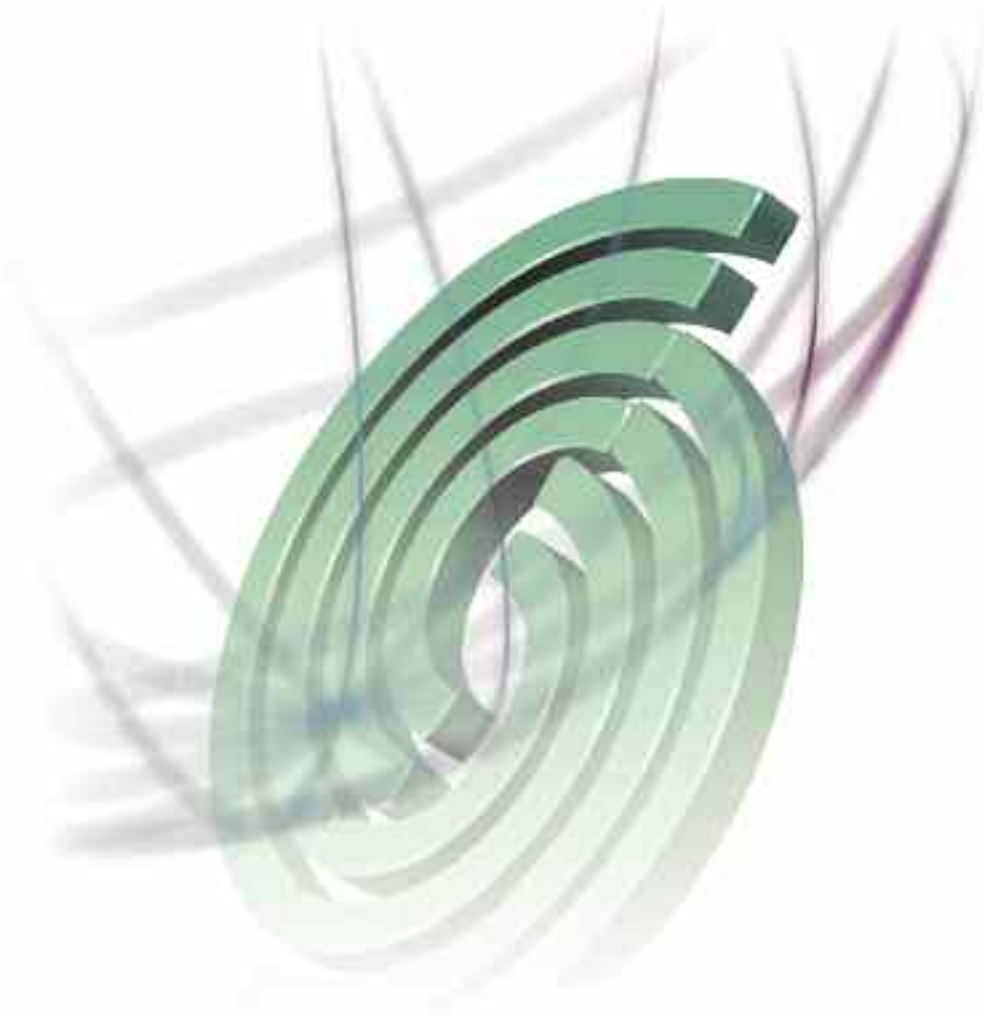

Standards Council of Canada
Conseil canadien des normes

SCC Monitoring Authority Requirements for the Recognition of GLP Compliant Facilities

CAN-P-1583
February 2008

Program Specialiaty Area
Good Laboratory Practice (PSA-GLP)

Canada

SCC MONITORING AUTHORITY REQUIREMENTS FOR THE RECOGNITION OF GLP COMPLIANT FACILITIES

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PROGRAM SPECIALTY AREA
GOOD LABORATORY PRACTICE (PSA-GLP)

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FOREWORD

The Standards Council of Canada ("Council") is a crown corporation established by an Act of Parliament in 1970 to foster and promote voluntary standardization in Canada. It is independent of government in its policies and operations, although it is financed partially by Parliamentary appropriation. The Council consists of members from government and the private sector.

The mandate of the Council is to promote the participation of Canadians in voluntary standards activities, promote public-private sector cooperation in relation to voluntary standardization in Canada, coordinate and oversee the efforts of the persons and organizations involved in the National Standards System, foster quality, performance and technological innovation in Canadian goods and services through standards-related activities, and develop standards-related strategies and long-term objectives.

In essence, the Council promotes efficient and effective voluntary standardization in Canada in order to advance the national economy, support sustainable development, benefit the health, safety and welfare of workers and the public, assist and protect consumers, facilitate domestic and international trade and further international cooperation in relation to standardization.

The Council serves as the government's focal point for voluntary standardization, represents Canada in international standardization activities, sets out policies and procedures for the development of National Standards of Canada, and for the accreditation of standards development organizations, of certification organizations, of calibration and test facilities, of quality management systems registration organizations, of environmental management systems registration organizations and of quality and environmental auditor certifiers. In addition, the Council promotes and supports the principle of recognition of accreditation or equivalent systems as a means of decreasing the number of multiple assessments and audits, both in Canada and with Canada's trading partners.

This document is one of several issued by the Council to define the policies, plans, and procedures established by the Council to help achieve its mandate.

INTRODUCTION

In order to promote international harmonization and cooperation, the Organization for Economic Co-operation and Development (OECD) developed *The OECD Principles of Good Laboratory Practice* (1) which were initially published in 1982. The OECD Principles of Good Laboratory Practice (GLP) are intended to promote the quality and validity of study data. They cover the organizational process and conditions under which studies are planned, performed, monitored, recorded and reported. A 1981 OECD Decision of the Council [C (81)30(Final)] recommended that Member countries apply these principles in the testing of chemicals, and decided that data generated in an OECD Member country in accordance with the OECD Principles of GLP shall be accepted in other Member countries for purposes of assessment and other uses relating to the protection of human health and the environment.

A 1989 OECD Council Decision-Recommendation [C(89)87(Final)] established that Member countries in which testing of chemicals for purposes of assessment related to the protection of health and the environment being conducted pursuant to the principles of GLP shall establish procedures for monitoring compliance with GLP based upon facility inspections and study audits [Part I, 1(i)]. In addition, Part II of the same Decision-Recommendation limited the 1981 Member country Mutual Acceptance of Data (MAD) requirements to those countries that establish such GLP Monitoring Authorities (GLP MA). OECD Decisions are legally binding on all Member countries who do not abstain when the ACT is adopted. Members are obligated to implement Decisions and they must take measures necessary for such implementation. As a result, most OECD Member countries have implemented the OECD Principles of GLP with supporting monitoring authorities.

In this regard, and in recognition of the Council's mandate, it has established a GLP Compliance Monitoring Authority (GLP MA) functioning in accordance with the OECD document *Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practice* (2). Health Canada's Pest Management Regulatory Agency (PMRA), responsible for the regulation of pesticides in Canada, and the New Substances (NS) program (Environment Canada and Health Canada) responsible for administering the regulation of new substances in Canada have recognized the Standards Council of Canada (SCC) in its role as a GLP MA of facilities submitting human health and environmental safety studies in support of pest control products, and the *New Substances Notification Regulations (Chemicals and Polymers)* (the Regulations), respectively.

A list that includes the identity of compliant GLP facility inspected by the SCC GLP MA and a summary of each facility's GLP Areas of expertise is available to the public, as well as national/international GLP MAs or Receiving Authorities on the SCC web site: www.scc.ca.

Applications for recognition of GLP compliance and the corresponding fee structure are available from the SCC's Conformity Assessment Division.

SCC MONITORING AUTHORITY REQUIREMENTS FOR THE RECOGNITION OF GLP COMPLIANT FACILITIES

1 SCOPE

This document describes the policies and procedures of the SCC GLP MA with respect to its granting of GLP compliance. The GLP MA activities focus primarily on inspections and study audits of domestic facilities completing non-clinical studies for submission to the PMRA (pesticides) or the Environment Canada/Heath Canada New Substances Program (Industrial Chemical). Facilities conducting other non-regulated GLP studies can, however, apply for GLP compliance recognition and be inspected by the GLP MA. The GLP MA functions in accordance with the *Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practice* (2) and on a full cost recovery basis between facilities and the SCC according to the Council's current published fee structure.

The PMRA GLP requirements are directed towards domestic test facilities, and test sites, including field sites, involved in pre-registration human health and environmental safety testing of pest control products. The PMRA GLP program's scope includes physical-chemical, analytical, residue and toxicological or ecotoxicological studies as defined by the PMRA receiving authority. A comprehensive list of studies requiring compliance to the principles of GLP is available from the PMRA [www.pmra-arla.gc.ca/english/pdf/dir/dir9801-e.pdf].

The New Substances GLP program's scope includes: acute mammalian toxicity; repeated-dose mammalian toxicity; genotoxicity; skin irritation; skin sensitization; acute fish, D*aphnia* or algal toxicity; and biodegradation studies (NSNR Chemicals and Polymers), section 15(2)) [www.ec.gc.ca/CEPARegistry/regulations/RegText.cfm?intReg=59&intDocument=334].

It is emphasized that the GLP MA is only involved in the recognition of compliance to the OECD Principles of GLP to support the validity of a facility compliance statement. It does not assess the suitability of a study's design, objectives, test system, or result interpretation: functions inherent to the regulatory role of the receiving authority to which the study is submitted.

2 OVERVIEW

Compliance with the conditions found in *The OECD Principles of Good Laboratory Practice* (1) is the prerequisite for obtaining GLP recognition. For short term studies, further guidance and interpretation of the principles are found in *The Application of the GLP Principles to short-term Studies* (7). Compliance is assessed based upon inspections and study audits conducted in accordance with the *Revised Guidance for the Conduct of Test Facility Inspections and Study Audits* (3).

Field site inspections are conducted in accordance with the guidance and interpretation of the GLP principles found in *The Application of the GLP Principles to Field Studies* (6). For organizations with multiple field sites in different geographical locations, initial GLP recognition is based on inspection of the Headquarters site and typically at least one remote site provided that all such sites are functioning under the same management and operational procedures. Subsequent routine inspections are conducted in a manner that would permit a rotation through those sites yet to be inspected and in a manner whereby all the field test sites and headquarters facility will be inspected within a 4-year time period...

Excluding the above policy for multi-site field locations, facilities are subject to a routine full inspection on a 2-year cycle with biennial inspections due on the anniversary date of the facility's GLP compliance recognition.

3 OECD GLP REFERENCES

The following documents from the *OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring* provide further guidance on GLP issues[1]

1) *OECD Principles on Good Laboratory Practice* (1998)

2) *Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practice* (1995)

3) *Revised Guidance for the Conduct of Laboratory Inspections and Study Audits* (1995)

4) *Quality Assurance and GLP* (1999)

5) *Compliance of Laboratory Suppliers with GLP Principles* (1999)

6) *The Application of the GLP Principles to Field Studies* (1999)

7) *The Application of the GLP Principles to Short-term Studies* (1999)

8) *The Role and Responsibilities of the Study Director in GLP Studies* (1999)

9) *Guidance for the Preparation of GLP Inspection Reports (1995)*

10) *The Application of the Principles of GLP to Computerised Systems* (1995)

11) *The Role and Responsibilities of the Sponsor in the Application of the Principles of GLP (1998)*

[1]The versions identified are current as of the publication date of this document but are subject to revision. It is recommended that facilities ensure that they are using the current versions of these documents, available on the internet under the *OECD GLP home page at:* http://www.oecd.org/department/; at time of document publication.

12) *Requesting and Carrying Out Inspections and Study Audits in another Country (2000)*

13) *The Application of the OECD Principles of GLP to the Organization and Management of Multi-Site Studies (2002*)

14) *The Application of the Principles of GLP to in vitro Stu*dies (2004)

17) *Establishment and Control of Archives that Operate in Compliance with the Principles of GLP* (2007)

4 DEFINITIONS

The relevant definitions from the OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, as referenced above, apply.

5 PERSONNEL AND TRAINING

The SCC maintains an inventory of qualified GLP inspectors with practical experience as required by the scope of the areas of expertise included in each receiving authority's GLP program.

Inspectors are obtained primarily from government Departments or Agencies. If qualified inspectors are not available from these sources, individuals are contracted from the private sector. However, in all instances, the SCC has in place conflict of interest protocols that will ensure the independence of the inspectors from the GLP facility, audited studies and corresponding study sponsors.

SCC inspectors have no powers of access to facilities or study data; however, once on site inspectors are tasked with conducting inspections, study audits, interviewing staff, and taking samples or documents as evidence of non-compliance. Any facility that refused such access or does not permit copying of evidence will be declared *Not-in-Compliance* and will be removed from the program.

6 CONFIDENTIALITY

The SCC safeguards the confidentiality of information disclosed in an application, or additional supporting documentation, and information obtained in conducting inspections and study audits. The requirement for confidentiality applies not only to inspectors, but also to any other individuals gaining access to such information as a result of inspection and/or review activities.

However, the names of facilities that have been subject to inspection, their current GLP compliance status and the dates of inspection are not considered confidential. This information is available to relevant parties, including appropriate Receiving Authorities, and is reported annually to the OECD by the GLP MA.

7 MONITORING AUTHORITY OPERATION

The GLP MA operation is consistent with the *Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practice* (2) with the recognition of GLP compliance based upon facility inspections and study audits conducted as per the *Revised Guidance for the Conduct of Test Facility Inspections and Study Audits* (3).

7.1 Application

7.1.1 A facility applies to the SCC GLP MA for recognition by submitting the following:

a) a completed application form;

b) facility information as described in the application form; and

c) the appropriate non-refundable application fee according to the current published SCC fee structure.

7.1.2 A SCC Officer is assigned to the file and acknowledges receipt of the application.

7.2 Pre-inspection Activities

7.2.1 The application and supporting documentation are reviewed by the SCC Officer and additional information is requested, if required. For a GLP-compliant facility undergoing a routine full reinspection, any new information will be reviewed prior to the visit.

7.2.2 When the submitted documentation is deemed complete, a team of inspectors is assembled and a mutually acceptable date is arranged for an inspection. The facility may veto the selection of the inspector(s) but must provide written rationale for such action to the GLP MA; however, depending on the circumstances, there might be instances where a facility must accept the assigned inspectors.

7.2.3 A facility is given appropriate advance notice of any impending inspection or specific study audit.

7.3 Facility Inspections and Study Audits

7.3.1 Inspections to assess GLP compliance fall into the following categories:

a) an initial complete full inspection, including a facility inspection and study audit(s) for facilities which have previously conducted GLP studies;

b) a facility-only inspection without a corresponding study audit(s) for facilities which have not conducted GLP studies. In this case, a pre-inspection is performed to determine that the necessary infrastructure is in place (facilities, equipment, staff, SOPs, archives, etc.) to permit the facility to successfully conduct GLP compliant studies. Once a complete study is available, it is subsequently audited on-site to fully complete the recognition process;

c) a reinspection to verify that identified GLP non-compliances from a previous inspection have been suitably addressed;

d) a regularly scheduled biennial full inspection completed within 3-months of the anniversary date of compliance recognition; or

(e) specific study audits requested by national or international receiving authorities.

7.3.2 Inspection costs are borne by the recipient facility. Costs associated with 7.3.1 (e) are covered internally by the GLP MA.

7.3.3 Inspection findings (including those of section 7.3.1 (b) are discussed with facility management during a Closing Conference in accordance with the *Revised Guidance for the Conduct of Test Facility Inspections and Study Audits* (3). During this meeting, a written list of findings signed and dated by the inspector(s) and facility management is presented to facility staff as evidence of any GLP non-compliances.

7.3.4 Following inspection and within ten (10) days, the facility may appeal any findings in the inspectors' report with which it disagrees.

7.3.5 In response to a request for a specific study audit, as per 7.3.1 (e), the GLP MA provides the requesting authority with a detailed report of its findings; without the option for facility appeal.

7.4 Post-inspection Activities

7.4.1 Upon completion of all required actions, the inspectors review the facility's response to the GLP inspection required actions. Depending upon the nature of the GLP non-compliances, a re-inspection might be needed to verify that actions have been implemented as per clause 7.3.1 (c). The inspectors review and approve the facility responses, but do not grant GLP compliance.

7.4.2 The inspectors' recommendation for approval is appended to the GLP inspection list of findings and forwarded to the SCC GLP Recognition Committee (GLPRC). If the GLPRC can not make a positive recommendation, the facility will be advised of further actions required for compliance. The facility may then either take appropriate action, terminate its application or appeal the GLP MA's decision

7.5 Granting or Continuing Recognition of GLP Compliance

7.5.1 Recognition of GLP compliance is based upon the acceptability of submitted documentation and evaluation of the facility inspection and associated study audits.

7.5.2 Initial recognition is dependent upon the type of the inspection:

a) full recognition of GLP compliance is granted to those facilities for which a satisfactory complete inspection has been conducted, as per clause 7.3.1 (a); or

b) acknowledgement of having the necessary infrastructure in place to complete GLP studies is issued to facilities which have undergone a satisfactory facility-only inspection but have not as yet completed a GLP study, as per clause 7.3.1 (b). Full GLP compliance will only be granted once a study has been completed and audited by the GLP MA.

7.5.3 Continued recognition is based upon the results of regularly scheduled biennial full routine inspections.

7.5.4 The SCC Director of Conformity Assessment grants a facility Recognition of GLP Compliance or continued *In-compliance status*.

7.5.5 If compliance is not granted the facility is advised of the reasons and may appeal the decision, following the procedures established by the SCC for this purpose. Following a final decision for not granting or continuing recognition of GLP compliance, the facility may reapply at a later date.

7.5.6 GLP compliance is recognized by issuing formal documentation to compliant facilities: a certificate and formal letter granting recognition or continued recognition of GLP compliance. Facilities inspected as per clause 7.5.2 (b) are issued a letter acknowledging that the necessary infrastructure is in place (facilities, equipment, staff, SOPs, archives, etc.) to permit the facility to successfully conduct GLP compliant studies.

Additionally, a list of GLP compliant facilities, their dates of compliance and their areas of expertise is maintained on the SCC website.

7.5.7 A recognized GLP facility must continue to comply with the requirements and conditions of the OECD Principles of GLP and to cooperate with the SCC in its performance as a GLP MA verifying such compliance. Specifically, the facility shall:

a) allow the SCC to carry out routine inspections, typically conducted at ~ two-year intervals, to support continued compliance;

b) allow the SCC to carry out specific study audits at the request of national or international receiving authorities; and

c) report immediately, to the SCC, any change that could affect its GLP compliant status. This includes, but is not limited to, changes in the area of studies conducted, personnel (particularly management, QA and Study Directors) or facility infrastructure.

7.6 Actions Resulting from GLP Non-compliance

7.6.1 Where only minor non-compliances have been found, such that the integrity of studies will not be compromised, the GLP MA may grant or continue to grant GLP compliance (as per clause 7.7.2) or, as appropriate, provide the Receiving Authority which requested a specific study audit with a detailed report of the findings.

7.6.2 Where major non-compliances are found, the action taken by the GLP MA is dependent upon the particular circumstances of each case. Actions may include:

a) issuing a recommendation to a Receiving Authority that a study be rejected;

b) issuing a statement to the facility and the receiving authority of the inadequacies or faults found which might affect the validity of studies conducted in the facility; or

c) refusing to grant or continue to grant recognition of GLP compliance. Such an action may include the removal of the facility from the program, a corresponding notation in the GLP MA list of inspected facilities described in clause 7.8, and notification to the applicable receiving authorities, and the OECD.

7.7 Facility GLP Compliance Status

7.7.1 OECD GLP MAs must report facility compliance to each other and do so as: *In-compliance*; *Pending;* or *Not-in-compliance.* However, being declared *Not-in-compliance* can have grave consequences to a facility as it could mean a world-wide receiving authority rejection of study submissions. The GLP MA will use the category *Not-in-compliance* only as a last resort.

7.7.2 If a facility inspection or study audit identifies GLP non-compliances which will not significantly compromise the integrity of studies, and the facility proposes to address them within an acceptable time frame, an *In-compliance* status may be granted to the facility.

7.7.3 If non-compliances are not or can not be addressed within an agreed period, the facility's compliance is deemed to be *Pending* until further notice of satisfactory completion of said actions. Typically, if the facility cannot complete the required actions within three months, it shall be subject to a *Not-in-Compliance* status. For a recognized facility the *In-compliance* status will be changed to *Pending* (with qualification) and can lead to a *Not-in-compliance* (Withdrawn) status.

7.7.4 A facility that does not adhere to the requirements of clause 7.5.7 shall be subject to a *Not-in-compliance* (Withdrawn) status, and shall be withdrawn from the program.

7.8 Reporting Facility GLP Compliance

The GLP MA maintains a list of inspected facilities including the identification of the facility, dates of inspection and decisions, nature of the inspection, fields of compliance, area(s) of expertise and compliance status. The list which also identifies facilities recognized in accordance with clause 7.5.2 (b) as having the necessary infrastructure in place to perform GLP compliant studies is annually reported to all OECD Member counties and observers, the European Commission, the OECD secretariat and applicable domestic receiving authorities. The GLPMA immediately informs all parties of all changes to a facility's GLP compliance status.

7.9 Withdrawal of GLP Recognition

A facility may voluntarily withdraw its GLP recognition by providing written notice to the SCC GLP MA. Voluntary or withdrawal of recognition of GLP compliance by the GLP MA does not preclude a facility from re-entry into the program at a later date as described in section 7.1.

8 APPEAL PROCEDURES

Appeals may result from disagreements with non-compliances identified in the GLP inspectors' reports or with interpretation of the report to decide on recognition of GLP compliance. Appeals resulting from the former situation are addressed by the GLP RC whereas those resulting from the decision of the Committee are resolved by the procedures established by the SCC for this purpose.

9 PUBLICITY GUIDELINES

A significant benefit of SCC recognition of GLP compliance is in the international acceptance of study data generated under the principles of GLP in a facility recognized by a GLP Monitoring Authority. Compliant domestic GLP facilities inspected by the SCC GLP MA may publicize their recognition status as per the following statement:

> "GLP compliance has been recognized by formal documentation issued on Yr/Mo/Day by the Standards Council of Canada GLP Monitoring Authority based upon an inspection and study audits conducted Yr/Mo/Day - Yr/Mo/Day in the area(s) of [type of study(ies)] of [Chemical Type]."

Should recognition be terminated by the facility, or withdrawn by the SCC GLP MA, the facility must immediately cease issuing all reference to its former GLP compliant status. Upon reinstatement, a facility may resume such publicity.