Overview

- SCC: who are we?
- OECD GLP Decisions-recommendations
- National GLP commitments
- SCC GLP Monitoring Authority
- Significant OECD GLP requirements
- GLP Non-compliances
- GLP Information exchange
GLP Historical Perspective

- 1970s: Data Fraud/Data Quality Issues
- 1978: US FDA GLP Regulations drafted
- 1989: Council Decision-Recommendation on Compliance with the OECD Principles of GLP
- 1997: Revision of the OECD Principles of GLP
- **1998**: SCC Monitoring Authority (MA); PMRA RA
- 1999: First Canada GLP Inspections
- 1999: EPA/PMRA MOU signed
- 2004: OECD MJV to Canada
- 2007: SCC MOU with Environment Canada; RA
- 20xx: Health Canada ??
Standards Council of Canada

- GLP Monitoring Authority
  - Pest Management Regulatory Agency (PMRA)
    - Pest Control Products ACT; Regulatory Directive 98-01
  - Environment Canada, New Substances Division
    - Canadian Environmental Protection Act (CEPA, 1999)
    - New Substances Notification Regulations (NSNR, 2005)
      (Chemicals and Polymers)
International Commitments

- Canada signatory to OECD Council Acts (1961)
  - Mutual Acceptance of Data (MAD) in the Assessment of Chemicals (1981)
  - Decision-Recommendation on Compliance with Principles of Good Laboratory Practice (1989)
Legal Status of OECD Acts

- Article 5 of the OECD convention states that the Organization may take decisions and make recommendations to Members. These are the Acts of the Organization.
  - **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 the measures necessary for such implementation.

- **Recommendations** are not legally binding but there is an expectation that Member countries will do their utmost to fully implement a recommendation.
OECD Council Decision on Compliance with GLP Part I

- "Decides that member countries shall":
  - Establish national procedures for monitoring compliance
  - Designate an authority (s) for monitoring
  - Require test facilities to issue a compliance declaration

[Annex 2 C(81)30 Final]
OECD Council Decision on Compliance with GLP Part II

- “Decides that member countries shall”:

- Recognize the assurance by another Member country that test data have been generated in accordance with the GLP principles if the member country complies with Part I and Part II paragraph 2

- MAD or Mutual Acceptance of Data
Council Decision on Compliance with GLP
Part II Paragraph 2

- “Decides that member countries shall”:

- Designate an authority for international liaison

- Exchange with other member counties information concerning procedures for monitoring compliance

- Implement procedures whereby GLP compliance status of facilities can be sought by other member countries
EPA/PMRA Cooperation
PMRA/EPA MOU

- MOU signed in June 1999
- Recognizes ‘comparable’ FIFRA/OECD GLP requirements
- Recognizes intent for consistent inspection procedures
- Confirm by joint training and inspections
- Information sharing, requests for inspections
  - Prior to OECD MJV program implemented
Mutual Acceptance of Data (MAD) in the Assessment of Chemicals (1981)

- OECD Council **Decision** (MAD): “Recognize the assurance by another Member country that test data have……”

- 2004 OECD MJV review of the SCC GLP Monitoring Authority
- MOUs no longer required between Canada and USA
  - Canada should accept EPA compliant studies
  - EPA should accept Canadian OECD compliant studies
  - Canadian Industrial Chemical and Pesticide studies accepted world-wide
OECD cf. EPA GLPs

- Recent GLP Forum Discussion
  - Study completed following EPA and OECD GLPs?
  - Is that possible? Perhaps; but OECD GLPs are not regs.
  - Is that necessary? Not for Canada/US studies
  - MAD and EPA/PMRA agreement

- Canada MA example
  - USA sponsored study; field phase completed at Canadian CRO
  - Submission to PMRA
  - Study to be completed following OECD GLPs; but
  - Study was designed as a mixture of EPA and OECD GLPs
  - Regardless of country; prepare/complete following country of origin requirements: accepted by EPA and PMRA
National Legislative Study Requirements*

- For each group of chemicals specify the type of testing for which GLP is mandated
  - **industrial chemicals**: EC/HC program
  - pharmaceuticals
  - veterinary medical products
  - **pesticides**: PMRA program
  - food additives
  - feed additives
  - cosmetics
  - **biocides**: PMRA program
  - other products (specify)

*NSNRs apply if a product group contains an industrial chemical
Council Recommendation on Compliance with GLP Part I

- “Recommends that member countries apply”:
  - The Guides for Compliance Monitoring for GLP (110) and
  - The Guidance for Conduct of Laboratory Inspections and Study Audits (111)
SCC GLP Compliance Monitoring Authority

- Follows OECD documents for operation of Compliance Monitoring Authorities (110), and conducting inspections/study audits (111)

- MA key requirements:
  - Maintain team of trained inspectors
  - Have published program documents
  - Maintain records of inspected facilities
SCC GLP MA Documents

- CAN-P-1583, SCC Monitoring Authority Requirements for the Recognition of GLP Compliant Test Facilities (2008)
- Facility specific checklists revised
  - Test Facility and associated Study Audits
  - Test Sites and associated Study Audits
  - Field Sites and associated Study Audits
- Application Form
SCC MA GLP Recognition Process

- Facility applies
- Documents requested and reviewed
- Inspection dates mutually arranged
- Inspection findings discussed
- Signed report left with management
- Facility responds to required actions
- GLP recognition granted
- Facility issued a Certificate of Recognition
- Areas of expertise posted on SCC website
- Re-inspection on 2-year cycle
CERTIFICATE OF RECOGNITION

Facility name
address

having been inspected under the authority of
the STANDARDS COUNCIL OF CANADA (SCC) Act
and found to comply with the requirements of the OECD
Principles of Good Laboratory Practice (1998) and the conditions
established by the SCC is hereby recognized as a
GLP COMPLIANT FACILITY
for specific areas of expertise
approved by the Standards Council of Canada.

CERTIFICAT DE RECONNAISSANCE

Facility No. Installation n°: XX
Reconnue le: XX
Recognition date: XX

Délivré le: XX
Issued on: XX

Date d’expiration: XX
Expiration date: XX

Chair (SCC) / Présidence (CCN)

Inspection performed according to the Guidelines for the Recognition of GLP Compliant Test Facilities, CAN-1563 (OECD, ENV/MC(94)9(9)) and the revised Guidance for the Conduct of Test Facility Inspections and Study Audits (OECD/IN/9647).

Inspection réalisée conformément aux lignes directrices pour la reconnaissance du respect des Principes de BPL, dans les installations d’essai (CAN-1563) (OECD, ENV/MC(94)9(9)) et aux directives révisées pour la conduite des inspections de laboratoires et de certification d’essai (OECD/IN/9647).

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Canadian GLP Facilities
(01-28-09)

- Total Recognized Facilities: 21
- Test Facilities: 11 (4 sponsors; 7 labs)
- Test Sites: 10
  - Field 8 (31)*
  - LAB 2
- Field Sites:
  - CRO (8) 14
  - Univ. 2
  - AAFC 9
  - Sponsor 6
- (Total)* 31

Standards experts. Accreditation solutions.
Canadian GLP Field Sites
GLP Definition

- “GLP is a quality system concerned with the organizational processes and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.” (ENV/MC/CHEM(98)17:section I)

- GLP applies to chemical pre-market phase

- Accreditation applies to chemical post-market phase

- “Data generated under ISO standards is unlikely to be accepted by regulatory authorities.” OECD November 1994.
SCC MA GLP Inspections

- Based on OECD, *Revised Guidance for the Conduct of Laboratory Inspections and Study Audits* (1995)
  - Full inspection
    - Facility Inspection and Study Audit
  - Study Audit (directed)
    - Receiving Authority Requested
  - Pre-inspection
    - Facility-only inspection
    - Study Audit after
Inspection Purpose

• To determine the degree of compliance of the facility and studies with the GLP Principles

• To determine integrity of data to assure that resulting data are of adequate quality for assessment and decision making by the receiving authority

  • Study Audits for study reconstruction
  • Study Audit directed by Receiving authority
Inspection Process

- “Inspectors should not be concerned with the scientific design of a study or the interpretation of the findings”

- “These are the responsibility of the regulatory authority to which the data are being submitted”
Inspection and Study Audit Procedures

- Organization and Personnel
- Quality Assurance Program (QAP)
- Facilities Suitable
- Apparatus, Materials, Reagents
- Test System
- Test and Reference Items
- SOPs
- Study Plan
- Final Report
- Archiving
GLP Study Plan Signatures

- QAP signed and dated **before** the Study Director signs
  - Signifies QAP reviewed
  - Might see signed same day as Study Director

- Study Director signature and date, becomes the study initiation date
- Any changes after that date are either deviations or amendments
- Sponsor signature not required in Canada
- Might see numerous signatures: only SD and QAP required
Quality Assurance Program (QAP)

- Must be independent of the study audited
- Must conduct audits of all studies

- Must provide a QAP statement in final reports
  - List types of inspections made
  - Phases of study inspected
  - Dates inspections reported to management, SD, PI and PI management, if applicable
  - Statement confirms the final report reflects the raw data

- Inspectors do not audit QAP reports
- Inspection reports must be archived
Study Director Compliance Statement

- **Decision** that: "management of test facilities issue a declaration that a study was carried out in accordance with GLP Principles and pursuant to any other…….”

- Study Director signed and dated final report becomes the date the study is completed
  - Any changes after that date are amendments
  - Statement indicates extent of compliance with the GLPs; list of any elements not done under GLP
  - SD acceptance of responsibility for the validity of the data
  - Any deviations must be specified

- **Sponsor signature not required in Canada**
Retention of GLP Records

- OECD GLPs: “Retained and in the archives for the period specified by the appropriate authorities”

- NSNR (Chemicals and Polymers) retention of information, Part 3, Clause 13: “the information and supporting documentation must be kept for a period of five years after the year in which the information is provided”
  - Applies to the person that is required to supply information to the Minister
Pest Management Regulatory Agency
Record Retention

- Retained at least until submission review complete
- Retained as long as sponsor holds research permit
- Specimens/samples kept as long as evaluation possible*
- Date, reasons, authority for disposal stored in archive*
- If test facility goes out of business sponsor or legal successor must retain documentation*
  - * GLP Principles
SCC GLP MA Audit Findings

- Missing amendments in final reports
- Missing QAP statement
- Personnel record deficiencies
- Organizational chart issues
- Archiving issues
- Missing SOPs
- SOPs missing elements
- Tardy SD approval of deviations

*Actions required but study integrity not impacted*
EPA Minor (III) Study Audit Findings

- Failure to maintain SOPs
- Failure to follow SOPs
- No QAP statement in the final report
- Failure to keep personnel records
- Final report does not include all, or has inadequate elements
- Final report not signed and dated by the SD

*Indicates lack of control over the study by the sponsor. May be able to accept study if sufficient raw data to reconstruct the study. Warrants careful monitoring of any future studies from registrant/test facility, EPA 1995*
Actions from Non-Compliance

- Minor non-compliances, study integrity not compromised: facility has 3 months to correct and submit documented evidence of completion of deficiencies
  - Facility/study *In-compliance*

- Major non-compliances, study integrity compromised: actions dependent upon circumstances of each case
  - Recommend to regulator that study be rejected
  - Advise regulator of inadequacies which might affect validity of studies conducted at the facility
  - Refuse to grant or continue to grant GLP compliance
  - Withdrawal of facility from the program
Monitoring Authority Information Exchange

Member countries shall: *implement procedures whereby GLP compliance status of facilities can be sought by other member countries*

- Monitoring Authorities report annually to each other, the OECD and the European Commission on all activities
- Any change in compliance status reported immediately to other Member counties
- Canada must report annually to domestic Receiving Authorities
- Receiving Authority ‘A’ communicate with Monitoring Authority ‘A’; who then communicate with Monitoring Authority ‘Z’ who communicate with Receiving Authority ‘Z’
Monitoring/Receiving Authority

- International MAs communicate with Member country MAs as per model

- Domestic:
  - Appointed contacts
  - Annual meeting (s)
  - Receive OECD Annual reports
  - Reports on domestic facility compliance
  - Recommend to RA that a study be rejected
  - Advise RA of the inadequacies or faults which might affect validity of studies conducted in the facility
More Information

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Compliant facilities at: