Good Laboratory Practice

EU-Serbia screening meeting

Brussels, 19 June 2014

DG Enterprise and Industry
Chemicals industry unit

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Purpose of GLP principles

- Principles of GLP ensure the **quality and validity of data** generated in non-clinical safety studies for regulatory purposes.
- GLP is a quality system and a management tool concerned with how safety studies are **organised, planned, performed, reported, reviewed and archived**, allowing the reconstruction of the study to test data integrity.
- Comparable quality of test data forms the basis for **mutual acceptance of data** among countries, which helps avoid duplicative testing, thereby saving time and resources.

Content of GLP principles

1. Test facility organisation and personnel
2. Quality assurance programme
3. Facilities
4. Apparatus, material & reagents
5. Test systems
6. Test & reference items
7. Standard operating procedures
8. Performance of the study
9. Reporting of the study results
10. Storage and retention of records and materials

History of GLP principles

- Cases of fabrication of data, removal of health effect findings from reports, unexplained changes in the animal data, uncovered by the FDA in the 1970s, led to the first local GLP Regulations

- OECD Council Act on **Mutual Acceptance of Data (MAD)** in the Assessment of Chemicals (C(81)30), *including the OECD Test Guidelines (Annex I) and the* ***OECD Principles of GLP*** *(Annex II)*

- OECD Council Act on **Compliance with Principles of GLP** (C(89)87), *including guidance for monitoring procedures, test facility inspections and study audits.*

- Implementation in **EEC Directives** 87/017/EEC and 88/320/EEC, later replaced by 2004/10/EC and 2004/9/EC

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EU legal basis for GLP

- **Directive 2004/10/EC** (11 February 2004) on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances
  (based on Council Directive 87/18/EEC)
  - **Includes the OECD principles of GLP in Annex I**

- **Directive 2004/9/EC** (11 February 2004) on the inspection and verification of good laboratory practice (GLP)
  (based on Council Directive 88/320/EEC)
  - **Includes the OECD guidance for compliance monitoring procedures, test facility inspections and study audits in Annex I**

Directives transposed into national legislation

EU legal basis for GLP

Directive 2004/10/EC

- **Article 1**: "Member States shall take all measures to ensure that laboratories carrying out tests on chemical products, in accordance with Directive 67/548/EEC, comply with the principles of good laboratory practice" [or] "where other Community provisions provide for the application of the principles of GLP"

- *Chemicals (Reg. 1907/2006 & 1272/2008)*
- *Human medicinal products (Dir. 2003/63/EC am. 2001/83/EC)*
- *Veterinary products (Dir. 2009/9/EC am. 2001/82/EC)*
- *Detergents (Reg. 648/2004)*
- *Feed additives (Reg. 429/2008)*
- *Food additives (Reg. 234/2011)*
- *GM food/feed (Reg. 503/2013)*
- *Pesticides (Reg. 1107/2009)*
- *Biocides (Reg. 528/2012)*
- *Cosmetics (Reg. 1223/2009)*

EU legal basis for GLP

Examples: chemicals & pharmaceuticals

Chemicals: REACH Regulation No 1907/2006

Article 13.4: *"ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of GLP provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or the Agency"*

Human Medicinal Products: Dir. 2003/63/EC am. 2001/83/EC:

Annex: *"Non-clinical (pharmaco-toxicological) studies shall be carried out in conformity with the provisions related to Good Laboratory Practice" (Annex)*

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Role of member states: compliance monitoring

Dir. 2004/9/EC, Art. 2(1):
"Member States shall verify the compliance with GLP of any testing laboratory within their territory claiming to use GLP in the conduct of tests on chemicals."

- **748** laboratories in compliance in the EU/EEA in 2012

Country	IC	Country	IC
Austria	16	Latvia	1
Belgium	18	Netherlands	30
Czech Rep.	12	Poland	24
Denmark	26	Portugal	4
Finland	12	Slovakia	13
France	110	Slovenia	2
Germany	155	Spain	75
Greece	7	Sweden	15
Hungary	31	UK	113
Ireland	4	Norway	5
Italy	75	Switzerland	31

Role of member states:
compliance monitoring

Dir. 2004/10/EC, Art. 3.1:
"Member States shall adopt the measures necessary for verification of compliance with the principles of good laboratory practice. These measures shall include, in particular, inspections and study checks in accordance with the recommendations of the OECD in this area."

Dir. 2004/9/EC, Art. 3:
"Member States shall designate the authorities responsible for the inspection of laboratories within their territories"

Compliance monitoring programmes are assessed by other countries through OECD / EU on-site evaluations

Role of member states:
compliance monitoring

ECJ Case C-95/08, Commission vs. Luxembourg:

"The Court declares that by not putting in place the authorities able to verify the implementation of the principles of good laboratory practice, the Grand Duchy of Luxembourg has failed to fulfil its obligations under Article 3 of Directive 2004/9/EC"

Role of member states: authorities

- **National monitoring authorities** set up GLP compliance monitoring programmes, inspect laboratories on a regular basis and conduct audits on studies carried out by laboratories in order to assess compliance with GLP.

- **Receiving authorities** receive GLP data (non-clinical safety data); they may verify the GLP compliance status of a test facility or request a study audit by a monitoring authority
  - European authorities: ECHA, EFSA, EMA
  - National authorities, e.g. clinical trial authorities

Role of member states:
internal market

Dir. 2004/10/EC, Art. 5:
"Member States may not, on grounds relating to the principles of GLP, prohibit, restrict or impede the placing on the market of chemical products if the principles applied by the laboratories concerned are in conformity"

Dir. 2004/9/EC, Art. 5:
"The results of laboratory inspections and study audits on GLP compliance carried out by a Member State shall be binding on the other Member States."

Role of member states:
information exchange

Dir. 2004/9/EC, Art. 4:
"Each year, Member States shall draw up a report relating to the implementation of GLP within their territory. [...] The reports shall be forwarded to the Commission each year, not later than 31 March."

Dir. 2004/9/EC, Art. 6:
"Where a Member State has sufficient reason to believe that a laboratory in another Member State claiming GLP compliance has not carried out a test in accordance with GLP, it may request further information from that Member State and in particular may request a study audit, possibly in conjunction with a new inspection."

Annual EU GLP working group meetings in Brussels

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Role of the European Commission

- Ensure uniform application of the GLP principles and compliance monitoring in all MS
- Facilitate acceptance of data among MS & by OECD MAD countries
- Regular meetings of MS experts in the EU GLP Working Group
- Coordination of information exchange on inspected laboratories
- Interaction between monitoring and EU receiving authorities
- Coordination of evaluation visits
- Participation in OECD working group meetings and coordination of EU MS views
  (all EU MS are OECD Members except BG/HR/CY/LT/LV/MT/RO)

Questions?

More information (including full legal basis, list of national authorities and Q&A document):
http://ec.europa.eu/enterprise/sectors/chemicals/documents/specific-chemicals/laboratory-practice/index_en.htm

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