Question and Answer document on Good Laboratory Practice

Which principles of Good Laboratory Practice (GLP) need to be taken into account in clinical trials?

• In accordance with article 25 (3) of the Clinical Trial Regulation non-clinical information submitted in an application dossier shall be based on data derived from studies complying with Union law on the principles of good laboratory practice as laid out in Directive 2004/10/EC, as applicable at the time of performance of those studies.

• Therefore these studies must be conducted in a test facility that is part of the national GLP monitoring programme of a European Union (EU) Member State, Organisation for Economic Co-operation and Development (OECD) Member Country or fully adherent to the Mutual Acceptance of Data (MAD), and found to be in compliance with the principles of GLP.

• Studies conducted at a facility located in a non-MAD adherent country may be accepted if the facility has been subject to a full monitoring inspection conducted by a monitoring authority from an EU member state country, OECD Member Country or full adherent to the MAD agreement and found to be compliant at the time the data was generated. However if the study is considered to be pivotal to the application, there is a possibility that a study audit will be required by some regulatory receiving authorities at the time an IMPD is received or at the time the Marketing Authorisation Application (MAA) is reviewed.

• Sponsors should include a statement confirming the GLP status of the studies or equivalent standards (i.e. principles of GLP recognised by other countries) within the IMPD (Annex I point 44), unless properly justified.

• **A summary table should be provided, listing the non-clinical studies and indicating the following for each study:**
  1. study title,
  2. study code (Unique identifier assigned to the study),
  3. date of completion of the Final Report,
  4. test facility and test sites in which the study was conducted,
  5. complete address of the test facility (and test sites where applicable),
  6. period in which the test facility(ies) and/or test site(s) was (were) used

• Sponsors should also indicate if in that period the facility was part of a European Union (EU) or an Organisation for Economic Co-operation and Development (OECD) Mutual Acceptance of Data (MAD) - accepted GLP monitoring programme.
Which principles of Good Laboratory Practice (GLP) need to be taken into account in relation to Advanced Therapy Medicinal Products (ATMPs)?

- It is generally expected that non-clinical safety studies\(^1\) are carried out in conformity with the principles of GLP. However, it is recognised that, due to the specific characteristics of ATMPs, it would not always be possible to conduct these studies in conformity with GLP. Exploratory pre-clinical studies, where safety information is obtained alongside with other information (e.g. in dose finding studies), are also not expected to be conducted under GLP.

- If a pivotal non-clinical safety study has not been conducted in conformity with the GLP principles, a proper justification should be submitted. This justification should also address the potential impact of the non-compliance on the reliability of the safety data.

- When pivotal non-clinical safety studies are not conducted in compliance with GLP, detailed documentation of study conduct and archiving of data should be ensured. Additionally, the conduct of the study should be in accordance with a prospectively designed study protocol. A summary of deviations from the protocol and their potential impact on the outcome of the study should be included in the relevant study report. The sponsor of the non-clinical study should consider appointing a person responsible for the oversight of the conduct of the study and the study reports.

- Applicants who submit pivotal safety studies that are non-GLP compliant in the context of an application for a clinical trial or a marketing authorisation may be asked to submit additional data to justify the reliability of the studies or to permit a site visit to verify the conditions under which the study has been conducted.

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\(^1\) The term “pivotal non-clinical safety studies” refers to toxicity studies which support the non-clinical safety conclusions. Among others, the following are not considered non-clinical safety studies: basic research (primary and secondary pharmacology), proof of concept studies, dose response studies, analytical quality control testing for clinical and commercial studies, stability testing on commercial products and feasibility studies.