What is GLP and when is it Indicated?[1]

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--- Prior to IND, only *in vivo* safety studies need to be performed under GLP ---

Good laboratory practices ("GLP") were first drafted by the U.S. Food and Drug Administration ("FDA") in 1976 (and finalized in 1978) in response to falsified and poorly documented toxicology data submitted by certain organizations seeking drug approvals, most notably the pharmaceutical company Industrial BioTest Labs ("IBT")[2]. GLP is the framework that enables regulatory agencies to be assured of the quality and integrity of safety data. It is an operating standard to which organizations seeking regulatory approval will adhere. The GLP requirements relate to the procedures by which laboratory studies are conducted rather the nature of the research itself. The 16-page 21 CFR Part 58 publication, under its subparts A-K, includes provisions relating to organization, personnel, facilities, equipment, testing facilities operation, test and control articles, protocols, recordkeeping, and test facility disqualification [1].

In parallel with the US FDA GLP guidelines, several other issuing authorities have drafted their own version of GLPs. The U.S. Environmental Protection Agency ("EPA") refers to 40 CFR Part 492. Europe's Organization for Economic Co-operation and Development ("OECD") has their own GLP series, currently comprised of 14 documents detailing GLP guidelines, advisory documents and other GLP specifications [3][4]. The European Medicines Agency ("EMA") provides GLP inspection advice and guidelines on bioanalytical method validation, and cross-contamination prevention in nonclinical safety studies.

Requirements listed within 21 CFR Part 58 for undertaking an FDA GLP study include [1]:

- Assignment of a study director for each study conducted, who will be responsible for overseeing all aspects of the execution and completion of the study;
- Appropriate standard operating procedures ("SOP"s) must be developed and followed by trained personnel;
- A separate quality assurance ("QA") unit must monitor the studies and periodically submit reports of compliance;
- Test articles must be fully characterized (for example, the active pharmaceutical ingredient ("API") must be characterized);
- The testing facility must have a system for archiving and retaining previous study data and reports.

As conducting a study under GLP involves an extensive operational burden, it can be important for a sponsor to be aware of which stages in the drug development process need to be GLP compliant. Early discovery and screening studies are not regulated for regulatory submission [2]. Though not required, some sponsors will opt for performing "functional preclinical studies" with GLP controls as a precautionary measure to maximize study controls if the study were to be submitted for regulatory approval later on [2]. However, GLP studies may drive up the cost of a study (sometimes significantly). Therefore the organization should consider whether filing is highly feasible, especially since professional non-GLP laboratories typically operate under procedures that more or less replicate GLP conditions and which provide reliable and quality results.

[1] This provides a brief introduction to GLP requirements; is not intended to be definitive. For formal guidelines the reader is referred to the appropriate regulatory guidelines [2][3][4]

In brief:

- Good laboratory practices (GLP) creates a standard baseline for the increased quality and integrity of data obtained from studies that assess the safety and efficacy of new drug filings;
- GLP is not required for early development stages such as concept assessment and screening;
- Prior to an investigational new drug application ("IND") filing, GLP is required only for safety studies. Such safety studies may comprise *in vivo* measurements of biocompatibility, metabolism, toxicology and pharmacology. For any *in vivo* preclinical animal safety tests, GLP will be required if a regulatory filing is anticipated.

References:

[1] Code of Federal Regulations, Title 21, Food and Drugs, Subchapter A – General, "Good Laboratory Practice for Nonclinical Laboratory Studies", Part 58 (US Government Printing Office, Electronic Code of Federal Regulations, current as of January 18, 2016). http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=58

[2] DeRoo, D., GLPs and GMPs: When are they necessary?. NAMSA White Paper (2014). http://www.namsa.com/LinkClick.aspx?fileticket=-Vm5VOgldvo%3D&portalid=0&language=en-US

[3] Code of Federal Regulations, Title 40, Protection of Environment, "Good Laboratory Practice Standards", Part 792 (US Government Printing Office, Electronic Code of Federal Regulations, current as of January 28, 2016). https://www.gpo.gov/fdsys/pkg/CFR-2011-title40-vol32/xml/CFR-2011-title40-vol32-part792.xml

[4] OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 14, Advisory Document of the Working Group on Good Laboratory Practice, The Application of the Principles of GLP to *in vitro* Studies, ENV/MJ/MONO (2004) 26. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?doclanguage=en&cote=env/jm/mono(2004)26