



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

January 22, 1992

MEMORANDUM

SUBJECT: Interpretation of the Good Laboratory Practice (GLP)
Regulation

GLP Regulations Advisory No. 42

FROM: David L. Dull, Director
Laboratory Data Integrity Assurance Division

TO: GLP Inspectors

Please find attached an interpretation of the GLP regulations as issued by the Policy & Grants Division of the Office of Compliance Monitoring. This interpretation is official policy in the GLP program and should be followed by all GLP inspectors.

For further information, please contact Francisca E. Liem at FTS-398-8265 or (703) 308-8265.

Attachment

cc: M. Stahl
C. Musgrove

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

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Dear

This is in reply to your letter of June 5, 1991 in which you requested clarification on several issues involving the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Good Laboratory Practice Standards (GLPS). Your questions were related to archiving requirements, test and reference substance characterization testing, and the separation of GLP work from non-GLP work in a testing facility.

Your first question was in reference to the archiving requirements for final report and protocols at the end of a study. You cited two of the EPA's responses (numbers 12 and 28) in the Draft Question and Answer document distributed on December 5, 1990, and two additional responses to direct inquiries which have been released as "advisory" documents (numbers 9 and 12). You were concerned with the EPA statements regarding the timing of the transfer of material to archives. EPA had stated that the archiving, which is required at 40 CFR 160.33 to be accomplished "during or at the close of the study", must be done before the compliance statement and the final report are signed. Your specific concern was that this appeared to cause problems since the signed document, (i.e., the compliance statement and the final report) are among the items that are required to be archived, and they must be archived after they are signed. Thus, it does not seem possible to complete all archiving before the compliance statement and study report are signed. Tangentially, you asked whether the requirement that "all ... protocols, ... and final reports" for a study be archived was inconsistent with the regulations since there should be only one protocol and final report for a study.

You are correct in assuming that a copy of the signed study report including the signed compliance statement are among the materials that must be archived during or at the close of the study EPA agrees that such archiving is technically unfeasible until after these documents have been signed. Consequently, the requirement at 40 CFR 160 33 that archiving occurring "during or at the close" of the study must be interpreted as requiring that copies of the compliance statement and study report must be archived immediately upon being signed by the study director. There is no substantial difference between the order in which these document are signed; the study director is accountable for the truth and accuracy of these documents in any case. There is also no inconsistency with the compliance statement being included in the final report for submission to the EPA.

In reply to your query about the pluralization of the terms

"protocol" and "final report" in regards to the archiving needs for a study (i.e., at 40 CFR 160 33 and 160 190), you are correct in noting that having more than one protocol and study report would be inconsistent with the GLPS. However, the issue dealt with in question number 28 was that retention of documents, which is specifically addressed at 40 CFR 160 190(a). The language from that section, which includes pluralization of the terms "protocol" and "report" even though the reference is to a single study, was copied directly into the Question and Answer document. In the regulation, the pluralization of those terms assures that all protocols and reports from numerous studies, as well as amendments and interim reports for any given study, must be kept. This is admittedly confusing in the limited context of the question which you cited, and we therefore intend to change these terms to the singular tense in the final draft of that Question and Answer document.

Your second question referred to 40 CFR 160.105 which requires test, reference and control substances to be adequately characterized before use in a study. Your specific concern was whether there were problems when characterization has been done as a part of a different study, i.e., to meet the data requirements for registration as stated at 40 CFR Part 158. You felt that a person citing such a characterization study in order to meet the requirements of 40 CFR 160 105 would not be able to assure GLP compliance since the characterization was performed by somebody else.

You may be confusing the characterization study requirements of 40 CFR Part 158 with the GLP characterization requirements at 40 CFR 160.105. These are not identical. The data requirements under 40 CFR 160.105 fulfill an entirely different purpose from the chemical characterization requirements under 40 CFR Part 158. The GLP characterization requirements are batch specific, and deal with the specific material used in the study. They also include data on control and reference as well as on the test substance, and require only that information stated at §160.105. The Part 158 requirements are general to the product and do not supply appropriately detailed information for characterizing that test substance which is used in a specific study.

In your third question you asked for comment on the situation where a facility performs both GLP and non-GLP studies. You suggested that such a facility might have standard operating procedures in place which are active only during GLP studies. For example, the standard operating procedures (SOPs) might state that they are only active during GLP studies.

There is no problem with having both GLP and non-GLP studies performed at the same facility as long as there is no interference

with the performance of the studies required to be under GLPS. For example, when facilities are shared between different studies, this may affect the availability of personnel or facility resources. Section 160.29© states that "there shall be a sufficient number of personnel..." and section 160.41 states that "each testing facility shall be of suitable size..." and "...shall be designed so that there is a degree of separation that will prevent any function or activity from having an adverse effect on the study. "In order to document that these sections were complied with, it would be necessary to document non-GLP activities that GLP personnel are also engaged in, and it would be necessary to document that non-GLP research does not interfere with available space for GLP Studies or interfere with test system, e.g., quarantine requirements. It is also necessary to assure that equipment "...be of appropriate design and adequate capacity..." (40 CFR 160.61) and "... be adequately...maintained... tested, calibrated and/or standardized..."(40 CFR 160. 63). This means that non-GLP work performed on equipment used for GLP studies must be documented to indicate that the equipment's capacity is not exceeded and to assure that maintenance and calibration requirements are met. (It may be necessary to perform certain maintenance or calibration procedures after so many hours of operation, number of analyses etc.).

If SOPs include a statement indicating that such SOPs need only be followed in the case that a study is under GLPS, this would cause problems if there were inadequate procedures to differentiate , at the technician level) GLP studies from non-GLP studies. If a study were incorrectly identified as non-GLP during the execution of a particular procedure it would result in non-compliance There should be no problems if there are procedures in place to clearly indicate at all times when a study is under GLPS.

If you have any questions concerning this response, please contact Steve Howie of my staff at (703) 308-8290

Sincerely yours,

/s/John J. Neylan III, Director,
Policy and Grants Division
Office of Compliance Monitoring (EN-342)

cc: David Dull

GLP File