UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

December 20, 1989

MEMORANDUM

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

GLP Regulations Advisory No. 9

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-475-9864.

Attachment

cc: C. Musgrove

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Dear

This Is In response to your letter of December 1, 1989 to David L. Dull, requesting information concerning the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Good Laboratory Practice standards (GLPs). That letter was referred to my office for response. Specifically, you asked for clarification on the following four points:

1. What is the definition of "quality assurance verification" at 40 CFR 160.190(a)? Can this be met through SOPs that are periodically inspected by the quality assurance unit (QAU)?

2.a. Must the compliance statement required at 40 CFR 160.12 be one sheet, or can the sponsor and applicant sign one sheet, with the study director signing the overall report containing a section on compliance? Can there be separate statements, and are three signatures required if the sponsor and applicant are the same?

2.b. Can the sponsor sign the study report after the study director?

3.Since test substances, as defined at 40 CFR 160.3 include degradation products or metabolites, is it necessary to include metabolites and reference substances to determine metabolites to the protocol?

Our staff has examined your questions and offer the following clarifications.

1. In the August 17 1989 GLP rule, 54 FR 34052, EPA clarified that quality assurance verification means that the material needs to bo retained until the QAU assures that its discarding does not negatively affect the quality of the study. This clearly implies that the verification Is a duty of the QAU, not the study personnel. It is not appropriate for the QAU to delegate its responsibilities to the personnel performing the study through SOPs or any other mechanism. Thus, the suggestion that verification be through S0Ps periodically checked by the QAU Is unacceptable.

2.a. EPA views the compliance statement as an Important document and does not believe that It fulfills Its Intended function unless it is signed by all parties as specified at 40 CFR 160.12. The regulations also specify at 40 CFR 160.185(b) that the study director must sign and date the study report. While it is clear that the regulations intend that both the compliance statement and the study report be signed by the study director this could be accomplished by including the compliance statement on the same page of the final report that the study director signs.

Regarding those situations where the sponsor and applicant are the same person, that person need sign only once provided that person is clearly identified on the compliance statement as both sponsor and applicant.

In response to your question on whether the individuals signing the compliance statement may sign separate copies the answer is yes. Where the sponsor, applicant, or study director sign separate copies of the compliance statement each copy must be identical in content and must be included in the study report with the appropriate signature.

2.b. The purpose of the study director's signature is to assure accountability for the contents of tho final report. Thus any amendments to the final report that reflect work that the study director Is accountable for require the study director's signature. However EPA has clarified, at 160.185(c), that reformatting or other modifications to conform with EPA's submission requirements (e.g. to conform with PR Notice 86-5) do not constitute amendments that require study director signature. Insofar as the sponsor signed items Included In the final report do not constitute products intrinsically related to the performance of the study EPA sees no reason to require that the submission of the report be delayed to acquire the study director's signature. Such contents should be clearly Identified as non-data Items, and the signature should be clearly identified as the sponsor signature.

3. The term "test substance”, as defined in section 160.2, does include any degradation product or metabolite which is used in a study to assist in characterization the toxicity, metabolism, or other characteristics of a substance that is the subject of an application for a research or marketing permit. However, in the case that determining metabolites or degradation products is the stated objective of the study, such determination constitutes tho characteristic that Is being determined. Thus, in such a study metabolites or degradation products do not constitute the test substance. However any reference substances intended to characterize such metabolites and degradation products should be identified in the protocol by amendment if necessary.

If you have any questions concerning this response, please call Steve Howie of my staff at (202) 475-7786.

Sincerely yours,

/s/John J. Neylan III, Director
Policy and Grants Division
Office of Compliance Monitoring

cc: David L. Dull
GLP File