UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

June 10,1993

MEMORANDUM

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

GLP Regulations Advisory No. 59

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 (703) 308-8333.

Attachment

cc: M. Stahl
C. Musgrove

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Dear

This is in response to your letter of December 18, 1992, to Dr. David L. Dull in which you requested clarification of issues related to compliance with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Good Laboratory Practice Standards (GLPS). Your letter was referred to my office for reply.

Specifically you asked for clarification regarding the allowable relationship of a study director to management during the conduct of a GLP study. You stated that within your company you represent the single point of control for all operations conducted by N personnel, including financial and technical oversight. Your company is about to conduct field studies program sponsored by an industry Task force, and has been required to provide the study director for the program. Industry representatives have expressed to you the belief that the top management person (i.e., the CEO, or yourself) of a management company cannot act as the study director. You asked whether it is necessary for you to assign a subordinate to the role of study director rather than assume the responsibility yourself.

You proposed an organization structure whereby: (1) a representative of the sponsoring company or the Task Force would serve as [testing facility] management. As defined at 40 CFR 160.31; (2) you would serve as study director, as defined at 40 CFR 160.33; (3) N's QA [quality assurance] officer would report to you [as study director] and to the sponsoring company of the Task Force representative (as management). All field testing facility QA Units would follow the same reporting structure; and (4) while you would delegate authority for many of the day-to-day filed or analytical activities, you would remain the single point of control for each study. You would approve the protocol for each study as well as all amendments or deviations within a given study [and] would sign the final study report.

The scenario that you proposed would not achieve full compliance with GLPS. As you appear to be aware, there are compliance problems that result from testing facility management responsibilities being assumed by the individual who is also the study director. These problems are not completely solved by your proposed approach.

Since you stated in your letter that you are responsible for all activities at it appears that, despite the proposed organizational structure, you retain significant testing facility management responsibilities. In particular this creates problems with 40 CFR 160.35 since the QA unit's independence from study personnel is compromised. It is also not clear how the responsibilities at 40 CFR l60.31(g) are met.

These conflicts cannot be solved simply by designating the sponsor as testing facility management. “Management” of a testing facility spanning several organizations may need to include management components of the different organizations, including in this case both the sponsor organization and N. When this occurs, it is critical that the responsibilities of each management component are known. In your scenario the division of management functions between the sponsor and N are not clearly defined.

Several modifications or clarifications would need to be made to the framework you proposed to resolve the problems mentioned above.

First, it would be necessary to use a QA Unit which is external to N. A QA Unit which is employed by the study director is not independent from the study director, even if a separate external “management” entity is interposed for the duration of the study.

Second, it must be made clear that "management” consists of both sponsor and N components. Certain duties must be assumed at a level above N, such a the responsibility to designate or replace, as necessary, the study director (40 CFR 160.31(a) and(b)), and the responsibility to designate the QA Unit (40 CFR 160.31(c)). On the other hand, other duties must be assumed by individuals responsible for on-site management, such as assuring that resources are available as scheduled (40 CFR 160.31(e)). This appears to require that N personnel (in this case, the study director) assume certain testing facility management duties.

Third, there must be clear documentation indicating which persons are responsible for executing which duties. The facility's standard operating procedures must accurately reflect the division of duties. A historical file of such standard operating procedures must be maintained as stated in 40 CFR 160.81(d).

Finally, there is a technical correction needed for some of the language in your proposal. Your scenario provides for the study director to approve the protocol and all amendments or deviation to it. Please note that it is the sponsor’s duty, not the study director’s, to approve the protocol including amendments. The study director is responsible for signing and dating the approved protocol as well as all changes in or revisions to the

protocol, but is not empowered under the regulations to “approve” the protocol or any changes to it.

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 L. Dull
GLP File