PROPOSED GLP QUALITY SYSTEM SPONSOR RESPONSIBILITY

AS THE PROCESS OF REVIEWING THE FDA PROPOSED GLP QUALITY SYSTEM CHANGES CONTINUES, WE WANTED TO BREAK DOWN THE PROPOSED CHANGES, RATIONALE, AND INDUSTRY IMPACTS IN MORE DETAIL.

The Quality Assurance Unit (QAU) is an integral part of any GLP regulated facility and/or study. If the proposed changes are accepted, the way study documents are reviewed and inspections are performed may be impacted. Below are some of the FDA proposed changes, reason for the changes, and potential industry impacts.

THE PROPOSED CHANGE

Addition of § 58.5 Sponsor responsibilities.

For each nonclinical laboratory study, the sponsor must:

(a) Ensure the nonclinical laboratory study protocol (the study protocol) meets the requirements in § 58.120.

(b) Ensure that the study protocol provides for humane care and ethical treatment of animals.

(c) Sign and date the study protocol to indicate approval.

(d) Contract with persons accredited as following appropriate animal welfare procedures for phases of a nonclinical laboratory study that include the use of animals. If these contracted persons are not accredited, document this fact, the reason for using a non-accredited person, and the qualifications of the non-accredited person. This information must be included in the compliance statement required in paragraph (k) in this section.

(e) Document that any contracted person conducting a phase of a nonclinical laboratory study is qualified according to the provisions in this part.

(f) Ensure that appropriate lines of communication are established among all persons conducting a phase of the nonclinical laboratory study and document all study-related communications that involve the sponsor.

(g) Document that test, control, and reference articles are prepared, characterized, and labeled according to subpart F of this part, and are appropriately shipped. Obtain, and provide to the study director as soon as available, information regarding test, control, and reference article characterization as specified in § 58.105.

(h) Inform the study director of any known potential risks of the test article to human health or the environment and any measures necessary to protect study personnel and the environment.

(i) Review, approve, sign, and date each protocol amendment before implementation.

(j) Document and update as necessary the archive location of all raw data and records as described in §§ 58.190 and 58.195.

THE REASON FOR CHANGE AS DISCUSSED IN THE PREAMBLE OF PROPOSED REGULATIONS

"The present regulations in § 58.10 cover only a sponsor's responsibilities to notify a consulting laboratory, contractor, or grantee that their service "is part of a nonclinical laboratory study that must be conducted in compliance with the provisions of this part [part 58]". FDA received many comments to the December 2010 ANPRM noting that there are other sponsor responsibilities implicit throughout the present regulations, and stating that the study sponsor must share in the responsibility for complying with part 58. We agree with those comments. Therefore, we propose adding § 58.5 Sponsor responsibilities, that provides explicit provisions for the presently implied sponsor responsibilities and adds new sponsor responsibilities. Our proposed sponsor responsibilities are consistent with the preamble to the original GLP proposed rule stating that the adequacy and validity of nonclinical laboratory tests remain the responsibility of the sponsor of the product as part of establishing the marketability of the product (41 FR 51206 at 51206) (Ref. 4). In addition, we propose adding provisions consistent with the OECD advisory document, The Role and Responsibilities of the Sponsor in the Application of the Principles of GLP (Ref. 9)."

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"A sponsor may transfer to another party responsibility for any or all of the obligations set forth in this part. A party that assumes any obligation of a sponsor must comply with the specific regulations in this chapter applicable to this obligation and must be subject to the same regulatory action as a sponsor for failure to comply with any obligation assumed under these regulations. Although a sponsor might transfer certain responsibilities, the sponsor is still ultimately responsible for compliance with all sponsor responsibilities provided in this chapter."

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POTENTIAL IMPACT OF THE PROPOSED CHANGE

As the preamble states, some of these changes are implied in the current regulations but the added specificity of sponsor responsibility encourages the sponsor to be more directly involved and aware of what is happening in the study. Since the sponsor is most knowledgeable about the applicable test article and the intended use, this is a positive change and a step in the right direction to promote a higher level of study integrity and better quality products. Though a higher level of study integrity is expected, the changes can still create some strain on sponsor resources and study timelines. A couple of the notable changes involve approving amendments, qualification of persons involved in the study, communication, and documentation of compliance.

Requiring sponsors to approve the protocol and "review, approve, sign, and date each protocol amendment" is essential to study integrity and in making sure the study maintains appropriate levels of compliance needed for submission. The concern in the proposed change is the requirement of approval and signature on amendments prior to implementation. This issue has the potential to be problematic when changes need to be made quickly or at inopportune times when the sponsor representative may be unavailable. Study directors would then be forced to delay changes or to create planned deviations which would, in turn, not require the approval of the sponsor. Therefore this change would likely have the opposite effect from what is intended.

Documentation of qualification of all persons conducting a phase of a study is also a significant change in the regulations. The current regulations require simply notifying a facility that the study must be conducted according to the regulations. Qualification of these persons will most likely require additional resources from the sponsor to perform these assessments. As a result, study start dates may be delayed (at least initially). This is a needed addition to the regulations as, currently, these qualifications can often fall through the cracks so to speak. A possible issue with this change is that it could potentially conflict with the study director being to single point of control of the study. For example, if a study director disagrees with the the use of a particular person that the sponsor has already qualified for a phase of the study.
If the proposed changes are accepted, another responsibility of the sponsor will be to maintain open lines of communication that are documented. This can be viewed as a positive change to promote sponsor involvement and accountability. The proposed regulations are currently lacking specific information regarding how this is to be addressed and to what level these conversations need to be documented.

Per proposed 58.5 (k), the sponsor is to provide a compliance statement which would be in addition to the compliance statement signed by the study director in the final report. This change is consistent with submission requirements but helps to notify the sponsor earlier in the process when they are directly involved with the study rather than later when they are ready to submit.

Though the proposed regulations allow for the sponsor responsibilities to be transferred, the sponsor will have the ultimate responsibility for these items. This will create more oversight and help ensure that the studies are conducted by the appropriate means. With these changes, it can be reasonably assumed that sponsors will need to account for additional resources for the documentation and/or transfer of these responsibilities.

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