Divisions of Document Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2010-N-0548 Good Laboratory Practice for Nonclinical Laboratory Studies

Dear Sir/Madam:

This letter is in response to the Food and Drug Administration’s (FDA) solicitation of comments regarding proposed changes to the regulations governing Good Laboratory Practice (GLP) to require a complete quality system approach for safety and toxicity studies intended to support applications and submissions for products regulated by the FDA.

The National Association for Biomedical Research (NABR) represents more than 360 public and private universities, medical and veterinary schools, teaching hospitals, voluntary health organizations, professional societies, pharmaceutical and biotechnology companies advocating sound public policy for the humane use of laboratory animals in biomedical research.

On behalf of its institutional membership, NABR appreciates the opportunity to provide comments on the proposed changes, which are intended to help ensure the quality and integrity of the data used to support FDA regulatory decisions. The comments that follow are similar to our comments submitted in response to Docket No. FDA-2010-N-0548 Advance Notice of Proposed Rulemaking Good Laboratory Practice for Nonclinical Laboratory Studies. In those comments we expressed our concerns that multiple animal welfare requirements already govern research facilities depending on their specific work (e.g. USDA’s Animal Welfare Regulations, the Guide for the Care and Use of Laboratory Animals, the European Convention for Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (ETS No. 123), etc.), and creating additional rules would be redundant and confusing. Those concerns have been amplified by some of the language used in the proposed rule, which we will address in our comments below.

I. Executive Summary
D. Cost and Benefits – Given current concerns expressed by the research community regarding the impact of regulatory burden on research productivity, we are concerned with the statement that the Agency lacks “…sufficient information to quantify the benefits of the proposed rule…” Given the language contained in Section 2034 (d) Animal Care and Use in Research of the 21st Century Cures Act (Public Law No. 114-255), the Agency should not
include in the final rule any new language regarding animal welfare for which the benefits to
the animals cannot be quantified, and no new regulations should be implemented until the
review required in Section 2034(d) is completed.

II. Description of the Part 58 Proposal
A. What did the FDA consider when drafting this rule
3. Animal Welfare – While NABR concurs that the humane treatment of laboratory animals
is essential to the quality and integrity of the data generated, we do not agree that the fact the
Animal Welfare Act has been amended since the GLP regulations were published requires
changes be made to the existing GLP regulations. In fact, we maintain the opposite is true.
While we recognize it was not the agency’s intention to duplicate the USDA/APHIS and NIH
regulations, the proposed language does in fact appear to duplicate existing regulations. It
also adds a level of confusion by the proposed use of undefined or inappropriately defined
terms which we will address later in our comments.

B. Part 8, Subpart A-General Provisions
3. Sponsor Responsibilities (§ 58.5) - In footnote 6 at the bottom of page 58351, the
following language appears, “Additionally, the protocol must meet the requirements in §
58.90 for animal care. USDA’s Animal Welfare Act regulations (Code of Federal
Regulations, Title 9, Chapter1, Subchapter A, Parts 1–4) and the Institute for Laboratory
Animal Research’s Guide for the Care and Use of Laboratory Animals (Ref. 11), provide
specifics regarding the veterinary care expected when animals are used for research.” The
requirements in this footnote are not currently part of the GLP regulations nor are they
contained in the language in the proposed rule. If such language was contained in the
proposed rule, it would allow the elimination of the confusing language that we will be
addressing below and would recognize the existing oversight process in place today.

Part 58-Good Laboratory Practice for Nonclinical Laboratory Studies

§58.1 Scope
(c) – the “definition” of “appropriate” seems unnecessarily complicated and confusing, and the
phrase “reasonably be expected” opens it up to a multitude of interpretations that could lead to
confusion and inadvertent incidents of noncompliance. We recommend deleting the word
“reasonably.”

§58.3 Definitions
Attending veterinarian - This term is currently defined in the Animal Welfare Regulations and
the FDA’s proposed definition differs from the currently recognized definition, thus the term
should be deleted. If the Agency needs to refer to the attending veterinarian within the proposed
regulations, they can do so without creating a definition that leads to confusion within the
regulated community. This could easily be accomplished by referencing the USDA definition.

Contributing Scientist – The inclusion of the phrase “any other service for a phase of a
nonclinical laboratory study” could apply to a very broad range of individuals within a testing
facility and thus would add an unnecessary regulatory burden to their duties to assure
compliance. This could be corrected by deleting the phrase “any other service.”
§58.5 Sponsor responsibility – The use of the phrase “provide for humane care and ethical treatment” in (b) would appear to require a regulatory definition of humane care and ethical treatment for the regulated community to be able to assure their facility’s compliance with the regulations. We recommend replacing the proposed language in (b) with the following; “Ensure the study protocol addresses the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used In Testing, Research and Training where appropriate.” The use of the requirement in (d) that persons contracted by the sponsor be accredited as following appropriate animal welfare procedures requires that the Agency define what is meant by accredited.

§ 58.33 Study Director - While the study director has overall responsibility for the study, when that study involves animals it appears that the requirements are greater for the Sponsor or a Contributing Scientist as it relates to the humane care and ethical treatment of the animals. The requirements in (b), (5) and (6) are consistent with the requirements of the USDA and the PHS, and with minor revisions should represent the requirements throughout §58. We recommend revising (5) to read “…are reviewed and approved as required in §58.120 (b) and (e) by the Institutional Animal Care and Use Committee (IACUC) or its equivalent before study initiation and the implementation of applicable amendments.” We recommend revising (6) by striking , “as defined in §58.3”. We recommend deleting the word “All” in (12) and revising that section to read “Document protocol related communication…”

§58.37 Contributing Scientist - (b)(3)(iii) should be revised to read, “Document corrective action required to address animal welfare concerns” to be consistent with language in § 58.33.

§58.120 Protocol – Section (b) should be revised to read “For studies that involve animals the Institutional Animal Care and Use Committee or its equivalent must review and approve…” Section (e) should be revised to read, “The Institutional Animal Care and Use Committee or its equivalent must review and approve…”

Conclusions

Consistent with the President’s Executive Order dated January 18, 2011 titled, “Improving Regulation and Regulatory Review - Executive Order,” NABR still believes the creation of new FDA animal welfare regulations would be duplicative and unnecessary. The United States Department of Agriculture (USDA), the federal regulatory agency charged with enforcing the federal Animal Welfare Act (AWA) currently performs unannounced inspections of research facilities at least annually and generates publicly available inspection reports. Institutional Animal Care and Use Committees (IACUCs), independent bodies required by the AWA, also monitor animal welfare based on USDA regulations and on the Guide for the Care and Use of Laboratory Animals (National Academies of Science 1996). IACUCs review and approve proposed animal use (protocols), inspect facilities, and oversee the institution’s animal care and use program. Documentation of IACUC activities is readily available in the form of inspection reports, meeting minutes and protocol files. In addition, most GLP-compliant
facilities are voluntarily accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International. Proof of accreditation in the form of formal letters from AAALAC is also available. FDA is currently able to determine animal welfare compliance by reviewing available USDA inspection reports, by reviewing existing IACUC documentation, by verifying AAALAC accreditation status, and by the direct observation of animals during FDA inspections.

Moreover, a longstanding Memorandum of Understanding (MOU) exists between the USDA, FDA and the National Institutes of Health (NIH). The current MOU dated April 29, 2016 states the agencies “…share a common concern for the care and use of laboratory animals, although there are necessary operational differences among the animal welfare programs of the cooperating agencies. Congress acknowledged the need for transagency cooperation in the AWA by calling for the Secretary of Agriculture to consult and cooperate with other Federal departments and agencies concerned with the welfare of animals used in research, and to consult with the Secretary of Health and Human Services prior to the issuance of regulations.” The agencies therefore agreed “to consult and coordinate with each other on regulatory or policy proposals and significant policy interpretations involving animal care and use under consideration by each agency.” As agreed to in the MOU, NABR urges the FDA to continue working closely with the USDA and NIH with respect to the care and use of animals in research rather than create unnecessary new regulations. In addition, Congress recognized the need to address the issue of regulatory burden in Section 2034 (d) Animal Care and Use in Research of the 21st Century Cures Act. Until the requirements contained in this section are met no additional regulations governing the care and use of animals in testing should be promulgated.

Since multiple animal welfare requirements already govern research facilities depending on their specific work (e.g. USDA’s Animal Welfare Regulations, the Guide for the Care and Use of Laboratory Animals, the European Convention for Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (ETS No. 123), etc.), the proposed rules are redundant and confusing in that several sections, as noted above, are not consistent with existing language in the AWA or PHS Policy. FDA’s efforts would be best focused on assuring that proper documentation is in place and allowing the federal regulatory agency responsible for the applicable statute or standard to determine whether the facility is in compliance.

Sincerely,

Matthew R Bailey
President