September 5, 2023

Robert M. Califf, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: E6(R3) Good Clinical Practice (GCP) (FDA-2023-D-1955)

Dear Dr. Califf:

The American Society of Hematology (ASH) appreciates the opportunity to provide comments to the U.S. Food and Drug Administration (FDA) in response to the International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use’s (ICH) draft guidance on E6(R3) Good Clinical Practice (GCP) (FDA-2023-D-1955).

ASH represents more than 18,000 clinicians and scientists worldwide committed to studying and treating blood and blood-related diseases. These disorders encompass malignant hematologic disorders such as leukemia, lymphoma, and multiple myeloma, as well as classical hematology (non-malignant) conditions. In addition, hematologists are pioneers in demonstrating the potential of treating various hematologic diseases and continue to be innovators in the fields of stem cell biology, transfusion medicine, and gene and cell therapies. ASH membership is comprised of basic, translational, and clinical scientists, as well as physicians providing care to patients.

ASH commends the FDA for its partnership with ICH in releasing this draft guidance. The Society shares the Council’s goal of maintaining and improving global common standards for good clinical practice (GCP), which will ultimately benefit all patients including those with hematologic diseases. We appreciate that the patient perspective is stressed throughout the document, and that this is a focus of the new revisions for E6(R3). ASH is pleased to share the following comments and recommendations that we encourage the Agency to consider as the draft guidance is finalized, implemented, and evaluated over time.

Overall, the Society is pleased to see this draft guidance. In future revisions, the Society notes that it would be helpful to have a redlined version so that updates and revisions can be easily identified between the draft guidance and previous iterations. One general suggestion is that the FDA include detailed information regarding how the recommendations in the guidance might differ for each trial phase. The addition of this detail will reduce the possibility of misinterpretation given the vague wording in some sections of the guidance. Furthermore, given that sponsors of clinical trials rely on the recommendations within guidance documents to design and execute on their trials, ASH encourages the Agency and the ICH to engage in conversations about potentially confusing or vague wording (e.g., defining risk, detailing differences in trial types) with relevant stakeholders prior to revisions to the GCP guidance.
The Society also encourages the Agency to continue examining ways in which clinical trials can be designed to enhance participation from diverse populations and to include in the GCP guidance, recommendations on diversity, equity, and inclusion (DEI) principles that are applicable to a wider international audience. This is important because designing inclusive and accessible clinical trials will bring significant benefits to product development for various diseases, especially those that impact underrepresented groups (e.g., sickle cell disease and multiple myeloma).

LINE SPECIFIC COMMENTS

Section 2.7. Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected.

- (Line 178) The word “risk” should be specifically defined for sponsors and principal investigators. The Society encourages the Agency and ICH to define risk beyond adverse events to include financial and emotional toxicity related to the trial and trial procedures. Defining risk more expansively will also incorporate strong DEI principles into the GCP, potentially allowing greater access to clinical trials. Risk in clinical trials is not something only related to medical harm, but also includes financial and emotional risk to participants, which can have downstream impacts on health. Incorporating these concepts into a risk-based framework will strengthen GCP for all populations and likely allow for more diverse clinical trials. The broader definition of risk should also be included in the glossary under Line 2283.

Section 2.8. Informed Consent of Trial Participants

- We note that in section 2.8.9, the institutional review board/independent ethics committee (IRB/IEC) is the arbiter of a patient’s rights, safety, and well-being in emergency situations. However, we ask that the Agency consider whether the IRB/IEC is the appropriate authority in emergency situations, or whether an impartial witness might be more appropriate similar to section 2.8.10 where the participant is unable to read.

Section 3.1. Trial Design

- (Line 940) This is another area that can benefit from a broader conceptualization of procedures necessary to capture difficult to reach populations for clinical trials. The Society recommends that language be developed that guides sponsors to include diverse enrollment by age, socioeconomic demographics, and accessibility into any study design. Additionally, the guidance should encourage decentralized trial design where possible to capture different subpopulations, as these types of trials help engage patients from communities that have historically not participated in clinical trials due to various barriers (e.g., costs associated with transportation to trial sites, availability and/or access to childcare). Data collection variables should also be expanded in a more granular fashion to include race and other socioeconomic identifiers where possible. This recommendation also applies for Line 1590.

ASH appreciates the opportunity to provide these comments. We look forward to supporting the implementation of this new policy. Please consider ASH a resource; we would be pleased to provide additional information or support. If you have any questions, please use ASH Deputy Director of Government Relations and Public Health Stephanie Kaplan (skaplan@hematology.org or 202-776-0544) as your point of contact.

Sincerely,

Robert A. Brodsky, MD
President