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Acting Commissioner
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10903 New Hampshire Avenue
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Re: Draft Guidance for Industry – *Core Patient-Reported Outcomes in Cancer Clinical Trials*

Dear Dr. Woodcock:

The American Society of Hematology (ASH) appreciates the opportunity to provide comments to the U.S. Food and Drug Administration (FDA) on the Agency's Draft Guidance for Industry – *Core Patient-Reported Outcomes in Cancer Clinical Trials*.

ASH represents more than 18,000 clinicians and scientists worldwide, who are committed to the study and treatment of blood and blood-related diseases. These disorders encompass malignant hematologic disorders such as leukemia, lymphoma, and multiple myeloma, as well as non-malignant conditions such as sickle cell disease, thalassemia, bone marrow failure, venous thromboembolism, and hemophilia. In addition, hematologists are pioneers in demonstrating the potential of treating various hematologic diseases and continue to be innovators in the field of stem cell biology, regenerative medicine, transfusion medicine, and gene therapy. ASH membership is comprised of basic, translational, and clinical scientists, as well as physicians providing care to patients.

In 2018, ASH founded the ASH Research Collaborative (ASH RC) to foster collaborative partnerships that accelerate progress in hematology, with the goal of improving the lives of people affected by blood diseases. The foundation of the ASH RC is its Data Hub and Sickle Cell Disease Clinical Trials Network. The Data Hub is a technology platform that facilitates the exchange of information by aggregating research-grade data on hematologic diseases. The core of the ASH RC programs is focused on patient centeredness and inclusion.

Overall, the Society is supportive of the Draft Guidance document and FDA's goal of increasing use of patient-reported outcomes (PROs) in cancer clinical trials. ASH believes strongly in the values of patient centeredness and inclusion and recognizes that standardizing the data collected by PRO tools will increase their utility and use in clinical trials. This is especially important for anti-cancer treatments, as therapies become increasingly personalized and as patient response and side effect profiles can vary widely.

In terms of the details included in the Draft Guidance, ASH has the following specific comments:

- **Applicability to blood cancers:** Throughout the document, there are references to tumor measures (starting with line 56). We believe that PROs also have utility in clinical trials for types of cancer without solid tumors, including hematologic cancers. For example, a number of studies have found that the use of PROs have strengthened clinical research related to lymphoid malignancies, such as chronic lymphocytic leukemia (CLL), multiple myeloma (MM); and myeloproliferative

disorders, such as acute leukemia and myelofibrosis. In fact, myelofibrosis represents an area in which the contribution of PRO data has been most critical in determining the most effective strategies for these patients¹. We hope that you will clarify in the final Guidance that PROs should also be considered in those trials.

- **Need for Disease-Specific PROs:** ASH recommends that FDA add language to the Guidance that recognizes the need for disease-specific PROs in hematologic malignancies that are used in addition to generic PROs. Hematologic malignancies have unique symptom/side effect profiles that differentiate them from other malignancies. Several examples of resources specific for hematologic malignancies include: (1) the Myelofibrosis Symptom Assessment Form (MFSAF); (2) QOL-E[©] instrument for the assessment of health-related quality of life in myelodysplastic syndromes (MDS); and the Quality of Life in Myelodysplasia Scale (QUALMS) for MDS.
- **Considerations for instrument selection to measure the core patient-reported outcomes:** ASH agrees that to contribute meaningfully to a therapy's benefit/risk assessment, the PRO instrument used should be well-defined and reliable so that the results presented are accurate. We also appreciate that you intend to release further Guidance documents related to PROs and the collection and analysis of clinical outcome assessments.
- **Assessment Frequency:** The Draft Guidance states that "A standard approach to assessment frequency over the first year of therapy would aid in consistency and interpretation across advanced cancer trials" (lines 216-217). This seems contradicted by a comment on the next page as the Draft Guidance acknowledges that different types of treatments – intravenous versus oral chemotherapy, for example – require different assessment frequencies. ASH would further suggest that in some trials, therapies are administered in structured phases, each of which may have a different intensity, which should also be taken into account when determining frequency. In the final Guidance, we suggest that you clarify how to reconcile a recommendation for standardized assessment frequencies with the nuances required for trials of different types of treatments.
- **Balance Impact of Patient and Research Sites:** As valuable as PROs are to research, it is important to be conscious of not over-burdening patients or clinical research sites. Therefore, ASH supports the FDA's aim to study more efficient ways of collecting data, like electronic self-reporting of outcomes by patients (e-PROs).

ASH also hopes that the FDA will consider developing future guidance on other types of clinical outcome assessments that are relevant to the patient experience. Examples of other valuable assessments that could be helpful in cancer, other hematologic conditions and other diseases include performance outcomes; and in the future, patient generated data from wearable health sensors. Additionally, we hope that the FDA considers developing a similar guidance for non-malignant diseases as our constituency would benefit from a similar resource for other hematologic diseases, such as sickle cell disease and venous thromboembolism

Again, ASH appreciates the opportunity to provide these comments. Please consider ASH as 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,



Martin S. Tallman, MD
President

¹ Fabio Efficace, Gianluca Gaidano, Francesco Lo-Coco; Patient-reported outcomes in hematology: is it time to focus more on them in clinical trials and hematology practice?. *Blood* 2017; 130 (7): 859–866. doi: <https://doi.org/10.1182/blood-2017-03-737403>