



August 26, 2010

**2010**

**President**

Hal Broxmeyer, PhD  
Walther Oncology Center  
Indiana University School of Medicine  
960 W. Walnut Street, Room 302  
Indianapolis, IN 46202  
phone 317-274-7510  
fax 317-274-7592  
hbroxmey@iupui.edu

**President-Elect**

J. Evan Sadler, MD, PhD  
Washington University Medical School  
660 South Euclid Avenue, Box 8125  
Saint Louis, MO 63110-1093  
phone 314-362-9029  
fax 314-454-3012  
esadler@wustl.edu

**Vice President**

Armand Keating, MD  
Princess Margaret Hospital  
610 University Avenue, Suite 5-303  
Toronto, ON M5G 2M9  
CANADA  
phone 416-946-4595  
fax 416-946-4530  
armand.keating@uhn.on.ca

**Secretary**

Charles Abrams, MD  
University of Pennsylvania  
School of Medicine  
421 Curie Boulevard, #912  
Philadelphia, PA 19104-6140  
phone 215-573-3288  
fax 215-573-7400  
abrams@mail.med.upenn.edu

**Treasurer**

Linda Burns, MD  
Division of Hematology,  
Oncology, and Transplantation  
University of Minnesota  
420 Delaware Street, SE  
Mayo MC 286/Room 14-154A Moos Tower  
Minneapolis, MN 55455-0341  
phone 612-624-8144  
fax 612-625-9988  
burns019@umn.edu

**Councillors**

Kenneth Anderson, MD  
Thomas Bensinger, MD  
David Bodine, PhD  
Stephanie Lee, MD, MPH  
Elaine Muchmore, MD  
Mohandas Narla, DSc  
Marilyn Telen, MD  
David Williams, MD

**Editors-In-Chief**

Cynthia Dunbar, MD, *Blood*  
Roy Silverstein, MD, *The Hematologist*

**Executive Director**

Martha L. Liggett, Esq.  
mliggett@hematology.org

Kristen Everett  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Ave., Building 51, Room 6228  
Silver Spring, MD 20993

Re: Draft Guidance for Industry on “Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications” (Docket No. FDA-2009-D-0461).

Dear Ms. Everett,

The American Society of Hematology (ASH) appreciates this opportunity to respond to the Food and Drug Administration’s (FDA) Request for Comments on the Draft Guidance for Industry on “Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications” (Docket No. FDA-2009-D-0461).

ASH represents over 16,000 clinicians and scientists committed to the study and treatment of blood and blood-related diseases. These areas include anemia (including sickle cell and thalassemia), thrombosis, bleeding disorders, transfusion medicine, and gene therapy, as well as the malignant hematologic leukemia, lymphoma, and myeloma. ASH members include clinicians who regularly render services to patients who require REMS as part of their treatment protocol.

ASH commends the FDA’s efforts to improve drug safety and for its ongoing efforts to gather input from stakeholders on issues related to REMS. In general, the Society supports the overall direction of the draft guidance and believes that the guidance will serve as a useful tool in the development and application of REMs. However, ASH would like to express its concerns regarding the process for developing REMS, the administrative burden of REMS, and the need to measure the quality and success of REMS.

**Expert Input Is Critical in Development and Implementation of REMS**

ASH is concerned that experts in relevant fields have not been included in the process of developing and implementing REMS. ASH recommends that the FDA require the pharmaceutical companies to consult relevant experts during a transparent REMS development process. This will ensure that the REMS are evidence-based and that their implementation is feasible for physicians. ASH and the Society’s member physicians are happy to serve as a resource to FDA and relevant pharmaceutical companies in developing and implementing future REMS.

### **REMS May Create Undue Burden on Physicians and Practices**

ASH is concerned that the current implementation of REMS poses an excessive burden on physicians and their practices. Due to the high toxicity and narrow therapeutic range of their treatments, hematologists, as a group, already devote much more time to educating patients regarding adverse effects than most other physicians. Specifically, ASH is concerned with the following:

- Requirement of Physicians to Administer REMS – Physicians are required to administer REMS when other qualified people in the practice can handle the administration. If the physicians had to go over the entire spectrum of adverse effects of every medicine they prescribe individually and face-to face with each patient, the access to care for patients might be compromised. ASH encourages the FDA to consider authorizing other qualified medical staff to administer the REMS.
- Uniformity and Redundancy of REMS – Some REMS are redundant, and there is a lack of consistency in the process for administering different REMS. For example, under the APPRISE Program, the REMS for erythropoiesis-stimulating agents (ESAs), physicians are required to give the same medication safety guide repeatedly. More effectively, the patients should receive the guide during their initial treatment. ASH recommends that the FDA establish a mechanism that will require pharmaceutical companies to develop REMS standards to ensure increased uniformity and efficiency.

### **Need for Evaluation and Proof of Principle of REMS Before Continued Expansion**

Finally, ASH is concerned that there is a lack of scientific evidence that REMS significantly improves the safety and quality of care of patients. ASH encourages the FDA to implement a formal data collection and evaluation system to determine whether the REMS are, in fact, effective before proceeding with expansion of this program.

The Society thanks you for the opportunity to submit these comments and looks forward to working with you to pursue the common goal of ensuring patient safety and the highest quality of care.

We welcome the opportunity to meet with you to further discuss the Society's concerns. If you have any questions or would like additional information, please contact ASH Government Relations Manager Stephanie Kart at [skart@hematology.org](mailto:skart@hematology.org) or 202-776-0544.

Sincerely,



Hal E. Broxmeyer, PhD  
President