



June 17, 2010

Members of the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) Joint Leadership Council
Division of Dockets Management [HFA-305]
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD, 20852

Re: The NIH and FDA Joint Leadership Council Request for Comments (FDA-2010-N-0233).

Dear Members of the NIH and FDA Joint Leadership Council:

The American Society of Hematology (ASH) appreciates this opportunity to respond to the National Institutes of Health (NIH) and the Food and Drug Administration's (FDA) Joint Leadership Council Request for Comments (FDA-2010-N-0233).

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 (including venous thrombosis, heart attack and stroke), bleeding disorders, transfusion medicine, and gene therapy, as well as the malignant hematologic leukemia, lymphoma, and myeloma. In addition, hematologists have been pioneers in the fields of bone marrow transplantation and stem cell research.

ASH supports the development of the NIH-FDA regulatory science program and the creation of the NIH-FDA Joint Leadership Council. The Society applauds the agencies' efforts to collaborate in order to advance the translation of biomedical research discoveries into approved diagnostics and therapies, as well as promote science to enhance the evaluation tools used for regulatory review. While the Joint Council has a broad charge, ASH encourages the group to focus its efforts on the following priorities: 1) harmonization of the clinical trial and regulatory mechanisms between the NIH and the FDA; 2) facilitate research translation and product development for regenerative medicine; and 3) provide support for specific preclinical research and product development of potential therapies for rare or neglected disorders.

PRIORITY 1: HARMONIZATION OF EXISTING POLICIES AND REGULATIONS ON CLINICAL TRIAL OPERATIONS.

The federal government, through the Office of Protection from Research Risks (OPRR), within the NIH and the Department of Health and Human Services (HHS), has promulgated regulations and policies that govern the protections for human subjects who participate in federally-funded research. The federal government also propagates regulations governing human subject protections through the FDA.

2010

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Unlike the NIH/HHS regulations, the FDA regulations apply to any FDA-regulated article, regardless of whether the research is federally-funded.

Investigators must comply with these complex regulations that not only lack harmonization between different agencies but, in fact, sometimes appear to be inconsistent with each other and with reimbursement policies established by the Centers for Medicare and Medicaid Services (CMS). In addition, most of these regulations were developed at a time when the vast majority of clinical research studies were taking place at single institutions and thus, rely heavily on local Institutional Review Boards (IRBs). Studies on the subject of research oversight have documented the adverse effects of regulatory burden on clinical, epidemiological, and health systems research¹.

ASH recognizes the importance of providing strict policies and regulations that govern protections for human subjects that participate in federally-funded clinical trials. At the same time, concerns have been raised that the various agencies that fund or provide oversight of clinical trials have instituted different regulations that are often inconsistent and unnecessarily burdensome, especially for multi-institutional trials. This has inhibited the initiation of new trials and access to promising treatments for patients. *ASH encourages the Joint Council to bring together leading researchers with experience in the operation of clinical trials and representatives from NIH, FDA, CMS, and other agencies to determine if changes could be made to better harmonize existing policies and regulations on clinical trial operations.*

One possible short-term goal for this harmonization process would be the establishment of a national IRB. The future of hematology in particular requires that research in diverse areas of basic and clinical science be integrated and translated into novel, decisive therapies that will effectively prevent and treat serious diseases. The integrated national IRB will lift the burden and increase the harmonization of multi-institutional trials, thus increasing access to promising treatments for patients. The centralized rules will increase collaboration between multiple investigators around common themes to supporting novel clinical trials. *ASH recommends that the Joint Council consider the establishment of a national IRB that will ultimately accelerate the translation of biomedical research discoveries into approved diagnostics and therapies.*

PRIORITY 2: FACILITATE RESEARCH TRANSLATION AND PRODUCT DEVELOPMENT FOR REGENERATIVE MEDICINE.

The field of regenerative medicine represents a multidisciplinary approach to treat diseases and disorders by enabling the body to repair, replace, restore and regenerate damaged or diseased cells, tissues and organs. The wealth of genomic information that became available from the successfully completed Human Genome Project has fostered the growth of the field of

¹ IDSA. Grinding to a Halt: The Effects of the Increasing Regulatory Burden on Research and Quality Improvement Efforts. *Clinical Infectious Diseases* 2009; 49:328–35.

regenerative medicine and targeted cell therapies that can lead to the development of treatments and cures for many of the major medical issues of our time.

The lack of coordination of research efforts, disjointed funding mechanisms and absence of harmonization of regulatory requirements of regenerative medicine research threaten to significantly delay the application of this research field into new therapies in the United States. In order to capitalize on the past decade's investments in biomedical and genomic research and significantly advance the field of regenerative medicine, there is a great need for:

1. Coordination of research efforts due to the unique nature of the field and its significant potential to develop treatment and cures for major diseases. Nearly 80 serious diseases have been treated by stem cell transplants, and some diseases such as leukemia, lymphoma and sickle cell disease can be cured by hematopoietic stem cell transplants.
2. New research methodologies, including clinical trial design and standardizing methods for characterizing cell-based products, and the use of animal models for both efficacy and toxicity evaluation.
3. Safety standards and Good Manufacturing Process (GMP) that address the development of cell-based therapy products.
4. Clinical database registries of recipients of cell-based therapies and tissue/DNA banking for future interrogations.

ASH urges the Joint Council to re-examine the current clinical trials methodologies and determine if these designs are useful in the utilization of cell-based therapies. These joined efforts should be directed towards building a consensus for the design of clinical trials across multiple disease disciplines that optimizes the opportunity for data collection and dissemination. The following should be addressed in this effort:

- Assurance of adequate characterization of the cellular product to be used in human trials.
- A defined long-term follow-up plan for all trials utilizing stem cell derivative products.
- A defined plan to bank a portion of all cell products infused into human patients, or at a minimum, DNA from donor samples for future interrogation.
- Solicitation of input from multiple disciplines to maximize opportunities for data collection.

PRIORITY 3: SUPPORT FOR SPECIFIC PRECLINICAL RESEARCH AND PRODUCT DEVELOPMENT OF POTENTIAL THERAPIES FOR RARE OR NEGLECTED DISORDERS.

Finally, ASH encourages the Joint Council to focus its efforts on providing support for specific preclinical research and product development of potential therapies for rare or neglected disorders. Hematologists research and treat many rare diseases, such as myeloproliferative disorders, hypereosinophilic syndrome, and systemic mastocytosis. ASH is eager to work with and be a resource for the Joint Council in this time of unprecedented scientific opportunity to begin the work to find solutions for millions of patients faced with rare or neglected illnesses. *ASH urges the Joint Council to establish a mechanism of support for development of therapies for rare hematological disorders, such as:*

- Myeloproliferative disorders
- Hypereosinophilic syndrome
- Methemoglobinemia and other acquired toxic red cell disorders
- Hemochromatosis
- Disseminated intravascular coagulation
- Acquired thrombosis
- Systemic mastocytosis
- Paroxysmal nocturnal hemoglobinuria
- Cutaneous peripheral T cell lymphomas
- Autoimmune neutropenia
- Amyloidosis
- Cold agglutinin disease
- Pyruvate kinase and other metabolic deficiencies of red cells
- Aplastic anemia
- Histiocytic disorders in adults
- Peripheral neuropathies associated with monoclonal proteins
- Hemoglobinopathies other than Sickle Cell Disease and HgbE, *e.g.*, Hgb Köln (unstable)

The American Society of Hematology and its membership of disease-specific experts are looking forward to being a resource for NIH-FDA regulatory science program and working with Joint Council to advance the translation of biomedical research discoveries into approved diagnostics and therapies. Please contact ASH Government Relations Manager, Stephanie Kart, at 202-776-0544 or skart@hematology.org for any additional information.

Sincerely,

A handwritten signature in black ink that reads "Hal E. Broxmeyer". The signature is written in a cursive, flowing style.

Hal Broxmeyer,
President