



**2012**

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February 7, 2012

Re: Request for Information: Scientific and Regulatory Issues to be Explored at an Upcoming Pluripotent Stem Cell Workshop Involving NIH and FDA (NOT-NS-12-004).

Submitted electronically to: [nindsstemcell@mail.nih.gov](mailto:nindsstemcell@mail.nih.gov)

To Whom It May Concern:

The American Society of Hematology (ASH) appreciates the opportunity to respond to the Request for Information: Scientific and Regulatory Issues to be Explored at an Upcoming Pluripotent Stem Cell Workshop involving NIH and FDA (NOT-NS-12-004) issued on December 12, 2011.

ASH represents over 16,000 clinicians and scientists committed to the study and treatment of blood and blood-related diseases. These diseases encompass malignant hematologic disorders such as leukemia, lymphoma, and myeloma; non-malignant conditions including anemia and hemophilia; and congenital disorders such as sickle cell anemia and thalassemia. In addition, hematologists have been pioneers in the fields of stem cell biology, regenerative medicine, bone marrow transplantation, transfusion medicine, gene therapy, and development of many drugs for the prevention and treatment of heart attacks and strokes.

Hematologists were instrumental in characterizing the first stem cell identified in the blood system and developing highly successful therapies from these cells that have resulted in a cure for some blood diseases and cancers. ASH believes that hematologists will continue to be pioneers in the field of regenerative medicine by manipulating induced pluripotent stem (iPS) cells to become blood stem cells and blood lineages. ASH supports all avenues of regenerative medicine research following appropriate standards and methodologies as well as public oversight.

ASH applauds NIH's recent efforts in expanding opportunities for translational application of stem cell research in the institutes' intramural program, especially the establishment of the Center of Excellence in iPS Cell Technology and the intramural Center for Regenerative Medicine. However, ASH urges the NIH to identify major opportunities and gaps in biomedical research and funding mechanisms for the field of regenerative medicine as a whole, especially in the Institutes' extramural program.

ASH recommends that the NIH review and improve its current funding mechanisms for regenerative medicine research to ensure that resources adequately meet the needs of basic discovery, translational and clinical applications of this evolving technology.

Specifically, ASH recommends the NIH:

- Establish a special “Regenerative Medicine Translational Review Panel/Study Section” that will review P01/R01 grants. This study section should include broad expertise in basic and clinical investigations.
- Encourage additional pharmaceutical/biotechnology partnerships and collaborative grants.
- Develop Requests for Applications that focus on studying both the potential efficacy and the safety of these therapies, including patient-specific database registries for effectively tracking outcomes and adverse events of subjects receiving cellular reagents as well as developing a consensus around the utility of animals and animal models to test efficacy and safety of cellular products.

ASH supports the increased coordination between the research and regulatory communities to enable more effective translation of regenerative medicine and pluripotent stem cell technology into clinical utility, including the recent series of joint NIH-FDA workshops. ASH urges the FDA to provide additional clarity on what it considers its purview with regard to regulatory aspects of regenerative medicine therapies. The Society recommends that the following themes be addressed during the workshop series:

1. Establishment of a unified regulatory process that would span all the stages of approval and use the same set of reviewers.
  - The recommendations in the past have been contradictory at different steps of the regulatory ladder; redundancy has been common, with few experts who effectively review iPS cell proposals.
  - Defined milestones should be linked to the gradual release of funds, and there should also be a single review decision at the beginning that would take into an account all the steps from the idea to clinical trial.
2. Support of collaborative, consortium-like efforts, as the conditions, at least initially, are going to be rare and the accrual will be slow.
3. Additional clarity on measures of clinical efficacy and the use of surrogate markers.
  - Specifically, issues associated with using gene-modified/gene-corrected stem cell derivatives for transplant (e.g., will there be/should there be additional safety guidelines related to off-target or clonal effects?)
4. Protection of high priority projects (such as support for current good manufacturing practice facilities) from budget fragmentation and repeated short-term funding justification.
5. Additional clarity on the structure of partnership when multiple parties are involved, such as academia, industry, patient-advocacy groups.

ASH looks forward to participating in this workshop series. In preparation for the final workshop in the series on clinical trial design, ASH urges the NIH and the FDA to re-examine the current clinical trials methodologies and determine if these designs are appropriate for the utilization of cell-based therapies.

These joint 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. ASH recommends that 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.

The American Society of Hematology looks forward to working with the NIH and the FDA on this important issue and will be happy to provide further information and be a resource for the agencies. Please contact ASH Senior Manager for Scientific Affairs, Ulyana V. Desiderio, Ph.D., at (202) 776-0544 or [udesiderio@hematology.org](mailto:udesiderio@hematology.org) for any additional information.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Armand Keating". The signature is fluid and cursive, with a prominent horizontal stroke at the end.

Armand Keating, MD  
President