



Advancing Transfusion and
Cellular Therapies Worldwide

January 25, 2005

The Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane Room 1061
Rockville, MD 20852

RE: Docket 2004D-0462, October 28, 2004, Draft Guidance for Industry: Criteria for Safety and Efficacy Evaluation of Oxygen Therapeutics as Red Blood Cell Substitutes

Dear Dockets Manager,

AABB is an international association dedicated to advancing transfusion and cellular therapies worldwide. Our members include more than 1,800 hospital and community blood centers and transfusion and transplantation services as well as approximately 8,000 individuals involved in activities related to transfusion, cellular therapies and transplantation medicine. For over 50 years, AABB has established voluntary standards for, and accredited institutions involved in, these activities. AABB is focused on improving health through the advancement of science and the practice of transfusion medicine and related biological therapies, developing and delivering programs and services to optimize patient and donor care and safety.

The draft guidance is intended to provide sponsors or investigators with suggested criteria for testing the efficacy and safety of oxygen therapeutics as substitutes for red blood cells, and guidance on the design of clinical trials to assess the risk/benefit ratio of such use. It is intended to discuss both hemoglobin-based products and perfluorochemical emulsions.

The draft guidance is very detailed about the criteria as they apply to the hemoglobin-based products, but rather cursory with respect to the perfluorocarbon products. This document would be improved by redressing this imbalance, or alternatively, limiting this document to discussion of the hemoglobin-based products, and issuing a separate guidance addressing the perfluorocarbon products.

8101 Glenbrook Road
Bethesda, MD 20814-2749
301.907.6977 MAIN
301.907.6895 FAX
www.aabb.org

Because the interest in development of perfluorocarbon products has decreased considerably, it is appropriate to assign a higher priority to issuing guidance with respect to the hemoglobin-based products.

The clinical uses discussed include elective surgery and trauma. There is little or no consideration of the use of oxygen therapeutics as a bridge to transfusion in patients with worsening anemia, where blood might not be available due to alloimmunization, for patients with autoimmune hemolytic anemia or sickle cell disease. Although these uses may not affect a large proportion of patients, they are likely to be lifesaving for some patients, and their use should be discussed and indications for their appropriateness should be considered.

There is also no discussion of how these materials might be used for patients who refuse blood, such as Jehovah's Witnesses.

Section IV, B, 1 appears to be recommending that clinical testing of each product should be performed in both the elective surgical setting and a trauma setting, since (III, C, 2) states "A trial to obtain an elective surgical indication alone, without evaluation of the product in unstable patients in a trauma setting is unlikely to assure the safety of an oxygen therapeutic in elective surgery patients who become unstable or in trauma patients." This suggests that every manufacturer is obligated to do a trauma trial for the purpose of eliciting toxicities. The draft guidance should be less prescriptive here. It is unclear what relevance trauma patients may have to some of the target patient populations for the primary indication e.g. elective orthopedic surgery. Secondly, a better way to elicit relevant toxicities may be to study more relevant patient populations, e.g. elective orthopedic surgery patients with greater co-morbidity. We suggest that FDA permit the manufacturers to define relevant, higher morbidity, patient populations.

Once these products are licensed, they are likely to be in short supply because of raw materials and manufacturing limitations. Their use in trauma or for the military could easily deplete the supply for other civilian indications such as alloimmunization. It would be useful for FDA to discuss or ask the manufacturers to discuss how these materials would be allocated when supplies are limited.

AABB strongly supports initiatives that improve patient safety and stands ready to interact with the FDA as necessary.

Questions concerning these comments may be directed to Kay Gregory, Director, Regulatory Affairs, AABB kayg@aabb.org.

Sincerely,



Karen Shoos Lipton, JD
Chief Executive Officer