FOR IMMEDIATE RELEASE
May 27, 2008

CONTACTS:

Larry Dumont, PhD, in Lebanon, New Hampshire:
+1.603.650.5480
or
Lorna Williamason, MD; Chair of the BEST Collaborative, in Cambridge, England:
+44.1223.548009

International Research Organization Responds to Recent Studies Purporting to Show that Transfusion of Older Red Blood Cells Leads to Greater Risk

Cambridge, United Kingdom — The Biomedical Excellence for Safer Transfusion (BEST) Collaborative will be presenting its concerns regarding the scientific validity and medical implications of several recent papers purporting to show that transfusion of older units of Red Blood Cells leads to greater risk. The organization will highlight its position during the U.S. Department of Health and Human Services (HHS) meeting of the Advisory Committee on Blood Safety and Availability (ACBSA) on May 30, 2008, at the Hilton Rockville Hotel, in Rockville, Md.

The BEST Collaborative is an international research organization that works collaboratively to explore ways to improve transfusion-related services through standardization of analytic techniques, development of new procedures and execution of clinical trials in hemotherapy. The position of BEST will be presented by Larry Dumont, PhD, Assistant Professor of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; and co-leader of BEST's Clinical Studies Team.

"Several retrospective studies have suggested a correlation between transfusion of older Red Blood Cells and poorer outcomes in certain clinical settings," said Dr. Dumont. "Such studies display several important shortcomings in their assumptions, designs and reporting."

- more -

In particular, the BEST Collaborative comments will focus on the recent *New England Journal of Medicine* article written by Colleen Gorman Koch, MD, and colleagues, noting the study had several key inadequacies, including:

1. The groups receiving units of different storage periods appeared not at all comparable.

   The groups differed in many important clinical features, including the frequency of left ventricular dysfunction, prior myocardial infarction, mitral valve regurgitation, body size, severity of heart disease, and the presence of peripheral vascular disease. These suggest that the patient groups were not similar and may have come to surgery in very different situations making a comparison of their outcomes meaningless.

   The groups displayed a skewed distribution of ABO groups and, furthermore, had an even more skewed distribution of ABO groups among the Red Blood Cells units transfused. This also suggests lack of comparability between the groups and in their clinical situations.

2. The survival curve shown in the paper was not adjusted for the many differences between the groups.

   Correction of results for confounding factors such as blood type, number of transfusions, and so forth would have been a legitimate and critical step in the analysis, but this was not performed for the results that were illustrated, and sufficient details of the analyses have not been provided to allow readers to judge the appropriateness of the analyses actually performed.

   Uncorrected survival curves present misleading pictures of the potential impact of red cell units' storage time. Presentation of stratified analyses should have been considered.

3. Storage age was treated as a dichotomous variable (i.e., "young" vs. "old") rather than investigating the association of increasing age with changing outcome.

4. No plausible mechanism explains the divergence of survival curves long after the natural removal of the transfused red cells at the end of their lifespan.

5. <u>Most important</u> is the indication that patients receiving older units of blood received more units of blood.

   The number of transfusions required by a recipient has been shown to correlate with outcome, but this association was not properly accounted for. Applying data published <u>from this same research group</u>, all the "excess mortality" they associated with the transfusion of older red cells can be attributed directly to the patients who received older units having received slightly more units of blood.

- more -

According to the BEST Collaborative, other studies using the more direct and powerful approach of prospective assignment of subjects to "younger" vs. "older" units of Red Blood Cells have not supported the contention of recent papers that older units convey significantly higher risk. These studies have used a variety of relevant physiologic endpoints.

"The only way to address the weaknesses of recent retrospective, epidemiologic studies is to properly design and execute a prospective randomized clinical trial with a clear, clinically relevant endpoint that is sufficiently powered to address the question," said Dr. Dumont. "The pathophysiology of the effects of red cell storage time on patient outcomes is not understood, and funding initiatives, such as the recent one announced by the National Heart, Lung and Blood Institute, should be expanded."

Overall, the BEST Collaborative finds the methodology of the Koch study inadequate to change transfusion policy. The organization encourages analyses of other data, particularly from randomized trials representing comparable groups of patients.

To learn more about the BEST Collaborative, visit: www.bestcollaborative.org.

# # #