Current and Future Cellular Transfusion Products

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• Novel transfusion products

Each year millions of life-saving and quality of life-enhancing blood components are collected and transfused. The cellular transfusion products, which include red blood cells (RBCs) and platelets, are collected and processed by approved methods to ensure their safety, purity, and potency. Novel transfusion products may be synthetic or may result from modifications to approved collection, processing, and storage procedures for existing cellular products and must be reviewed by the Food and Drug Administration (FDA) before being legally marketed in the United States. Manufacturers of novel transfusion products typically have performed in vitro studies, small Phase I and Phase 2 clinical trials, and larger Phase 3 trials to evaluate their products. For modified components, the extent of studies required depends, in part, on whether the novel RBC or platelet product is collected using methods that are significantly different from approved methods. Novel RBC products include RBCs collected in new storage bags or bags with new anticoagulants, RBCs derived from stem cells, RBCs subject to extended storage, and RBCs undergoing pathogen reduction procedures. Novel platelet products include pathogen-reduced platelets, extended-storage platelets and lyophilized platelets used for intravenous hemostasis, stem-cell derived platelets, and platelet products stored or derived in other ways that may influence product safety or quality. Artificial particles with platelet-like hemostatic functions also are being developed. Evaluation of these novel products involves testing to establish whether the product is safe, pure, and potent.

Current transfusion therapies and practices are the culmination of major scientific and technological advancements during the last 7 decades. Nevertheless, innovative technologies have the potential to improve blood and blood products. The FDA

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regulates biologic products, including blood and blood products, to ensure that they are safe, pure, and potent. Thus, novel products that seek to further improve currently available products (eg, extending the shelf life) are evaluated by the FDA. In this article, we discuss certain novel products of potential interest in transfusion medicine that are described in the literature.

RBC TRANSFUSION PRODUCTS

RBCs are a life-saving therapeutic transfusion component. Approximately fifteen million RBCs units are collected and transfused in the United States each year[1] with the intent of providing increased capacity to deliver oxygen to tissues of patients who are anemic.

The FDA evaluates novel RBC products to ensure that they are safe, pure, and potent and at least equivalent to other RBC transfusion products already on the market. The FDA evaluation process relies, in part, on in vitro tests and on RBC recovery based on in vivo radiolabeling clinical studies. The in vitro tests characterize RBC morphology and biochemical status that include red cell shape, size, hemoglobin concentration, hemolysis, cell surface markers, glucose use rates, lactate production rates, ATP levels, and use rates. Some of these tests have been in use for decades while others have been recently developed and adapted. These tests do not include evaluation of oxygen-carrying capacity because, historically, it has been assumed that minor modifications to storage conditions do not alter the RBC ability to deliver oxygen. Extrapolation of in vitro tests results to predict the in vivo function of RBCs has had, over the years, only limited success. Highly abnormal tests are usually predictive of poor in vivo performance but normal or slightly abnormal in vitro tests may also be associated with decreased in vivo performance.

It is well accepted that the viability of a sample of stored red cells cannot be accurately predicted from any measurement made in vitro. Therefore, measurements of posttransfusion survival are necessary to assess potential new methods of collection and storage.[2] Because of the difficulty of extrapolating in vitro results to clinical performance the FDA has relied on in vivo studies as the gold standard for evaluation of RBC products. The in vivo test involves radiolabeling of autologous RBCs donated by a healthy volunteer and reinfusion of these cells into the same volunteer. The percentage of the RBCs recovered 24 hours after transfusion has been used to evaluate the quality of RBCs. This criterion for evaluating in vivo recovery of RBCs has evolved over time along with new procedures and technologies.

In 2008, the Blood Products Advisory Committee (BPAC) addressed the issue of RBC recovery. The BPAC supported (15 yes, 2 no) that radiolabeling studies for RBC recovery should be performed in at least two separate laboratories with a total of 20 to 24 healthy donors. The mean recovery at 24 hours for each unit should be greater than or equal to 75% with SD less than or equal to 9%; and the one-sided 95% lower confidence limit for the population proportion of successes greater than 70%.[3]

Recent studies have highlighted potential risks associated with RBCs stored for longer periods before transfusion. Two retrospective analyses indicated that transfusion of older RBCs to critically ill patients may lead to adverse events and ultimately death.[4,5] Prospective studies evaluating clinical outcomes of patients transfused with different aged RBCs are needed to determine if older RBCs may be detrimental for certain patient groups.[6,7] Several large prospective studies evaluating different clinical outcomes are being initiated in the United States (the Red Cell Storage Duration Study [RECESS]) and Canada (the Age of Red Cells in Premature Infants