FDA Workshop: Use of Computer Simulation of the United States Blood Supply in Support of Planning for Emergency Preparedness and Medical Countermeasures

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ISSUE SUMMARY

FDA Center for Biologics Evaluation and Research (CBER)

FDA seeks discussion with industry, academia and other government agencies about the application of computer simulation models of the U.S. blood supply in support of emergency preparedness and planning for potential disruptions of blood availability resulting from mass-casualty events and pandemics. FDA will present an example of a blood supply system model and seeks discussion of the structure, capabilities, and limitations of the model; on data needs for modeling; and on how simulation models may inform and complement current blood supply management approaches.

Background

Planning for a response to a mass-casualty event or a pandemic is a national priority and involves the coordination of personnel, non-medical and medical resources. An important medical resource is the supply of blood components, including red blood cells, platelets and plasma. FDA has developed a computer-based simulation model of the supply of red blood cells (RBC) in the U.S., which we will refer to as the U.S. blood supply or blood for the purposes of this workshop. The U.S. blood supply relies on volunteer donation and may be vulnerable to the effects of chemical, biological, radiological, or nuclear (CBRN) threats, incidents or pandemics since donors may be prevented from or not wish to donate blood; or may need to care for ill family members; or fear exposure to influenza. As the blood supply system is a complex network of collection, handling, processing and distribution facilities it is difficult to develop realistic scenarios describing behavior of the supply under conditions of mass casualties or pandemic. However, understanding the limits and the dynamics of the U.S. blood
supply is essential for informing and developing effective strategic planning for emergency preparedness to prevent avoidable blood shortages. Mitigation of associated adverse health consequences can have a profound effect on the overall mortality and morbidity of potential patient populations impacted by a mass-casualty event or pandemic.

FDA is sponsoring a one-day workshop to initiate a dialogue with stakeholders of the blood community to discuss the utility and application of simulation models, and possible approaches for collecting necessary information for use in the development of robust computer simulation models of the U.S. blood supply. The FDA model is a pilot model that can illustrate and be used to discuss possible applications and scenarios for pandemic and mass-casualty events which may be of interest to stakeholders and the public. The dynamics of the entire national blood supply system are complex, making it difficult to model at a level of detail that accurately represents the actual system. Recognizing these potential limitations, FDA seeks feedback during workshop discussions on the capabilities of the current version of the example pilot model; on desired model improvements; and on the level of additional, high-quality data that would improve the model and further reduce uncertainty. The level of development of the model and data acquisition required to better support regulatory decision-making and protect public health is a key outcome of the workshop. This public workshop will help also to increase the transparency of the risk assessment process used by FDA-CBER.

**FDA Example of a Computer Simulation Model of the U.S. Blood Supply**

1. **Model elements**

   FDA has developed a computer-based simulation model of the blood supply based on multiple years of daily RBC collections data gathered from America’s Blood Centers (ABC) for several U.S. blood centers. Blood utilization was estimated using three years of daily data using Centers for Medicare and Medicaid Services (CMS) billing data. The computer simulation model allows for the evaluation of the daily availability of blood units in response to a pandemic or a mass-casualty event. The stochastic discrete-event stock-and-flow simulation model is able to simulate two simplified blood systems models independently: one that provides national estimates and a second that provides regional estimates of blood availability, and the associated uncertainty, by ABO/Rh blood type. Each blood system model uses Monte Carlo techniques to simulate 10-years of daily blood collection and blood utilization data. One model outcome is the average daily number of RBC units, which is obtained by analyzing 10-years of simulated outcomes and generating the average for each day of the year. Data from the Nationwide Blood Collection and Utilization Survey (NBCUS, 2009) on annual U.S. donations (17,159,000) and annual U.S. transfusions (14,855,000) for the year 2008 were used in the model.
The national blood system simulates a single in-flow of daily donations and a single out-flow of daily transfusions and two stocks: a blood collector bank and a hospital. In the system, the blood collector bank represents the collection, inventory and management of the blood donations, while the blood distributor or hospital, which is assumed to not have its own collector center, represents the inventory and management of the blood that is available for use in transfusions. Each stock has its own inventory of blood units organized by blood types. Blood units move from the hospital inventory into patients based on a daily stochastic simulated demand algorithm. The hospital inventories keep track of end of day levels and request blood units of specific blood types to keep inventories at target levels. In the simulation model, the hospital seeks to maintain 6 days of reserve of blood units of each type in its inventory. The model implements ABO/Rh blood type predictions based on donor patterns and U.S. phenotype prevalences and a system of rules which allows for compatible blood to be selected and removed from the inventory when the exact match of a specific blood type is not available (cross-matching) during the simulation of blood demand.

The inter-regional blood system consists of connections among 5 different local systems, representative of 5 different regions. Each local system is structured to be similar to the national blood system but with around 1/5 of the national blood system levels described above. Different regional distributions of annual U.S. donation and transfusion levels have been considered for the inter-regional blood system to differentiate among the regions. In this case, it is possible to explore the system by accounting for regions with a higher or lower collector bank and/or distributor. The inter-relationship among regions is accomplished by allowing the establishment of five regional blood centers with inter-regional demand for blood generated from one region and surplus supply shared by other regions. The blood transfer system at the inter-regional level accommodates the needs of simulated regions and communicates the information to other regions with surplus supply to address the imbalance. The blood transfer system integrated into the model is scaled by individual blood type. Modeling inter-regional blood transfers is relevant for capturing the specific dynamics at the national level of the U.S. blood supply. With further enhancements and data, simulation models could provide more realistic national estimates on a daily basis of availability for national emergencies.

The simulation model also integrates the effects of different approaches for managing blood transfers from the blood collector to the distributor; and for allocating blood from the distributor for transfusion. These approaches can be tested in order to evaluate the potential impacts on the U.S. blood supply. While transfers from the blood collector to the blood distributor occur using a strict First-In-First-Out (FIFO) approach for the management of the blood units; the model explores the impact of several allocation methods for blood use at the distributor/hospital level, which is usually not strictly FIFO. We developed two independent algorithms that select blood units from the inventory according to the daily blood demand to
explore the impact of allocation methods. The first algorithm, “Likely Oldest” (LO), is similar to FIFO but is not as strict since the most likely blood selected is older blood, but younger blood can be occasionally selected instead of older blood. The second algorithm provides a contrast to the first algorithm and is called “Likely Newest” (LN). This second algorithm is like the first in that it probabilistically selects units of blood from the inventory based on demand, but selects newer blood in preference to older blood. These different allocation methods can be tested to explore the impact on the steady state levels of the blood supply.

2. Preliminary model findings

Preliminary results on the steady-state level of the U.S. blood supply have been obtained by independently running the national blood system model over a 10-year simulation both under normal conditions (Baseline) and for a Pandemic. For a typical Pandemic simulation we assume that the amount of donations have been reduced on a weekly level by selected percentages following the start of the Pandemic. After some time, donations begin to recover on a per week basis until supply returns to pre-pandemic levels in a manner that mirrors the decrease. Any specific decrease in donations or rate of decrease and recovery of donations may be explored by the model. At present, the impact of a Pandemic on the blood collection and distribution system (i.e. reduced staffing causing reduced capacity) is not modeled; however, future enhancements to the model can incorporate this aspect.

A Pandemic scenario has been simulated by assuming a 5% reduction in the number of donations each week at the start of the pandemic in the middle of January. The overall result is a reduction of 35% by week 7, followed by a recovery of 5% each week for each of the next seven weeks until the pre-pandemic normal supply level is reached. We present results in this summary, assuming that blood units are allocated by the hospital for transfusion using a Likely Oldest (LO) protocol. Figures 1.A and 1.B show the difference in the impact on the steady-state level of the Total (Collector Bank + Hospital) U.S. blood supply for the Baseline model (Figure 1.A) compared to a Pandemic scenario. The simulation results on Pandemic show that the recovery time to pre-pandemic steady-state levels occurs more than six months after the start of the Pandemic (Figure 1.B) in mid-January.

Simulation results are summarized in the Table 1, which include the annual average daily number of RBC units as well as the absolute and percent reduction in the average daily number of units for each of the simulated scenarios (Baseline (LO) and Pandemic (LO)). In the case of Pandemic, on average, an absolute reduction of 402,000 RBC compared to baseline has been estimated by the simulation, reducing the average number of RBC units by 26% of baseline levels, as shown in Table 1.
Table 1. Absolute Simulation results on Baseline vs. Pandemic impact on the steady-state level of the U.S. Blood Supply for the overall blood.

<table>
<thead>
<tr>
<th>Model type</th>
<th>Annual average daily number of RBC units (95% CI)</th>
<th>Absolute reduction in average daily number of RBC from Baseline</th>
<th>Percent reduction in average daily number of RBC from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1,547,000 (1,520,000-1,570,000)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pandemic</td>
<td>1,145,000 (1,110,000-1,180,000)</td>
<td>402,000</td>
<td>26%</td>
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Figures 2.A and 2.B show simulation results for Baseline LO and Pandemic LO scenarios by blood type. Note that the steady-state level of each of the ABO/Rh blood types significantly decrease during a Pandemic compared to Baseline. O positive is the most prevalent blood type across both the Baseline and Pandemic scenarios, while AB negative is the least prevalent. Each blood type shows a similar pattern of reduction in the quantities available following the start of the pandemic.
Figure 1. Total (Collector Bank+Hospital) U.S. blood supply for the overall blood. Figure 1.A represents Baseline, while Figure 1.B represents the Pandemic scenario. Pandemic scenario assumes a 5% reduction in donations each week at the start of pandemic (mid-January) and a total reduction of 35% by week 7, followed by a recovery of 5% each week for each of the next seven weeks.

**Figure 1.A**

Average daily number of RBC units
1.55 million (1.52 million – 1.57 million)

**Figure 1.B**

Average daily number of RBC units
1.14 million (1.11 million – 1.18 million)

Beginning of Pandemic

Average over 10-year simulation
Figure 2. Total (Collector Bank+Hospital) U.S. blood supply by ABO/Rh blood type. Figure 2.A represents Baseline LO, while Figure 2.B represents the LO Pandemic Scenario. Pandemic scenario assumes a 5% reduction in donations each week at the start of pandemic (mid-January) and a total reduction of 35% by week 7, followed by a recovery of 5% for each of the next seven weeks.
Modeling the supply by blood groups is valuable in capturing the specific dynamics of the system. For instance, shortages of some rare blood types may have important public health impacts. The results from the example model are intended to show how possible outcomes for pandemic scenarios can be modeled, and at this time should not be construed as representing a likely outcome of a pandemic. Further elements of the model and preliminary results obtained by running the inter-regional system for a mass-casualty scenario will be presented at the workshop.

The current version of the FDA computer simulation model is extremely versatile and allows for the addition of appropriate features as needed. Further refinements of the model through the extension to the sub-regional and local levels may allow the use of the model at different levels of planning. The development of representative scenarios of changing blood supply and demand help demonstrate how the model can be used to predict and explore “what-if” scenarios to better support regulatory decision-making. The example FDA model suggests that simulation models may be useful tools to support emergency preparedness and planning that may minimize adverse medical consequences during public health emergencies.

This FDA Workshop will provide opportunities for FDA and other stakeholders to discuss the following goals:

1. provide a forum for discussion of data needs and to obtain feedback on possible modeling scenarios to explore emergency supply situations should a pandemic, or epidemic diseases or other events that could adversely impact the blood supply in the United States occur;

2. discuss simulation modeling of the U.S. blood supply including the possible application of an FDA computer simulation model of the U.S. blood supply in support of emergency preparedness and planning for potential disruptions in blood donations;

3. discuss with the blood community the utility of simulation methods as a complementary approach to support planning for daily inventory needs and forecasting for future blood donations and demand;
4. discuss the capabilities and limitations of the U.S. computer simulation model, assumptions used in the model and data gaps for model validation;

5. describe and prioritize future model enhancements to extend the model predictions from red blood cell units to other blood components such as plasma and platelets;

6. discuss the level of detail required for a model to characterize the U.S. blood supply and to develop possible scenarios in which shortages may be addressed through countermeasures such as use of local and inter-regional transfers of blood and blood components.

Presentations and panel discussions with experts from academia, regulated industry government and other stakeholders will be included in this public workshop.