



**STATEMENT OF
AMERICAN ASSOCIATION OF BLOOD BANKS
AMERICAS BLOOD CENTERS
AMERICAN RED CROSS**

BEFORE THE BLOOD PRODUCTS ADVISORY COMMITTEE

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Nucleic Acid Testing of Blood Donors for Human Parvovirus B-19 Virus

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Parvovirus B19 infection is widespread in the human population. Transmission generally occurs by the respiratory route. By adulthood, 50% of the population shows antibody evidence of previous infection and presumably retains immunity to reinfection. Parvovirus B19 infection is usually either asymptomatic or results in a mild self-limited illness in immunocompetent individuals. Parvovirus B19 infection can rarely result in severe, clinically significant outcomes in three patient groups: transient red cell aplasia with accompanying anemia may occur in patients with chronic hemolytic anemias, pure red cell aplasia may occur in immunocompromised patients, and hydrops fetalis with spontaneous abortion may rarely occur in pregnant women.

Frequent transmission of Parvovirus B19 infection by transfusion of Factor VIII concentrates prior to the widespread use of viral inactivation technology has been well documented. Due to the relative resistance of Parvovirus B19 to viral inactivation and to the high level of viremia in acutely infected persons, such transmission continued, though at lower levels, even after the introduction of virally inactivated concentrates. Data from the transfusion experience with SD plasma indicate that seroconversion in recipients occurred frequently when high titer viremia ($10^{7.5}$ to $10^{8.5}$ copies/ml) was present but did not occur when viremia was present at $< 10^4$ copies/ml. These observations have lead most manufacturers of plasma derivatives to introduce nucleic acid amplification testing (NAT) for high titer parvovirus B19

viremia performed on relatively large pools of donor samples. To the best of our knowledge, comprehensive data on the effectiveness of these procedures in decreasing transmission by factor concentrates have not been published.

Despite the historically high transmission rates of parvovirus B19 to recipients of pooled plasma products, very few adverse clinical outcomes have been reported in patients with hemophilia; a 1999 review article cites only three cases of erythema infectiosum and one case of hypoplastic anemia. Similarly, cases of clinical disease associated with Parvovirus B19 transmission by blood component transfusion in North America and Europe are rare; we are aware of only 3 published cases. In each case, the recipient developed anemia; one case was successfully treated by IVIG, one case spontaneously resolved, and one case did not report follow-up data. Parvovirus B19 does not appear to be transmitted by albumin or IVIG.

Because blood centers supply recovered plasma for manufacture of plasma derivatives, these collectors plan to begin parvovirus B19 minipool NAT to ensure that plasma sent for fractionation does not contain high titers of B19. Preliminary data from the American Red Cross using pools of 512 and an assay that detects $10e^7$ copies/ml per donation shows donor viremia rates of 1:12,800.

Blood centers intend to perform Parvovirus B19 NAT on minipools as an in-process manufacturing control, according to previously defined FDA policies. This can be termed phase 1 of parvovirus testing. Under this mechanism, Parvovirus B19 testing would not be regarded as donor screening and there will be no need to resolve the positive minipool to the level of the individual donation. This would accomplish the aim of interdicting Parvovirus B19 viremic plasma units prior to pooling for manufacture.

Given the important and compelling competing safety priorities of implementing West Nile Virus donor screening and performing bacterial detection in platelets for the whole blood sector in the next 6 to 9 months, the additional capacity and work that would be required to perform Parvovirus B19 NAT as a donor screening test cannot be absorbed. For example, performing Parvovirus B19 as a donor screening assay would require the addition of another on-line assay requiring completion prior to all product release, the pulling of samples and further testing to resolve positive pools, the need for a confirmatory assay, and the alteration of 510k cleared computer systems to accommodate Parvovirus B19 results as a release criteria. Furthermore, current FDA policy would require that donor screening be performed under an IND or IDE which would be an additional burden for test kit manufacturers who are turning their efforts to WNV screening test development.

We believe this practical solution of performing Parvovirus B19 testing as an in process control at this time is supported by the available scientific and medical data on the clinical significance of Parvovirus B19 infection.

?? Parvovirus B19 infection in a blood donor is of no consequence to the donor's health and secondary transmission of the infectious agent does not occur by preventable parenteral routes. Realistically, donor notification for any agent cannot be accomplished until 7 to 14 days after donation. By this time, a donor with a previously high viremia would likely

have resolved the viremia and/or developed antibody and would be very unlikely to still be infectious. Furthermore, notification of contacts of the donor to alert them to the possibility of recent exposure would have no value in preventing virus transmission or in helping either the donor or the contacts to receive treatment or undergo diagnostic laboratory testing. The most likely effect of donor notification would be a high degree of donor confusion and/or anxiety as has been demonstrated with other agents.

?? Identifying and deferring the individual donor with high viremia would not significantly enhance safety for recipients of blood components. Since such infections spontaneously resolve rapidly, donors would be safe at the time they became eligible for their next whole blood donation.

?? As a consequence of not identifying the individual donor, it will not be possible to prevent the transfusion of the red cells and platelet units from that positive donation. Although it might be desirable to do so, the data indicate that the enhancement of safety that would be provided by such component removal is likely to be minimal. Continued transfusion of such components, as occurs currently, very rarely results in reported clinical disease.

At the present time, blood centers must prioritize their efforts and implement procedures that deal with the highest level risks to transfusion recipients. At a later date, it is possible that Parvovirus B19 testing can move into a phase 2 in which positive results are linked to an individual donation and all components of that donation are removed from inventory. The policy issues associated with such phase 2 testing (in which Parvovirus B19 is performed as a screening test) and the logistics of implementing such a policy will need further discussion.

In conclusion, the issue of prioritization of blood safety initiatives and the capacity of the system to absorb multiple changes simultaneously is a reality that must be recognized.

America's Blood Centers (ABC) is an international network of community-based blood centers that collects nearly half of the U.S. blood supply and about 25% of the Canadian blood supply. The largest provider of blood components and services, America's Blood Centers' members are located in 45 states, serving more than 125 million people at 450 blood donation sites. For 40 years, America's Blood Centers' members have been committed to serving the needs of their local communities by saving lives through volunteer blood donation.

The American Red Cross (ARC) is an independent, non-profit organization dedicated to saving lives, easing suffering and restoring hope at home and around the world. The Red Cross, through its 36 Blood Services regions, supplies approximately half of the nation's blood for transfusion needs. Its primary focus is providing high quality blood and blood products to the patients who need them, but ARC is also a large supplier of human allograft tissue including heart valves, skin, bone and associated connective tissues. Additionally, the Red Cross is engaged in research and other efforts to support donation and processing of such human derived products as umbilical cord blood and bone marrow for use in treatment of malignancies and other serious diseases.

The American Association of Blood Banks (AABB) is the professional society for over 8,000 individuals involved in blood banking and transfusion medicine and represents approximately 2,000 institutional members, including blood collection centers, hospital-based blood banks, and transfusion services as they collect, process, distribute, and transfuse blood and blood components and hematopoietic stem cells. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. For over 50 years, the AABB's highest priority has been to maintain and enhance the safety and availability of the nation's blood supply.