

**Blood Products Advisory Committee Meeting  
March 14-15, 2002**

**FDA's Current Thinking on Parvovirus B19 NAT for Blood and Plasma**

Issue:

FDA seeks to clarify the circumstances under which the Agency would regard NAT testing for Human parvovirus B19 to be "in-process" testing, medical diagnostic testing and/or donor screening.

Background

Consistent with the advice of BPAC (held in September 1999), FDA has allowed the testing of plasma pools for parvovirus B19 by NAT as "in-process" tests to ensure the quality of Source Plasma and Solvent/Detergent Treated Pooled Plasma. Test results were used to reject reactive units, but donors were not notified or deferred. BPAC did not recommend resolving the reactive manufacturing pool to the individual donor. FDA has reviewed these NAT methods as analytical procedures with respect to sensitivity, specificity and reproducibility under license supplements for the manufactured products, and in the absence of "free-standing" approvals for the NAT tests per se.

FDA has become aware that Source Plasma fractionators have been performing high-titer minipool testing and resolving reactive to individual donors. FDA understands that such high-titer, i.e., insensitive, screening may not capture all infectious donors and hence products (especially unpooled components). The viremic period for B19 infected donors can be very lengthy. The infectivity is largely depending upon the balance between virus and the presence of anti-B19 antibodies (which can potentially complex with or neutralize the virus). A sensitive test may remove low-level B19 DNA and anti-B19 IgG positive donations, which may adversely affect anti-B19 levels in plasma pools and resulting products.

FDA is also aware that Whole Blood industry would like to implement similar high-titer B19 NAT screening as those by Source Plasma fractionators. It has been proposed that such testing should be regarded by FDA as "in-process" testing on recovered plasma, and not as donor screening. At least initially, reactive minipools would not be resolved to identify individual reactive donors. Additionally, it has been stated that pre-release testing and labeling are not feasible for blood components, for lack of an appropriate technology infrastructure. As proposed, test kit manufacturers may provide their systems and reagents for such testing. The validation of these test methods would be reviewed under the license supplement mechanism submitted by fractionators.

FDA's Current Thinking

The following points summarize FDA's current thinking on parvovirus B19 NAT for Blood and Plasma. FDA is considering recommending that:

- When tested, high-titer parvovirus B19 reactive plasma donations should not be used for further manufacturing into injectable products. This is to ensure that the FDA's proposed limit,  $<10^4$  IU of B19 DNA/mL, for manufacturing pools destined for making plasma derivatives can be met.
- For Whole Blood donations, when feasible, B19 reactive minipools should be resolved to identify the individual reactive donors prior to release of components for transfusion, and that units from reactive donors should not be used for transfusion.
- When testing is done subsequent to product release, in-date components from potentially reactive donors should be retrieved and discarded so that they are not used for transfusion or further manufacturing into injectable products.
- Even when performed as an "in-process" test (i.e. not performed pre-release as part of a determination of donor suitability or product labeling), testing and identification of the individual reactive donor constitutes medical diagnostic testing. Therefore, such testing would require the use of an investigational test under an FDA approved investigational mechanism.
- Informed consent should be obtained from blood and plasma donors subjected to such high-titer NAT testing. Reactive donors should be identified, be informed of the reactive status, and be provided with medical counseling. Because of the transient nature of the infection and a rapid development of the immune response, such donors would be suitable to donate when they test non-reactive.