American Red Cross

National Headquarters

BSL 86-28

To Responsible Heads
Directors/Medical Directors
Directors, Technical Services

Date June 27, 1986

From Dr. Sandler

Subject Phase-In of ALT Testing

Proposed BSD 6.53, Testing for Alanine Aminotransferase (ALT), and a proposed revision of BSD 4.9, The Donor Deferral Register: Function, Content and Use are being sent to regions for comment. This letter provides information on phasing-in ALT testing. Please share the proposed directives and this letter with appropriate staff in your region.

Protocols for Introduction of ALT Testing: Initial evaluations of analyzer performance, assay accuracy and reproducibility should facilitate prompt resolution of instrument or methodology problems. The following protocols, designed by Dr. James P. AuBuchon, should be followed by blood services staff performing ALT testing in order to determine proficiency:

1. Replication Protocol - Obtain 20 serum or plasma samples that cover a wide range of ALT activities. Five of these should be at the expected lower cutoff level (about 45-60 International Units per Liter), and another five should be at the expected upper cutoff level (over 100 IU/L). These samples may be obtained from a local clinical laboratory or from donors tested in early familiarization runs on the analyzer.

   Test each sample at least nine times: three times a day, in separate runs, for at least three days. Run other samples during this time, so that the instrument is handling typical operational volumes. At the end of this data collection, calculate the arithmetic mean, standard deviation (SD) and coefficient of variation (CV) for each sample, and submit the results to

   Mr. Chyang Fang
   Quality Control Laboratory
   Laboratory Services
   American Red Cross
   Auburn Avenue Facility
   4915 Auburn Avenue
   Bethesda, MD 20814

2. Comparison Protocol - Quality Control Laboratory/Infectious Diseases Section (QCL/IDS) will distribute a panel of five serum samples, including three freeze-dried aliquots of each sample. One aliquot of each sample must be tested each day for three days, and results submitted to Mr. Fang, QCL/IDS.

3. Technical Proficiency - The QCL/IDS will determine whether or not a center has established proficiency based on the results of the protocols outlined above.

Run Controls: At the request of national headquarters staff, Dr. AuBuchon has provided the following recommendations for quality control of the test procedure.

Enzymatic analyses are inherently more likely to exhibit drifts and shifts during a run than other tests performed during donor unit processing. Documentation that analyses are being performed within acceptable limits are important even in screening tests such as ALT because:

1. Slight changes in temperature, spectrophotometer function or reagent characteristics may have disproportionate effects on measured enzymatic activity.

2. The disease state that ALT screening is being implemented to detect, characteristically has only very mild elevations of ALT. Slight changes in analytical performance may greatly affect this screening test's efficacy in preventing post-transfusion non-A, non-B hepatitis (NANB).

3. The cutoff level used to determine acceptability of a donation for transfusion is based on a population distribution. Unless the screening tests are performed in the same analytical system as the population distribution analysis (as defined by run controls that are performing according to expectation), a greater or lesser proportion of donations may be excluded.

It is strongly recommended that each region begin their work with their test system by employing frequent run control samples, one every 8-15 samples. The results of the run may be considered acceptable only so long as the values for the run controls are acceptable according to the Multi-Rule Shewhart procedure*. If a run control is found outside this control procedure's limits of acceptability, all samples since the last acceptable control should be retested.

Once familiarity has been gained with the instrumentation, the degree of variability attributable to reagent lot variations and other such factors that may affect analytical performance, the region may elect to reduce the frequency of control samples.

* Westgard JO, Barry PL, Hunt MR (1981). A multi-rule Shewhart chart for quality control in clinical chemistry. Clin Chem 27/3:493-501.

At least two different serum, plasma, or freeze-dried control samples should be employed alternately in a run. One of these should have an ALT activity near the lower cutoff; the activity of the other should be near the mean of the donor population distribution. Control materials may be produced locally by regions, by freezing aliquots of plasma from donor units. The mean and standard deviation should be characterized by the region on multiple runs prior to the institution of the plasma as a control sample.

Establishing Cutoffs: Two cutoffs will be used routinely in ALT testing - a lower cutoff to determine the disposition of the donated blood, and an upper cutoff for donor management. Mr. Wayman Ng of the Office Systems and Telecommunications division of Corporate Management Information Systems has written a computer program that will perform the computations required for setting cutoffs. This software can be used on Molecular, IBM and IBM-compatible computers.

A copy of the software may be obtained by sending a TWX to Ms. Kay Ennis, Medical Operations, stating the type of computer to be used. Additional information on determination of cutoffs is provided in proposed BSD 6.53, Attachment I, Determination of Cutoff Values for ALT Testing, June 1986.

Establishing the Date-of-Record: Upon notification of the region by QCL/IDS that technical proficiency has been established, all donated blood should be tested and found to have an ALT level below the lower cutoff before being issued for transfusion. The date upon which such routine testing begins is the date-of-record for ALT testing.

Testing of Blood in Inventory: ALT testing of existing inventories of whole blood and blood components is not required. Plasma that has not been ALT tested by the date-of-record should be sent for fractionation into albumin.

Notification of Hospitals: No more than 42 days from the date-of-record, transfusion services should be notified that all blood and components distributed by the center have been tested and found to have acceptable ALT levels unless otherwise labeled. A sample letter has been provided by Dr. AuBuchon (Attachment I). A modified Circular of Information should accompany the letter. (See Special Labels, below.) A similar message should be sent from regional blood services that export to other centers on contract.

Special Labels: The following labels are being printed and will be shipped to regions when available.

1. Overlabel for Circular - At the time of notification, an add-on label should be applied to Circulars of Information. This label states, "All products distributed by American Red Cross Blood Services have been tested and found to have ALT levels that are acceptable for transfusion unless otherwise indicated by an additional label." Alternatively, this statement may be overprinted onto existing stocks of the circular.

2. Untested Product - Beginning at the time of notification, all blood components that are issued without having been tested for ALT must bear the label stating, "CAUTION - Test for _____ has not been done", with ALT legibly and indelibly printed in the blank space.

3. Elevated ALT - If whole blood and components with ALT levels not acceptable for transfusion are shipped for further manufacture or research, the products should bear one of the special labels, "Biohazard" or "Not for Transfusion", or one of the new labels, "CAUTION - Elevated ALT" or "Based on ALT test result, this plasma unit is designated for manufacture of Albumin only".

If it becomes necessary to release untested blood in an emergency, include ALT test results (or untested) on the "For Emergency Use Only" special label in the "other" space.

No modifications of recovered and source plasma labels are planned at this time.

Donor and Patient Safety Brochure: At the next revision of Form 1786, *Donor and Patient Safety - What You Should Know About Giving Blood*, the paragraph on testing of blood will be modified to include ALT testing.

Disposition of Blood Products: Whole blood and components with ALT levels less than the lower cutoff may be issued for transfusion if otherwise acceptable. Products with ALT levels equal to or greater than the lower cutoff should be sterilized and destroyed according to BSD 6.53, Section XI.D (except as provided for liquid plasma, below).

Plasma with ALT levels equal to or greater than the lower cutoff may be labeled with Form 6247, "Recovered Plasma Liquid", or Form 6274, "Recovered Plasma", and the additional new special label, "Based on ALT test result, this plasma unit is designated for manufacture of Albumin only", and shipped as recovered liquid plasma for production of Albumin (Human).

Donor Management: If a donor's ALT level is equal to or exceeds the lower cutoff, the donor's health history and test results should be reviewed by the center physician or the physician's designee.

- If the donor's ALT level is equal to or exceeds the lower cutoff but is less than the upper cutoff, the donor's information should be entered into local surveillance Category 1.

- If the donor's ALT level is equal to or exceeds the upper cutoff, the donor should be notified and deferred indefinitely by entry of the donor's information into Category L.

- A donor's information will be transferred automatically into Category L if it is entered into Category 1 a second time within a 12 month period.

Any donor entered into Category L must be notified of the deferral. Sample letters for donor notification have been provided by Dr. Frans Peetoom (Attachments II and III).

The regional responsible head may review a donor's history and test results, and determine that the evidence supports removing the donor's name and other information from the DDR (either Category 1 or Category L). BSD 4.9 I.E.4 applies.

Computer Systems: Corporate Management Information Systems will modify the IBIS and BMIS programs to include the new DDR categories and will interface the ALTAIRE and EPOS systems with IBIS.

Questions About ALT Testing may be directed to the following Medical Operations staff:

Medical Evaluation, Donor Notification	Joseph P. O'Malley, M.D. Medical Associate (202) 639-3017
Technical Proficiency, Quality Control	Delores Mallory, MT(ASCP)SBB Director, Laboratory Services (301) 652-4618
	or
	Chyang Fang Coordinator, Quality Control Laboratory (301) 652-4618
Reagent and Equipment Contracts	Jeany Mark, MBA, MT(ASCP) Business Analyst (202) 639-3070
Blood Services Directives	Kay Ennis, SBB(ASCP) Director, Medical/Technical Services (202) 639-3331

Comments on this letter and the proposed directives will be welcomed and should be directed to Ms. Ennis.

S. Gerald Sandler, M.D.
Associate Vice President
Medical Operations