

Changes in Equipment for Processing Blood Donor Samples (7/21/92)

DATE: July 21, 1992

FROM: Director, Center for Biologics Evaluation and  
Research

SUBJECT: Changes in Equipment for Processing Blood Donor  
Samples

TO: All Licensed Blood Establishments

The Code of Federal Regulations, 21 CFR 640.5(b) and (c) requires that each container of Whole Blood be classified as to ABO and Rh group. Routine blood bank practice also includes performing blood group related antibody screening tests on a sample from each donor. In the past, this testing was most often performed using manual slide or tube procedures. In recent years, however, various automated methods and equipment have been developed to perform this testing.

It has been the policy of the Center for Biologics Evaluation and Research (CBER) both to review automated blood grouping and antibody test systems as medical devices used in blood and blood component manufacturing prior to marketing, and to also consider a licensed blood establishment's original or modified use of the medical device to be an important change in manufacturing methods [21 CFR 601.12(b)] that required review and acceptance by this Center prior to implementation.

We have evaluated the Center's past experience in the review and approval process for use of these devices. The results of our evaluation indicated that blood safety will not be adversely affected if licensed blood establishments implement use of medical devices approved for automated blood grouping after appropriate installation and on-site instrument qualification in the licensed blood establishment. The establishment should report the changes in procedures or equipment to the Director, CBER, consistent with 21 CFR 601.12(a) not less than 30 days in advance of implementation. However, the establishment does not need a specific approval from CBER prior to implementing. The FDA will review documentation supporting the change at the time of the next scheduled inspection.

A copy of the change notification sent to CBER, and acknowledgment of receipt by CBER, should also be available at the facility for review during FDA inspections.

Henceforth, any establishment electing to use automated blood grouping or antibody test systems approved for testing blood donor samples may do so consistent with the manufacturer's directions, following on-site instrument qualification, parallel testing as appropriate, and documentation of staff proficiency in

each facility. Any departure from the manufacturer's instructions, however, represents an unapproved method and will continue to require review and approval in the form of a product license application amendment prior to implementation.

Establishments that are currently awaiting approval of license amendments for the use of such equipment should submit a letter requesting withdrawal of the amendment application, if appropriate.

FDA will review the documentation in support of the procedural change at the firm's next inspection to determine that the manufacturer's directions are being followed, that adequate standard operating procedures are in place and being followed, that staff are appropriately trained and that appropriate qualification testing was performed, evaluated and documented prior to implementation of the change. The addendum further explains the kind of information that should be available for evaluation upon request by FDA.

Questions regarding this policy may be directed to the Division of Product Certification, (301) 295-8428, FAX (301) 295-8528; technical questions should be referred to the Division of Transfusion Science, Laboratory of Blood Bank Practices, FAX (301) 227-6431.

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Addendum to FDA Memorandum Regarding:  
Documentation of Changes in Equipment for ABO/Rh  
and Antibody Screening Processing Blood Donor Samples

As automation becomes an integral part of all laboratories, many blood establishments are purchasing equipment for use in the collection, processing, and testing of blood and blood products. Equipment used in blood establishments is subject to approval by the Center for Biologics Evaluation and Research and/or the Center for Devices and Radiological Health (CDRH) through the process of a 510(k) Pre-Market Notification or a Pre-Market Approval Application (PMA). Test kits and reagents to perform required tests for licensed blood products are also subject to approval by FDA.

In the past, the implementation of automated equipment for ABO/Rh blood grouping tests and related antibody screening tests has been considered a major change in manufacturing, requiring approval of a product license amendment (PLA from the Food and Drug Administration (FDA/CBER). The attached memorandum informs establishments that review of implementation procedures for new

equipment already cleared by the FDA and used according to the manufacturer's directions will now be performed during routine inspections. This step will eliminate duplication of review and streamline procedures for blood establishments implementing changes that include new equipment.

Documentation for changes that include use of new equipment should include the following procedures prior to acceptance for testing blood and blood components. Deviation from the manufacturer's instructions requires justification; licensed establishments also need written approval from CBER for the variation.

#### General Procedures

##### 1. Calibration

Automated equipment should be calibrated after installation and periodically according to the manufacturer's recommended schedule for maintenance. This may be performed by the device manufacturer at the time of installation. The blood establishment should keep a record of the calibration procedures performed, identifying the name of the person(s) performing the calibration, and listing the date(s) of calibration and any subsequent re-calibration.

##### 2. Validation (Qualification)

Validation establishes that a specific process will consistently produce a product meeting predetermined specifications. Blood establishments should have written specifications for automated equipment performance and the equipment should be evaluated to determine that it meets these specifications. Performance qualification is a part of validation involving rigorous testing to demonstrate effectiveness and reproducibility of the specific process being tested. Qualification includes testing a process with challenge conditions that simulate conditions that will be encountered during equipment use. The number of specimens tested or the number of test runs performed should be sufficient to ensure that the equipment meets the specifications determined by the blood establishment. There should be written records of qualification testing, including the names of personnel performing the testing and the date(s) of testing.

##### 3. Parallel Testing

Because it is very difficult to evaluate the precision and accuracy of some serological tests (e.g., blood grouping tests) in any other way, testing in parallel with an FDA licensed reagent used by another approved method has been a primary part of some types of new equipment validation.

Parallel testing is functional testing performed using both the new test method and the reference method on the same samples to determine that the new method provides accuracy comparable to or better than the reference method. The number of specimens tested should be sufficient to show that the new method is equivalent to or better than the reference method.

- a. Test adequate numbers of samples to document consistent determination of accurate ABO and Rh groups. Compare to results with licensed reagents used by a method accepted by the FDA for testing donor samples. The number of tests necessary to demonstrate adequacy of the new method is dependent upon many factors including the number of discrepancies and the range of phenotypes encountered. It may be necessary in most situations to supplement the routine donor samples with known examples of less common blood groups such as group A2B or weak D(Du).

If during the evaluation process the protocol changes or equipment adjustments are made, it will be necessary to test additional samples. The number of tests should be adequate to show both proficiency of technologists and reproducibility of results. In all cases the number of parallel tests to be performed should include:

A minimum of 500 samples. A minimum of 3 days testing under representative conditions.

- b. Maintain a summary of all of the experience with the instrument. (i.e., a complete history of testing performed, including test data, problems, equipment adjustments or repairs, protocol changes, and conclusions.)
- c. Maintain documentation regarding discrepant results, identification of the problems, and the resolution of problems. All additional testing done on problem samples should be fully documented.
- d. The NTD (no type determined) rate should not be greater than 6% of the total number of tests performed. An SOP should be prepared describing in detail how NTD samples will be handled.
- e. Record the names, lot numbers and manufacturers of all reagents used. If tests were performed to determine dilutions of reagents to be used, there must be documentation of these tests and consistent application of a protocol to choose correct dilution of each lot.

4. Quality Control

Quality control should be performed on all automated equipment prior to implementation and periodically thereafter as required by the manufacturer and the establishment SOP. Quality control data should meet predetermined acceptability criteria. If these criteria are not met, corrective actions should be taken and documented. The corrective action should be evaluated to ensure that the problem was corrected.

5. Maintenance

A schedule for preventative (routine) maintenance and a maintenance log should be developed prior to implementation of new automated equipment. The log should also include procedures for re-qualification after preventive maintenance and repairs, and documentation that these procedures were followed. Simple calibration may be sufficient following scheduled preventive maintenance, whereas complete re-qualification may be necessary following major repairs. The SOP should clearly define what will be required and/or the criteria for decisions concerning the extent of quality control or validation testing before donor testing is resumed.

6. Emergency Plans

The blood establishment should have a back-up system for providing test results in the event of equipment failure. The SOP should describe the alternative system(s), and staff proficiency for employing the alternative system should be documented.