Use of the Recombigen HIV-1 LA Test (2/1/89)

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From : Director, Center for Biologics Evaluation and Research

Subject: Use of the Recombigen HIV-1 LA Test

To: All Register Blood and Plasma Establishment

On December 13, 1988, the Food and Drug Administration licensed Cambridge Bioscience Corporation, Worcester, MA to manufacture and distribute a rapid latex agglutination screening test for antibodies to HIV-1 called "Recombigen" HIV-1 LA Test." The test is labeled for use "by properly trained personnel as a screening test in hospital laboratories, medical clinics, physicians' offices, and emergency care situations, and in blood banks or other settings where enzyme immunoassays are not practical or available." The purpose of this letter is to clarify FDA's concept of the appropriate use of this test in blood and plasma establishments.

The latex agglutination test can be performed in as little as five minutes with a sample of venous or capillary whole blood, serum or plasma which is diluted on a card and then mixed-with a suspension of microscopic latex particles which have been coated with a recombinant DNA-derived protein related to the virus envelope. The test endpoint is determined by visual inspection for an agglutination reaction in comparison with a negative control. As documented in the package insert, this test, when properly performed, is at least as sensitive as the licensed EIA screening tests.

Several clinical studies have shown that the Recombigen test may frequently give rise to false positive results. The primary cause of this problem is that the agglutination reaction can be easily overinterpreted by inexperienced operators. For this reason, the manufacturer requires that users familiarize themselves with the test by the use of a training panel and an "Interpretation Guide." In addition, the test can be falsely . positive in a variety of medical conditions including common viral infections and the presence of certain abnormal serum immune globulins. Also, the format of the test, which lacks automated procedures and objective read-out, may dispose to errors inherent with tests that utilize subjective reading and interpretation.

The particle agglutination test is not recommended for routine use in registered blood and plasma collection establishments because of the procedural difficulties and hence errors that would be likely to arise in handling large numbers of samples and because of the likelihood of false positive tests. Users of the test should be aware that donors with repeatably reactive tests

by this procedure should be counseled and permanently excluded from donating blood or plasma unless they can be requalified by the reentry algorithm defined in a letter of April 29, 1987. In the event that a donor is deferred on the basis of the latex agglutination test, the latex test should be read in place of the initial EIA or "iEIA" mentioned in the document on reentry. Since the latex test uses a purified and genetically engineered polypeptide related to the viral envelope protein, the different screening test referred to in the algorithm as "dEIA" may be a test based on virus cultured in either the H-9 or the CEM cell line.

As is the case for other licensed screening tests for antibodies to HIV, it is recommended that additional more specific tests such as Western blot be performed prior to notification of donors who have been deferred. It is not appropriate to "validate" the results of the latex agglutination test with other licensed screening tests prior to notification. Also, it is not appropriate to "re-screen" donors previously positive by the latex agglutination test with licensed EIA tests prior to distributing units for transfusion or further manufacture. Routine "pre-screening" of donors such as on mobile collection facilities would not be a valid use since that practice would be likely to generate a large number of false-positive tests leading to excessive donor exclusion and further testing.

Medical discretion should be used to decide whether the latex agglutination test is indicated in a particular instance because screening by the EIA is impractical or unavailable. Emergency situations involving donations of rare blood types, or urgent management of disasters might be examples. It is expected that the test will be used as the primary blood screen in some developing countries. It should be noted by such users that the manufacturer has made no claim for test sensitivity for detection of antibodies to HIV-2.

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