Use of Fluorognost HIV-1 Immunofluorescent Assay (IFA) (4/23/92)

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FROM: Director, Center for Biologics Evaluation and Research

SUBJECT: Use of Fluorognost HIV-1 Immunofluorescent Assay (IFA)

TO: All Registered Blood and Plasma Establishments

On February 5, 1992, the Food and Drug Administration licensed Waldheim Pharmazeutika, GmbH, Vienna, Austria, to manufacture and distribute the Fluorognost HIV-1 IFA, an immunofluorescent assay (IFA) for the detection of antibodies to human immunodeficiency virus type 1 (HIV-1) in human serum or plasma. The kit package insert states that the IFA test

> "... is intended to be used as an additional, more specific test for antibodies to HIV-1 in human serum or plasma specimens found to be repeatably reactive by screening procedures, such as the Enzyme-Linked Immunosorbent Assay (EIA). Fluorognost HIV-1 IFA can also be used 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 memorandum is to provide further information on the approved use of this test in blood and plasma establishments.

The Fluorognost HIV-1 IFA uses infected, immortalized human T-cells that express antigens of HIV-1 (type IIIB). The cells are fixed in wells on the surface of a glass slide. Separate wells of fixed, uninfected T-cells are provided as controls for reaction with the test sample. When antibodies to HIV-1 are present in a serum or plasma specimen, they will bind to the infected cells but should not bind to the control, uninfected cells. Bound antibodies are detected with anti-human immunoglobulin conjugated to fluorescein isothiocyanate. The conjugate becomes fixed to the bound human antibodies and emits light by fluorescence when exposed to UV light. The interpretation of the test result is based on a microscopic, visual evaluation of the degree and pattern of fluorescence of the infected cells compared with the uninfected cells. It requires approximately 1.5 hours to test one IFA slide containing five test wells.

As documented in the package insert, the Fluorognost HIV-1 IFA test, when properly performed, is equivalent in sensitivity to a licensed EIA for detection of antibodies to HIV-1 in human serum or plasma. Clinical studies have also shown that the Fluorognost HIV-1 IFA is equivalent in sensitivity and specificity to a licensed

Western blot for additional, more specific testing of EIA repeatably reactive serum or plasma samples obtained by screening in low or high risk populations. The data also suggest that the Fluorognost HIV-1 IFA may be useful in resolving the status of samples with an indeterminate Western blot result for purposes of medical counseling.

1. Use of the Fluorognost HIV-1 IFA as an additional, more specific test for validation of antibodies to HIV-1 in serum or plasma

   The primary intended use of the Fluorognost HIV-1 IFA is as an additional, more specific test for the presence of HIV-1 antibodies in samples of human serum or plasma that are repeatably reactive by an EIA screening test. Therefore, the IFA can be used instead of an HIV-1 Western blot whenever an additional, more specific HIV-1 test is indicated. Such uses include testing for the purpose of donor notification and counseling, possible donor reentry, disposition of "lookback" product retrievals and "lookback" recipient notification. These uses are described below:

   For purposes of donor notification, the licensed IFA may be used as an alternative to the HIV-1 Western blot. Also, if the IFA is performed subsequent to an indeterminate Western blot, the additional information from a negative IFA result may be used in donor counseling to alleviate anxiety over a test result that is unlikely to indicate HIV infection. Conversely, a positive IFA result would demonstrate the presence of antibodies to HIV, and the donor could be counseled accordingly.

   When used to qualify a donor for reentry, the licensed IFA can be performed instead of the Western blot in any part of the recommended reentry algorithm (see Memorandum to All Registered Blood Establishments, February 5, 1990). Positive, negative and indeterminate results by the IFA should be treated the same way as the corresponding results of a licensed HIV-1 Western blot. Unlike the use in donor counseling, if a licensed Western blot has been performed as the additional, more specific test for reentry purposes, additional IFA testing may not be used to negate or resolve a positive or indeterminate Western blot result. For example, if a licensed western blot test result is indeterminate, whether on the initial, substituted, or follow-up sample, a negative IFA result obtained subsequently is not sufficient to qualify a donor for reentry.

   Products from prior donations by persons currently found to have repeatably reactive HIV screening tests may be released from quarantine based on a negative result of either a licensed IFA or Western blot. The results of additional testing on the donor sample by either IFA or Western blot may be provided to the consignees of such products as a basis for

the decision to trace and notify recipients of previously collected units from currently positive donors. In this context, use of the IFA to resolve Western blot indeterminate results is recommended.

2. Use of the Fluorognost HIV-1 IFA for screening

The IFA is not recommended for routine use as a screening test for blood and plasma donations. Errors may be more likely to occur in these settings because the test format is not conducive to handling large numbers of samples and because the test end-point is operator-dependent. Medical discretion should be used to decide whether the HIV-1 IFA test is indicated as a screening test in a particular instance because screening by the EIA is unavailable or impractical. Emergency situations involving donations of rare blood types, urgent screening of an HLA matched platelet donor, or urgent management of disasters might be examples when the IFA is appropriate.

When used for donor screening, the results of a single IFA test are sufficient to determine the HIV-1 status of the donor. Donors with reactive test results must be deferred, although they remain eligible for reentry. If the IFA is used as a screening test for HIV-1 antibodies, a different type of test, such as the Western blot, should be used as the additional, more specific test for validation of the presence of HIV-1 antibodies and for possible reentry. It should be noted by users that the licensed HIV-1 IFA test is not approved for detection of antibodies to HIV-2.

The format of the IFA lacks automated procedures and an objective read-out, therefore, results may be disposed to errors inherent in tests that depend on human judgement, both in reading and interpretation. For this reason, individuals reporting Fluorognost HIV-1 IFA results should have demonstrated proficiency at interpreting IFA results. The manufacturer provides both a Product Education Manual which contains a program of study, and a proficiency panel of coded samples for assessment of user proficiency. Each individual who intends to report IFA results is strongly advised by the manufacturer to qualify as a reader by completing this program of training and assessment.

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