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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Biologics Evaluation
and Research
1401 Rockville Pike
Rockville MD 20852-1448

October 23, 2002

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

William M. Dugan, Jr., M.D.
President and Medical Director
Universal Reagents, Inc.
2858 North Pennsylvania Street
Indianapolis, IN 46202

Dear Dr. Dugan:

The Food and Drug Administration (FDA or the agency) conducted an inspection of Universal Reagents, Inc. (URI), 2858 North Pennsylvania Street, Indianapolis, IN, between May 29 and June 3, 2002. Additionally, FDA conducted an inspection on ———— , of ———— ————, which performs infectious disease testing for URI under a contract agreement. FDA determined, through its investigation and inspections of both URI and————, that significant deviations from the standards in your license and the applicable requirements of Subchapter F, Parts 600-640 of Title 21, *Code of Federal Regulations* (21 CFR) exist at Universal Reagents, Inc. FDA has also documented that URI has willfully engaged in violative record keeping practices and falsified records it submitted to the agency. The findings of our investigation and the deficiencies noted on the Form FDA-483, Inspectional Observations, issued at the conclusion of the inspection at URI include, but are not limited to

1 Test results for the hepatitis B surface antigen (HBsAg) and the antibody to the human immunodeficiency virus types 1 & 2 (anti-HIV-1/2) on the ———— ————Report, which is a computer-generated report, dated and time stamped February 11, 2002, 17:23, for Source Plasma, units 0730900, 0730911, and 0730912, were missing. During the closeout discussion on June 3, 2002, URI provided the FDA investigator with what the firm identified as the missing test results on a ———— ————Report. The firm indicated that the tests were performed by ———— This document noted the HBsAg and anti-HIV-1/2 test results for Source Plasma, units 0730900, 0730911, and 0730912, were negative or "N", however, this document did not bear a date or time in the designated fields on the report. Contrary to the documents obtained at the URI inspection, FDA's inspection at————disclosed that the required infectious disease testing for HBsAg and anti-HIV-1/2 was not completed or performed for Source Plasma, units 0730900, 0730911, and 0730912. [21 CFR 610.40(a), and 606.160(b)(2)(i)]

2 HBsAg and anti-HIV-1/2 test results for Source Plasma, unit 0729859, were missing on a Transfer Report, which is a computer-generated report, dated and time stamped June 2, 2001, 14:50, and on a Testing Status Report dated and time stamped June 19, 2001,

15:43. An additional notation on the Testing Status Report stated "sample too old to complete testing." An additional record that FDA collected during the URI inspection showed that all test results for unit 0729859, including HBsAg and anti-HIV-1/2, were documented as "NR" or non-reactive on a Laboratory Request form dated June 4, 2001. During the close-out discussion on June 3, 2002, the firm provided the FDA investigator with a Testing Status Report dated and time stamped June 19, 2001, 15:43, which provided that the testing had been performed at ——— and that test results for HBsAg and anti-HIV-1/2 were "N" or negative for unit 0729859. There were no additional notations or comments noted on this document. Contrary to the documents obtained at the URI inspection, FDA's inspection at——— disclosed that infectious disease testing for HBsAg and anti-HIV-1/2 was not performed on Source Plasma, unit 0729859. [21 CFR 610.40(a), and 606.160(b)(2)(i)]

3. On a Transfer Report dated and time stamped May 5, 2001, 17:26, Source Plasma, unit 0729718, which was tested by ———, tested reactive for anti-HIV-1/2. The sequence number for the batch run that was noted on the Transfer Report for unit 0729718 was —— During the closeout discussion on June 3, 2002, the firm provided a Testing Status Report for unit 0729718 that noted an "N" or negative test result for anti-HIV-1/2. No date or time was documented on the report, however, a notation on the report stated that it was reviewed by URI on May 9, 2000. The sequence number noted on this Testing Status Report was —— An additional record that FDA collected during the inspection of URI, a Laboratory Request form dated May 7, 2001, showed that all infectious disease testing results for unit 0729718 were documented as "NR" or non-reactive. FDA's inspection at ———disclosed that anti-HIV-1/2 testing for unit 0729718 was performed on or about May 5, 2001 and tested initially reactive. Results of repeat duplicate anti-HIV-1/2 testing on unit 0729718, which was performed by ——— on May 7, 2001, were negative All infectious disease testing related to anti-HIV-1/2 that was performed on unit 0729718 at ——— was associated with sequence number ——— Contrary to the documents obtained at the URI inspection, FDA's inspection at ———disclosed that sequence number ——was not used for infectious disease testing of Source Plasma, unit 0729718. In addition, FDA determined that discrepancies existed in documents obtained during the inspections of URI and ——— Specifically, FDA's investigation disclosed that infectious disease testing of Source Plasma, unit 0729718, was performed on or about May 5, 2001; however, on the Laboratory Request form, which was a document provided by URI during the closeout discussion, the date that infectious disease testing results were reviewed by URI was documented as May 9, 2000. [21 CFR 606.160(b)(2)(i)]

In your June 7, 2002, response to the May 29 - June 3, 2002, inspection, you promised to implement corrective actions to address the deficiencies noted at your firm and, as part of your response, included copies of the discrepant records which the firm previously provided to the FDA investigator during the inspection. Our review of your response disclosed continuing inconsistencies with the results of our investigation.

For example, the FDA investigator noted that infectious disease testing results for Source Plasma, units 0730900, 0730911, 0730912, and 0729859, were missing or incomplete In your

response, you stated that infectious disease testing was performed on these units and that the results were misplaced. You also stated that you were able to obtain copies of the missing test results for these units from your testing laboratory. However, our review of the testing records that you provided in your response to this issue disagree with the testing results that were obtained during FDA's inspection of ——— your contract testing laboratory, and with our investigation.

Additionally, the FDA investigator determined that your firm provided discrepant information regarding infectious disease testing records for Source Plasma, unit 0729718. You responded that the test results for unit 0729718 may have been tampered with and changed by an employee prior to being terminated by URI. You additionally stated that you obtained a copy of infectious disease testing results for unit 0729718 from the testing laboratory demonstrating that the tests were performed and found acceptable. Again, our review of the testing records that you provided in your response to this issue disagree with the testing results that FDA collected during the inspection of ——— your contract testing laboratory, and with our investigation.

Based on our investigational and inspection results, FDA has determined that URI willfully engaged in violative record keeping practices and provided false manufacturing records to FDA as corrective actions for the above-noted deficiencies. Additionally, your June 7, 2002, response to the FDA Form-483 demonstrates that you willfully continue to submit falsified documents to FDA.

While these deviations were documented during the most recent inspection, we note that your establishment has a history of non-compliance with the applicable regulations and standards as evidenced by the significant deviations that were documented during previous inspections at URI. The seriousness of these deficiencies was emphasized in letters to URI, including a Notice of Adverse Findings letter dated October 20, 1988; a Notice of Adverse Findings letter dated September 26, 1989, a Warning Letter dated October 19, 1992; and a Warning Letter dated July 20, 2000 [Enclosures A-D].

21 CFR 601.5(b)(1) and (2) provide that when the Commissioner of the FDA finds an establishment or any location thereof, or the product for which the license has been issued, fails to conform to the applicable standards established in the license and regulations designed to ensure the continued safety, purity, and potency of the manufactured product, he may institute proceedings for the revocation of the license In situations involving willfulness, the FDA need not provide an opportunity for the licensee to demonstrate or achieve compliance. As previously stated in this letter, the agency has determined that your establishment willfully engaged in the falsification of manufacturing records. Pursuant to 21 CFR 601.5(b), this letter is to provide you with notice that it is the agency's intent to revoke U.S. license number 0887 issued to Universal Reagents, Inc., and to issue a notice of opportunity for a hearing. If you wish to waive the opportunity for a hearing, you may do so within ten (10) working days of receipt of this letter by contacting Mr. Steven A. Masiello, Director, Office of Compliance and Biologics Quality (HFM-600), Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200N, Rockville, Maryland 20852-1448. Mr. Masiello may be reached by telephone at (301) 827-6190

The waiver must be confirmed in writing and may be accomplished by your voluntarily requesting that U.S. license number 0887 be revoked. If we do not hear from you within the prescribed time, we shall proceed pursuant to the regulations governing formal evidentiary public hearings, as found in 21 CFR 12.21(b), and publish in the Federal Register a notice of opportunity for hearing on the proposal to revoke the license. A request for a hearing may not rely upon mere allegations or denials but is required to set forth specific facts showing that there is a genuine and substantial issue of fact that warrants a hearing [21 CFR 12.24(b)]. The appropriate state officials will also be notified of this administrative action.

Sincerely,

Kathryn C. Zoon, Ph.D.
Director
Center for Biologics Evaluation and Research

Enclosures:
A - Notice of Adverse Findings letter dated October 20, 1988
B - Notice of Adverse Findings letter dated September 26, 1989
C - Warning Letter dated October 19, 1992
D - Warning Letter dated July 20, 2000