Use of Donor Screening Tests to Test Donors of Human Cells, Tissues and Cellular and Tissue-Based Products for Infection with *Treponema pallidum* (Syphilis)

Guidance for Industry

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Contains Nonbinding Recommendations

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I. INTRODUCTION

We, FDA, are providing you, establishments that make donor eligibility determinations for donors of human cells, tissues and cellular and tissue-based products (HCT/P Establishments), with updated recommendations concerning donor testing for evidence of *Treponema pallidum* (*T. pallidum*) infection, the etiologic agent of syphilis. As required under 21 CFR 1271.80(a) and (c) (§ 1271.80(a) and (c)), you must test a donor specimen for evidence of the communicable disease agents specified in 21 CFR 1271.85, including *T. pallidum*, using appropriate FDA-licensed, approved, or cleared donor screening tests, in accordance with the manufacturer's instructions, unless an exception to this requirement applies under 21 CFR 1271.90. This guidance clarifies that we do not consider cleared or approved diagnostic tests or pre-amendment devices (which have not been licensed, approved, or cleared) to be adequate for use in donor testing for *T. pallidum* infection under the criteria specified in § 1271.80(c).

This guidance applies to all HCT/P Establishments. This guidance finalizes the draft guidance of the same title, dated October 2013. This guidance supersedes the recommendations on compliance with the requirements for testing of HCT/P donors for *T. pallidum* infection under § 1271.80(c), that are contained in the FDA guidance entitled "Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)," dated August 2007 (2007 Donor Eligibility guidance) (Ref. 1).

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II. BACKGROUND

This guidance updates previous recommendations contained in the 2007 Donor Eligibility guidance concerning donor testing for evidence of infection with *T. pallidum* and clarifies the type of tests FDA considers appropriate to adequately and appropriately reduce the risk of transmission of *T. pallidum*. We are providing this clarification to assist HCT/P Establishments in complying with the requirements under 21 CFR Part 1271, subpart C, for donor-eligibility determinations based on donor screening tests for *T. pallidum*.

Under 21 CFR 1271.45(b), a donor-eligibility determination, based on donor screening and testing for relevant communicable disease agents and diseases, is required for all donors of cells or tissues used in HCT/Ps, except as provided under § 1271.90. To adequately and appropriately reduce the risk of transmission of relevant communicable diseases, and except as provided under § 1271.90, you must test a specimen from the donor of cells or tissue, whether viable or nonviable, for evidence of infection due to relevant communicable disease agents, including *T. pallidum* (see § 1271.85(a)(5)). As stated previously in this guidance, under § 1271.80(c), you must test for evidence of infection using appropriate FDA-licensed, approved, or cleared donor screening tests in accordance with the manufacturer's instructions to adequately and appropriately reduce the risk of transmission of the disease agent.

The 2007 Donor Eligibility guidance contains recommendations for complying with the requirements in 21 CFR Part 1271, subpart C, and applies to all HCT/Ps recovered on or after the effective date of the regulations, May 25, 2005. In footnote 6 of the 2007 Donor Eligibility guidance, we stated, "For purposes of this guidance, we consider FDA-cleared diagnostic serological tests to be adequate for use in donor screening for syphilis." The 2007 Donor Eligibility guidance did not address the use of pre-amendments devices to meet the requirements of § 1271.80(c), as applied to donor screening for syphilis. The term "pre-amendments device" refers to a device legally marketed in the United States before May 28, 1976, when the Medical Device Amendments of 1976 (Pub. Law No. 94-295, 90 Stat. 539 (1976)) became effective. A device can be a pre-amendments device if it has the same intended use as that marketed before May 28, 1976, has not been significantly changed or modified since then, and if a regulation requiring a premarket approval application for the device has not been issued by FDA. Pre-amendments devices meeting the above criteria are exempted from requirements for premarket submission and review requirements under the Medical Device Amendments of 1976.

When the 2007 Donor Eligibility guidance was issued, few screening tests for evidence of *T. pallidum* infection in donors were licensed, cleared, or approved. HCT/P Establishments expressed concern that the adoption of platform based donor screening tests would be overly burdensome during the early implementation of Part 1271. After considering these issues, and as an interim measure pending greater availability of and access to these tests, we advised in the 2007 Donor Eligibility guidance that we would consider all cleared serological diagnostic tests for evidence of *T. pallidum* infection to be adequate for donor screening purposes. We are now updating the recommendation provided in the 2007 Donor Eligibility guidance regarding use of

all cleared serological diagnostic tests to test for *T. pallidum*[1]. In this guidance, we also are clarifying the status of pre-amendments devices used to test for *T. pallidum*. Since the 2007 Donor Eligibility guidance issued, several donor screening tests have been cleared. We believe that the technology for donor screening tests has evolved such that FDA-licensed, approved, or cleared test systems with an indication for use in donor screening to test for evidence of *T. pallidum* infection are now widely available, and that laboratories now are proficient in their ability to utilize such systems. The wide availability of this testing technology and widespread testing laboratory proficiency with these systems no longer support a policy for the use of diagnostic syphilis tests for use as a donor screening test. We now clarify that, as of the implementation date of this guidance, we do not intend to exercise enforcement discretion related to the use of such tests as donor screening tests.

III. RECOMMENDATIONS

This guidance updates prior recommendations and clarifies that:

1. We no longer intend to exercise enforcement discretion with respect to the use of diagnostic tests for evidence of infection with *T. pallidum* for use as HCT/P donor screening tests. Rather, we intend to enforce the requirements provided under § 1271.80(c) that establishments must use appropriate FDA-licensed, approved, or cleared donor screening tests in accordance with the manufacturer's instructions to adequately and appropriately reduce the risk of transmission of disease agents such as *T. pallidum*.
2. Pre-amendments devices are not acceptable for use as a donor screening test for evidence of infection with *T. pallidum*.
3. This guidance applies to all HCT/Ps recovered after the implementation date of this guidance.

You must, under § 1271.85(a), test all donors of HCT/Ps for evidence of infection due to relevant communicable diseases including syphilis, except as provided under § 1271.90(a). You must test using appropriate FDA-licensed, approved, or cleared donor screening tests, in accordance with the manufacturer's instructions, to adequately and appropriately reduce the risk of transmission of the disease agent (§ 1271.80(c)). Current FDA-licensed, approved or cleared donor screening tests are listed on the FDA's website at http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm.

IV. IMPLEMENTATION

We recommend that you implement the recommendations in this guidance as soon as feasible, but not later than 6 months after issuance of this guidance.

[1] FDA provides additional discussion of syphilis assays, including information about nontreponemal and treponemal assays, in section VI.A of FDA's Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps), dated August 2007 (Ref. 1).

V. REFERENCE

1. FDA Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps), August 2007. http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/default.htm.