THE AMERICAN MEDICAL EDUCATION AND RESEARCH ASSOCIATION

# Guidance for Industry

*Advisement for the Use of Gen-Probe Procleix Ultrio Plus Assay for NAT Testing on Cadaveric Donors*

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## Disclaimer:

*This Guidance Document is not intended to be used as a legally binding advisement. It is not intended to interpret federal or state law, nor does it replace or otherwise circumvent these laws. It is intended as an informative advisement for AMERA accredited institutions and general industry. AMERA guidance documents do not endorse any company, product or process. AMERA guidance documents are designed to aid and advise AMERA accredited institutions and general industry on current topics of interest, industry warnings and relevant issues that are critical to the mission of AMERA.*

**Introduction:**

The Gen-Probe Procleix Ultrio Plus Assay (Human Immunodeficiency Virus Type 1 and/or Hepatitis C Virus and/or Hepatitis B Virus (HIV-1 and Hepatitis C Virus and Hepatitis B Virus/Nucleic Acid Pooled Testing/Synthetic) is an FDA licensed nucleic acid amplification test intended:

1. For use in testing plasma and serum specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing blood specimens from cadaveric (non-heart-beating) donors.
2. For use in testing individual samples from living donors of whole blood, blood components, or source plasma, other living donors and heart-beating organ donors, and for testing individual blood specimens from cadaveric (non-heart-beating) donors.
3. For use in testing pools of human plasma comprised of equal aliquots of not more than 16 individual donations from donors of whole blood, blood components, or source plasma.
4. To be used in conjunction with licensed tests for detecting antibodies to HIV-1, HCV, and hepatitis B core antigen (anti-HBc), and with licensed tests for hepatitis B surface antigen (HBsAg).

*NOTE: The newer Gen-Probe Procleix Ultrio <u>Plus</u> Assay should not be confused with the older Gen-Probe Procleix Ultrio Assay. AMERA understands that there are still a few laboratories using this older assay for donor screening.*

Traditionally, this test is a component of serological testing panels required by the FDA for blood, plasma and to determine donor eligibility under 21 CFR 1271.80 for HCT/Ps donors. For more information on how this test is used to determine eligibility for HCT/Ps refer to FDA's *Guidance For Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based products*. Though required (as part of a testing panel) for FDA regulated environments, this test is not required for serological screening of cadaveric donors intended for the sole use in medical research and education (not for transplant or therapy).

**AMERA's Position:**

AMERA is the only entity in the United States that requires the use of specific serological assays for donor eligibility for the non-transplant tissue banking industry. AMERA's *Standards for Accreditation for Non-Transplantable Tissue Banks & Bioskills Facilities* require the following serological assays be used to determine donor eligibility:

1. Anti-HIV 1/2 AB plus O
2. Anti-HCV AB
3. HBsAg

The use of the Gen-Probe Procleix Ultrio Plus Assay is not required under AMERA Standards, as AMERA feels it should only be used as a supplemental test in compliment with standard antibody assays if a bank chooses to perform both. The Procleix assay is not intended to be the sole test used to determine donor eligibility and is not suitable as a stand-alone assay for the following reasons:

1. It does not detect HIV-2 infected donors
2. It does not detect past exposures to HIV or HCV or HBV viruses that traditional antibody tests can detect.
3. It may not detect an individual that is receiving Anti-Retroviral Therapy (ART) where the free viral load of the donor is under the detection limits of the assay.
4. There is no documented evidence to support that a donor receiving ART treatment has been cleared of the virus in its entirety even though no detectible viral copies are found in the donor's serum. The donors Sustained Virologic Response (SVR) can suppress the viral load to undetectable levels though it may still be resident in different areas of the body. For example: It is well established that patients carrying the HIV virus can establish a dormant reservoir of the virus which consists of latently infected CD4 T cells. This reservoir can persist in patients receiving ART and re-emerge within weeks of discontinuing ART treatment.

It is AMERA's position that donors screened with a minimum of the AMERA required assays represent the best approach to serologically determining donor eligibility for use in medical research and education.

AMERA is aware that there may be multiple banks using only the Gen-Probe Procleix Ultrio Plus Assay for determination of donor eligibility for medical research and education donors. AMERA strongly asserts that using only the Gen-Probe Procleix Ultrio Plus Assay as their sole method of determining serological donor eligibility is not adequate and may be represent a significant safety issue for the industry and those the industry serves.

**Industry Advisement:**

The Gen-Probe Procleix Ultrio Plus Assay is FDA licensed to screen serum or plasma from cadaveric donors (non-heart beating). However the package insert for the test has the following specimen condition for cadaveric donors:

*Specimens should be collected within 24 hours of death if the cadaver was refrigerated (1°-10°C) within 12 hours of death. Specimens should be collected within 15 hours of death if the cadaver was not refrigerated (1°-10°C). Specimen stability is affected by elevated temperatures.*

AMERA understands that if an organization chooses to use the assay for serological donor eligibility determination in either its sole method or as a compliment to traditional

antibody assays, the organization must adhere to the package insert requirements for sample acceptability. In order to be in compliance with this requirement, the organization must draw the sample within 24 hours of death (if refrigerated) and within 15 hours of death (if not refrigerated) to have a valid sample result. Any serological result obtained outside of package insert requirements would be considered Invalid by the manufacturer and the testing laboratory. An invalid sample result cannot be relied on (under any circumstances) for proper donor eligibility determination by the organization.

In most cases, non-transplant tissue banks are not able to draw within 15-24 hours from death. This is due to many issues that include: death notification to the organization, transportation of the donor, delay in obtaining consent, backlog in donor volume, etc. This is a historical norm for our industry. Therefore, any organization that has used and/or is using the NAT test as a stand-alone assay is at a significant risk for these results being invalid or having previously obtained results being invalidated retro-actively depending on when the donor was drawn in relation to the date and time of death. With no other serological results obtained by the organization at the time of testing (through alternate assays), there may be no recourse for the organization to rectify this situation.

**Recommended Course of Action:**

AMERA is advising that all institutions that have utilized the Gen-Probe Procleix Ultrio Plus Assay as its sole method for serological determination of donor eligibility for medical research and education perform the following steps:

1. Determine the period of time to which this test was the sole assay in use.
2. Perform a lookback to determine which donors were tested using this assay.
3. Calculate which donors did not meet the package insert requirements for sample acceptability.
4. Consult with your medical director to determine if additional testing can be performed using a retention sample to come into compliance with AMERA requirements for serological donor eligibility.
5. Identify any tissue that is still under your control and quarantine tissue until such time as additional testing can be performed to properly determine serological donor eligibility.
6. Identify any tissue that is outside of your control, but not yet disposed of and perform a recall.
7. Perform client notification for any/all donors that did not meet the sample acceptability criteria.
8. If accredited, notify your accrediting body for further instructions and/or support.

A copy of the Gen-Probe Procleix Ultrio Plus Assay can be reviewed at:

http://www.fda.gov/BiologicsBloodVaccines/ucm335203.htm

Any questions or comments can be made to AMERA via the following:

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