



Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps): Donor Testing

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CBER/FDA

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Learning Outcomes

At the completion of this session, you should be able to:

- Identify the testing requirements used by HCT/P establishments when determining donor eligibility
- Identify the criteria used to determine if an HCT/P poses a risk to public health
- Identify general donor testing requirements and recommendations

Abbreviations

- DE = Donor Eligibility
- RCDAD = Relevant Communicable Disease Agent or Disease
- HIV = Human Immunodeficiency Virus
- HBV = Hepatitis B Virus
- HCV = Hepatitis C Virus
- HTLV = Human T-lymphotropic virus
- WNV = West Nile virus
- ZIKV = Zika virus
- CMV = Cytomegalovirus
- CLIA = Clinical Laboratory Improvement Amendments
- § = Section (of the rule) ex. § 1271.3
- PI = Package Insert
- IFU = Instructions for Use
- ID = Individual Donor
- NAT = Nucleic Acid Amplification Technology or “Nucleic Acid Test” (includes Polymerase Chain Reaction (PCR) and Transcription-Mediated Amplification (TMA))
- aka = also known as

Donor Testing Requirements

§§ 1271.80, 1271.85

- General requirements for donor testing – § 1271.80
 - a) Requirement to test for RCDADs
 - b) Timing of specimen collection
 - c) Types of tests that are required & laboratory certifications
 - d) Ineligible donors -- Reactive test results
- Testing requirements for different types of cells and tissues – § 1271.85
 - a) All donors
 - b) Donors of viable, leukocyte-rich HCT/Ps
 - c) Donors of reproductive cells or tissue
 - d) Retesting anonymous semen donors



General Testing Issues

Regulatory Basis for Donor Testing

§ 1271.80(a)

- Must test a donor specimen for evidence of infection due to communicable disease agents listed in § 1271.85 to adequately and appropriately reduce the risk of transmission of relevant communicable diseases
 - Except as provided under § 1271.90
 - May require more than one test to adequately and appropriately reduce the risk

Timing of Specimen Collection

§ 1271.80(b)

- The specimen to be used for donor testing must be collected at the time of recovery of cells or tissue from the donor; or up to 7 days before or after recovery of HCT/Ps

Timing of Specimen Collection

§ 1271.80(b)

- Specimen collection for donor testing for RCDADs for oocyte donors, you may collect the donor specimen for testing up to 30 days before recovery
 - Oocyte donors
 - Hormonal stimulation of the donor is usually begun a month prior to a scheduled date of recovery. There is a desire to be sure communicable disease test results are acceptable before these drugs are administered.
 - Note: this 30-day period does not extend to semen donors

Infectious Disease Testing

The 'window period'... time from infection to antibody detection:

- HBsAg & HBcAb \approx 5-7 weeks (ID HBV NAT \approx 28 days)
- HCV Ab \approx 70 days (ID HCV NAT \approx 7.4 days)
- Syphilis testing \approx 3 months
- HIV Ab from 3 weeks to months (ID HIV NAT \approx 9 days)
- HTLV Ab \approx 45 days

**Based on experience in the
US with blood donors**

This assumes: 1) qualification of the blood specimen was evaluated without error, 2) specimen handling requirements are met, 3) an appropriate test kit was selected for use, 4) each test was performed following the test kit manufacturer's instructions, and 5) lab technicians made no errors when testing or reporting....

General Testing Issues

§ 1271.80(c)

- Testing must be performed:
 - Using appropriate FDA-licensed, approved, or cleared donor **screening** tests
 - Exceptions for chlamydia, gonorrhea, and syphilis will be discussed later
 - Tests FDA considers to be appropriate will be discussed later
 - According to manufacturer's instructions for use in the package insert
 - In a CLIA-certified laboratory (Clinical Laboratory Improvement Amendments of 1988) or equivalent as determined by the Centers for Medicare and Medicaid Services (CMS)
 - International testing establishments are not likely to have access to FDA-licensed, approved, or cleared tests

Screening vs. Diagnostic Tests

- Tests are specifically labeled as a screening and/or diagnostic test
 - “intended for use as a donor screening test”
 - For general population; risk is not suspected (low-risk, asymptomatic)
 - “intended for use as an aid in diagnosis”
 - For patient population; risk may be suspected (at risk, may be symptomatic)
- Because of the way the performance characteristics are evaluated, cannot directly compare sensitivity and specificity between diagnostic and screening tests

Intended Use Labeling

§ 1271.80(c)

- Note: A “more generally labeled test” includes tests labeled for screening donors of blood and blood products as well as those specifically labeled for screening of other living donors.
 - Other living donors include reproductive cell and tissue donors, organ donors, donors of hematopoietic progenitor/stem cells (HPCs), and donor lymphocytes for infusion, and cellular and tissue donors
- A listing of available tests can be found at <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm>

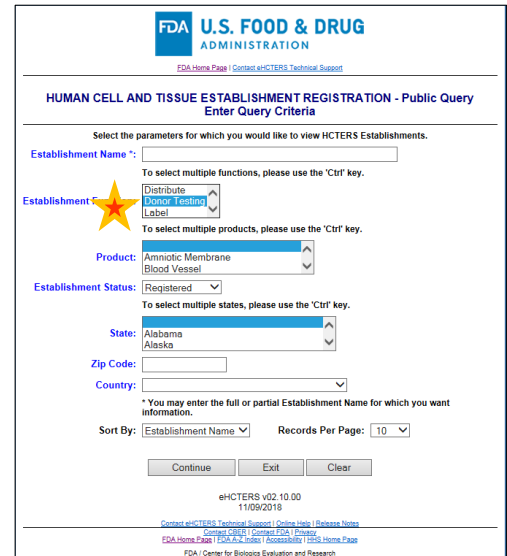
Manufacturer's Instructions for Use

§ 1271.80(c)

- Storage and testing of specimen
 - Must follow the **manufacturer's instructions for use** in the package insert for the test kit – most have time limits on how long after collection specimens can be tested under certain storage conditions
 - If no time limits are mentioned, we recommend testing as soon as possible after a donor's specimen is collected
- Testing algorithms and interpretation of test results
 - Follow the **manufacturer's instructions for use** in the package insert
 - Most tests are software-driven and fully automated

Reminders about Testing Laboratories

- Must register and list with FDA (§ 1271.1)
- Must maintain documentation of results and interpretation of all testing for at least 10 years after performing the test (§ 1271.55(d))
 - CLIA’s retention is only 2 years so § 1271.55(d) is more strict





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Note that “Test” is now “Donor Testing”

Ineligible Donors

§ 1271.80(d)

A donor must be considered ineligible if:

- Their specimen tests **reactive** on a screening test for a communicable disease agent in accordance with § 1271.85
 - Except for a donor whose specimen tests reactive on a non-treponemal screening test for syphilis and negative on a specific treponemal confirmatory test
- Plasma dilution sufficient to affect the results of communicable disease testing is suspected

Repeat Anonymous Semen Donors

§ 1271.85(d); DE Guidance, VII.D.

- At least 6 months after the date of donation of semen from anonymous donors:
 - Must collect a new specimen from the donor and test for required communicable disease agents (§ 1271.85(d))
 - In the case of a repeat semen donor from whom a specimen has already been collected and tested, and for whom retesting is required under §1271.85(d), you are not required to collect a donor specimen at the time of each donation (§ 1271.80(b)(2))
- In other words:
 - All semen from a donation event must be quarantined for ≥ 6 months
 - Must have at least one complete set of test results both before and after the 6 month quarantine period

Repeat Anonymous Semen Donors

§ 1271.85(d); DE Guidance, VII.D

- If the donor discontinues donations, should wait at least 6 months then retest/re-screen
 - Except you can use results of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and WNV tests obtained at the final donation, or any time after, as the follow-up test for those RCDADs

Directed Reproductive Donor

§ 1271.3(l); DE Guidance, VII.D.

- A donor of reproductive cells or tissue to a specific recipient, and who knows and is known by the recipient before donation
 - Includes semen, oocytes, and embryos to which the donor contributed the spermatozoa or oocyte
 - Does not include a sexually intimate partner

Directed Semen Donor Testing

§ 1271.85(d), DE Guidance, VII.E.

- Quarantine and retest are not required, but a firm may elect to perform quarantine of semen and retesting of the directed donor as described for anonymous semen donors (§ 1271.85(d))
- If quarantine and retesting are not performed:
 - Must collect a specimen for testing within 7 days of each collection

Other Reproductive Donor-Specific Information

DE Guidance, VII.G.

- Gestational carriers/gestational surrogates:
 - Are considered recipients (not donors), regardless of whether an embryo or only semen is transferred
 - Screening and testing is not required for the carrier
 - DE Guidance provides specific scenarios for testing and screening donors used for a procedure involving a gestational carrier

Q&A-1

Q1: If a manufacturer performs a test but does not follow the package insert (PI) instructions, is there a violation of the DE regulations?

Q&A-1

- A1:** If it is for an RCDAD for which testing is required, then yes
- § 1271.80(c) requires that “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 relevant communicable disease agents or diseases”
 - If the test is not for an RCDAD, but is an additional test that the establishment chooses to use, then regulations are not violated when using that test kit in a manner that is different than the manufacturer’s PI instructions (example: genetic testing for reproductive donors is not required by 1271 regs but may be ‘standard practice’)

Q&A-1 F/U

Q1 Follow-up: In the situation where the test is for a disease agent that is an RCDAD, would this result in a reportable HCT/P deviation?

A1 Follow-Up: If it is used as the test of record for a nonreproductive 361 HCT/P, then “yes”

- § 1271.350(b) requires reporting of HCT/P deviations relating to core CGTP requirements if the HCT/P has been ***distributed***. Donor testing is a core CGTP requirement.
- Subpart E **only applies to nonreproductive HCT/Ps** regulated solely under section 361 of the PHS Act (see §1271.330 Applicability)

Q&A-2

Q2: Under CLIA, testing laboratories are permitted to validate testing methods other than those specified in the product insert. Is this acceptable for laboratories performing donor testing?

Q&A-2

A2: No; according to § 1271.80(c), test kits used for HCT/P donor testing must be “appropriate FDA-licensed, approved, or cleared donor screening tests, in ***accordance with the manufacturer’s instructions***”. Though validating alternate testing methods is a common practice for diagnostic tests, laboratories may not validate alternate testing methods if the results are to be used to determine donor eligibility.

Q&A-3

Q3: Are all semen donors required to be tested within 7 days of collection, then the semen be stored for 6 months in quarantine to allow for re-testing of the donor prior to using the semen?

Q&A-4

A4: No. Directed semen donors must have testing performed within 7 days of collection, but there is no requirement that the semen then be quarantined and the donor be re-tested. This must occur, however, with anonymous semen donation.



SPECIFIC DONOR TESTING – ALL HCT/PS

Donor Testing: § 1271.85

Agent or Disease	Applies to	Screening	Testing*
HIV-1 and -2	All	X	X
Hepatitis B Virus	All	X	X
Hepatitis C Virus	All	X	X
Syphilis	All	X	X
TSE	All	X	
WNV	All	X	LIVING DONORS
ZIKV	All	X	
Sepsis	All	X	
Vaccinia (recent smallpox vaccination)	All	X	
HTLV-I and II	Viable, leukocyte-rich HCT/Ps	X	X
CMV**	Viable, leukocyte-rich HCT/Ps		X
<i>Chlamydia trachomatis</i>	Reproductive HCT/Ps	X	X
<i>Neisseria gonorrhoea</i>	Reproductive HCT/Ps	X	X

*** More than one test may be necessary to adequately and appropriately test for a single RCDAD (e.g. serology and NAT).**

**** CMV is not a RCDAD. Donors of viable leukocyte-rich HCT/Ps must be tested for CMV, and positive test results must be communicated to the responsible physician.**

Screening Test Technology

NAT

- Detects: RNA or DNA
- Technology: PCR, TMA
- Multiplex (MPX) assays use NAT to detect multiple pathogens

Serologic

- Detects: antigen, antibody
- Technology: ELISA, ChLIA, Agglutination, Other Immunoassays

NAT: Nucleic Acid Test (aka “molecular testing”)

PCR: Polymerase Chain Reaction

TMA: Transcription-Mediated Amplification

ELISA: Enzyme-Linked Immunosorbent Assay

ChLIA: Chemiluminescent Immunoassay



The following slides describe the tests FDA considers to be appropriate in order to adequately reduce the risk of transmission of RCDADs for all HCT/Ps

Information on these recommendations can be found in sections VI. & VII. of the DE Guidance

A listing of available tests can be found at <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm>

Additional screening tests acceptable for living donors may be found at <https://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm080466.htm>



Human Immunodeficiency Virus (HIV)-1/2

DE Guidance, VI.A

- **HIV, type 1**

- FDA-licensed screening test either for anti-HIV-1 *or* combination test for anti-HIV-1 and anti-HIV-2; *and*
- FDA-licensed screening NAT for HIV-1 (or combination NAT);

Note: Establishments not utilizing an FDA-licensed screening test for HIV group O must defer donors who are at risk for HIV group O infection as described in section IV.E.27-28 of the DE guidance.

- **HIV, type 2**

- FDA-licensed screening test either for anti-HIV-2 *or* combination test for anti-HIV-1 and anti-HIV-2

Licensed Donor Screening Tests – Anti-HIV Assays



Anti-HIV-1 and Anti-HIV-2 Assays (Detects antibodies to HIV Types 1 & 2)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
Alinity s HIV Ag/Ab Combo Reagent Kit	HIV-1, HIV-2	CMIA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Serum	Donor Screening: Qualitative detection of HIV p24 antigen and antibodies to HIV-1 (including groups O and M) and HIV-2	Abbott GbmH & Co KG Wiesbaden, Germany US License 2095	7/23/2019	BL125679
ABBOTT PRISM HIV O Plus assay	HIV-1, HIV-2	ChLIA	<i>Living:</i> Plasma Serum <i>Cadaveric:</i> Serum	In Vitro Diagnostic, Donor Screening: Qualitative detection of antibodies to HIV-1 groups M and O and/or antibodies to HIV-2	Abbott Laboratories Abbott Park, IL US License 0043	9/18/2009	BL125318
Genetic Systems HIV-1/HIV-2 Plus O EIA	HIV-1, HIV-2	EIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	In Vitro Diagnostic, Donor Screening: Qualitative detection of antibodies to HIV-1 (Groups M and O) and/or HIV-2	Bio-Rad Laboratories Redmond, WA US License 1109	8/5/2003	BL125030

Licensed Donor Screening Tests – HIV NAT



HBV/HCV/HIV Multiplex NAT

(Detects HBV/HCV/HIV Nucleic Acids)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
cobas MPX Test	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	1/17/2020	BL125576
Procleix Ultrio Elite Assay	HBV, HCV, HIV-1, HIV-2	TMA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HCV RNA, HIV-1 RNA and HIV-2 RNA	Grifols Diagnostics Solution., San Diego, CA US License 2032	5/03/2018	BL125652
cobas TaqScreen MPX Test version 2.0	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Serum, Plasma	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	12/19/2014	BL125459
Procleix Ultrio Plus Assay	HBV, HCV, HIV-1	TMA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HCV RNA, and HIV-1 RNA	Grifols Diagnostics Solution., San Diego, CA US License 2032	5/25/2012	BL125113
cobas TaqScreen MPX Test	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	8/27/2009	BL125255

Hepatitis B Virus (HBV)

DE Guidance, VI.A. & 2016 HBV Guidance

- **Hepatitis B virus and antibody tests:**
 - FDA-licensed screening test for Hepatitis B surface antigen (HBsAg);
 - FDA-licensed screening test for total antibody to Hepatitis B core antigen (anti-HBc)(IgG and IgM); **and**
 - FDA-licensed screening NAT for HBV or multiplex assay that includes HBV NAT

HBV

- Published Aug. 1, 2016; 6-month implementation (**Feb. 1, 2017**)
- Recommends that you test HCT/P donors for HBV using an FDA-licensed NAT donor screening test
 - This is in addition to HBsAg and total anti-HBc (IgG and IgM)
- Donor specimen should be negative/nonreactive on all three assays (i.e., HBsAg, total anti-HBc (IgG and IgM), and HBV NAT) to be considered eligible

Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products

Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

For questions on the content of this guidance, contact OCOB at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
August 2016

<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/UCM516650.pdf>

Licensed Donor Screening Tests – HBsAg Assays

HBsAg Assays (Detects Hepatitis B surface Antigen)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
ABBOTT Alinity s HBsAg; and Alinity s HBsAg Confirmatory	HBV	CMIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	Donor Screening: Qualitative detection of HBsAg Confirmatory: To confirm the presence of HBsAg in samples found to be repeatedly reactive by the ABBOTT Alinity s assay	Abbott Ireland Diagnostics Division Sligo, Ireland US License 2094	6/14/2019	BL125674
ABBOTT PRISM HBsAg; ABBOTT PRISM HBsAg Confirmatory	HBV	ChLIA ChLIA - specific antibody neutralization	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	Donor Screening: Qualitative detection of HBsAg. Confirmatory: To confirm the presence of HBsAg in samples found to be repeatedly reactive by the ABBOTT PRISM HBsAg assay	Abbott Laboratories Abbott Park, IL US License 0043	7/18/2006	BL103766
Genetic Systems HBsAg EIA 3.0; Genetic Systems HBsAg Confirmatory Assay 3.0	HBV	EIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	In Vitro Diagnostic, Donor Screening: Qualitative detection of HBsAg. Confirmatory: To confirm the presence of HBsAg in reactive specimens	Bio-Rad Laboratories Redmond, WA US License 1109	1/23/2003	BL103590

Licensed Donor Screening Tests – Anti- HBc Assays



Anti-HBc Assays

(Detects antibodies to Hepatitis B core antigen)

Note: The following anti-HBc donor screening assays detect total antibody (IgG + IgM) to HBc.

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
ABBOTT Alinity s Anti-HBc	HBV	CMIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	Donor Screening: Qualitative detection of total antibody to hepatitis B core antigen	Abbott GbmH & Co KG Wiesbaden, Germany US License 2095	8/09/2019	BL125681
ABBOTT PRISM HBcore	HBV	ChLIA	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of total antibody to hepatitis B core antigen	Abbott Laboratories Abbott Park, IL US License 0043	10/13/2005	BL103785
ORTHO HBc ELISA Test System	HBV	ELISA	<i>Living:</i> Serum, Plasma	In Vitro Diagnostic, Donor screening: Qualitative detection of total antibody to hepatitis B core antigen	Ortho-Clinical Diagnostics, Inc Raritan, NJ	4/23/1998	BL103062

Licensed Donor Screening Tests – HBV NAT



HBV/HCV/HIV Multiplex NAT

(Detects HBV/HCV/HIV Nucleic Acids)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
cobas MPX Test	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	1/17/2020	BL125576
Procleix Ultrio Elite Assay	HBV, HCV, HIV-1, HIV-2	TMA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HCV RNA, HIV-1 RNA and HIV-2 RNA	Grifols Diagnostics Solution., San Diego, CA US License 2032	5/03/2018	BL125652
cobas TaqScreen MPX Test version 2.0	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Serum, Plasma	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	12/19/2014	BL125459
Procleix Ultrio Plus Assay	HBV, HCV, HIV-1	TMA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HCV RNA, and HIV-1 RNA	Grifols Diagnostics Solution., San Diego, CA US License 2032	5/25/2012	BL125113
cobas TaqScreen MPX Test	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	8/27/2009	BL125255

Hepatitis C Virus (HCV)

DE Guidance, VI.A.

- **Hepatitis C antibody and virus tests:**
 - FDA-licensed screening test for anti-HCV;
 - and*
 - FDA-licensed screening NAT test for HCV or combination NAT

Licensed Donor Screening Tests – Anti-HCV Assays



Anti-HCV Assays (Detects antibodies to HCV)

Tradename	Infectious Agen	Format	Specimen	Use	Manufacturer	Licensure Date	STN
ABBOTT Alinity s Anti-HCV	HCV	CMIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	Qualitative detection of antibodies to hepatitis C virus	Abbott GbmH & Co KG Wiesbaden, Germany US License 2095	7/15/2019	BL125677
Ortho HCV Version 3.0 ELISA Test System	HCV	EIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum, Plasma	Donor Screening: Qualitative detection of antibodies to hepatitis C virus	Ortho-Clinical Diagnostics, Inc Raritan, NJ US License 1236	2/18/2009	BL103065
Abbott PRISM HCV	HCV	ChLIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum	Donor screening: Qualitative detection of antibodies to hepatitis C virus	Abbott Laboratories Abbott Park, IL US License 0043	7/11/2007	BL103762

Licensed Donor Screening Tests – HCV NAT



HBV/HCV/HIV Multiplex NAT

(Detects HBV/HCV/HIV Nucleic Acids)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
cobas MPX Test	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	1/17/2020	BL125576
Procleix Ultrio Elite Assay	HBV, HCV, HIV-1, HIV-2	TMA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HCV RNA, HIV-1 RNA and HIV-2 RNA	Grifols Diagnostics Solution., San Diego, CA US License 2032	5/03/2018	BL125652
cobas TaqScreen MPX Test version 2.0	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Serum, Plasma	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	12/19/2014	BL125459
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cobas TaqScreen MPX Test	HBV, HCV, HIV-1 (group O and M), HIV-2	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Simultaneous qualitative detection of HBV DNA, HIV-1 Group M and Group O RNA, HIV-2 RNA, and HCV RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	8/27/2009	BL125255

Syphilis

§ 1271.80(d)(1), DE Guidance, VI.A. & 2015 Syphilis Guidance

- ***Treponema pallidum***

- FDA-cleared screening test for syphilis*
- Remember – If the specimen tests reactive (or positive) on a non-treponemal screening test for syphilis and negative or nonreactive on a specific treponemal confirmatory test, the donor may be eligible (§ 1271.80(d)(1))
 - Specific treponemal confirmatory test: any legally marketed treponemal test
 - If any treponemal screening test is reactive or positive, then the donor is ineligible (even if a confirmatory test is negative)

*Syphilis guidance:

<http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM373311.pdf>

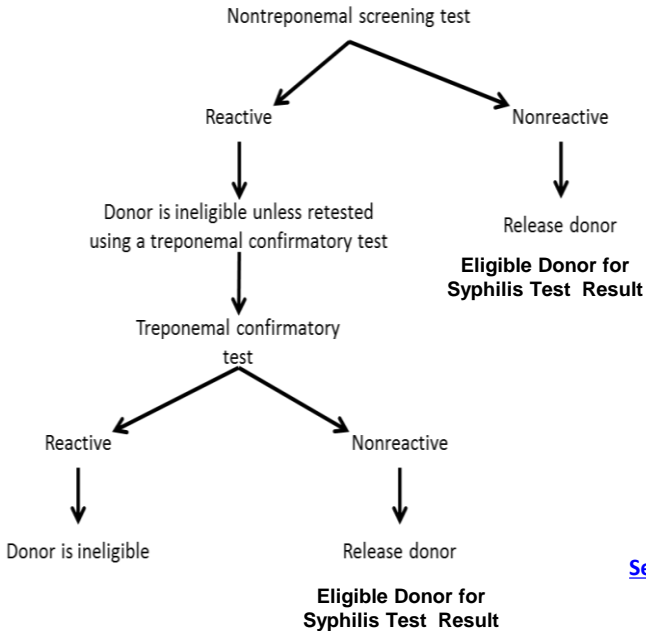
Use of Donor Screening Tests to Test Donors of Human Cells, Tissues and Cellular and Tissue-Based Products for Infection with *Treponema pallidum* (Syphilis)

Guidance for Industry

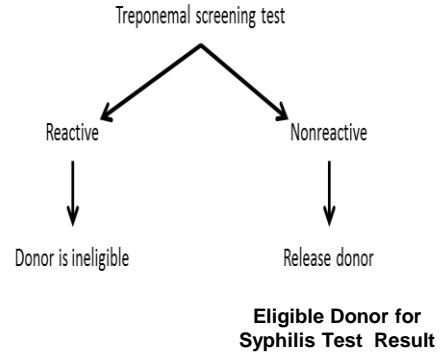
- FDA no longer intends to exercise enforcement discretion with respect to the use of diagnostic tests for evidence of infection with *T. pallidum* for use as HCT/P donor screening tests.
- Intend to enforce the requirements provided under § 1271.80(c) that establishments must use appropriate FDA-licensed, approved, or cleared donor screening tests in accordance with the manufacturer's instructions.
 - Pre-amendments devices are not acceptable for use as a donor screening test for evidence of infection with *T. pallidum*.
 - Published Sept. 9, 2015; Implementation within 6 months of publication (**March 9, 2016**)

<http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM373311.pdf>

Traditional Algorithm



Reverse Sequence Algorithm



[Section VI.A. of the DE Guidance](#) contains additional useful information regarding syphilis tests.

Cleared Donor Screening Tests – Syphilis



Specific Treponemal Confirmatory and Non-treponemal Screening Assays (Detects antibodies to *T. pallidum* and other serological tests)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Clearance Date	STN
PK7400 TP HA	<i>T. pallidum</i>	Hemagglutination (Treponemal)	<i>Living:</i> Serum, Plasma	Donor Screening: detection of IgG and IgM antibodies to <i>T. pallidum</i>	Newmarket Biomedical, Ltd. Kentford, Suffolk, UK	8/1/2019	BK180301
ASiManager-AT™ ↗	<i>T. pallidum</i>	RPR (Non-treponemal)	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum, Plasma	Donor Screening: Qualitative detection of reagin antibodies	Arlington Scientific, Inc. Springville, UT	2/19/2015	BK140192
TPHA Screen ↗	<i>T. pallidum</i>	Hemagglutination (Treponemal)	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of IgG and IgM antibodies to <i>T. pallidum</i>	Immucor, Inc Norcross, GA	10/24/2012	BK120021
Olympus PK TP System ↗	<i>T. pallidum</i>	Micro-hemagglutination (Treponemal)	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of IgG and IgM antibodies to <i>T. pallidum</i>	Fujirebio Diagnostics Inc. Malvern, PA	2/21/2003	BK030007
ASI TPHA Test ↗	<i>T. pallidum</i>	Micro-hemagglutination (Treponemal)	<i>Living:</i> Serum	Donor Screening: Qualitative detection of IgG and IgM antibodies to <i>T. pallidum</i>	Arlington Scientific, Inc Springville, UT	1/30/2003	BK020031
CAPTIA Syphilis (T. Pallidum)-G	<i>T. pallidum</i>	EIA (Treponemal)	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of IgG antibodies to <i>T. pallidum</i>	Trinity Biotech Wicklow, Ireland	01/24/2002	K014233

Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

Guidance for Industry

- Living HCT/P donors should be tested for WNV using a licensed NAT donor screening test.
 - U.S. (50 states + D.C.): June 1st – October 31st
 - Other locations: year-round
- Donor specimen should be negative/non-reactive for WNV by NAT to be considered eligible

WNV Testing – Repeat Semen Donors

2016 WNV Guidance

Published Sept. 8, 2016; Implementation March 8, 2017

- Under § 1271.85(d), you are not required to collect a new blood specimen for testing at the time of each donation
 - However, you should collect a specimen for WNV NAT testing at the time of (or within 7 days before/after) the first donation that is recovered within the June 1st through October 31st testing period (even if an earlier blood specimen was already collected and tested).

WNV Testing – Repeat Semen Donors

- “Due to the increased potential for donors to contract WNV infection from June 1st through October 31st, establishments may want to consider collecting a specimen for WNV NAT testing at the time of (or within 7 days before or after) each donation made during this time period. Although ***this additional testing for subsequent donations is not required***, any reactive results must be considered when making a donor eligibility determination.”
- If a repeat anonymous semen donor discontinues donations, may use the results for WNV obtained at the final donation, or any time later than that, as test of record to qualify final donation (i.e., not necessary to wait 6 months to retest)
 - **This is the same testing expectation for chlamydia and gonorrhea (DE Guidance, VII.D.)**

Licensed Donor Screening Tests – WNV NAT

West Nile Virus (WNV)

WNV NAT

(Detects WNV RNA)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
cobas WNV Assay	WNV	PCR	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Qualitative detection of West Nile Virus (WNV) RNA	Roche Molecular Systems, Inc. Pleasanton, CA US License 1636	1/17/2020	BL125575
cobas TaqScreen West Nile Virus Test	WNV	PCR	<i>Living:</i> Plasma <i>Cadaveric:</i> Plasma	Donor Screening: Qualitative detection of West Nile Virus (WNV) RNA	Roche Molecular Systems, Inc., Pleasanton, CA US License 1636	8/28/2007	BL125245
Procleix West Nile Virus (WNV) Assay	WNV	TMA	<i>Living:</i> Plasma <i>Cadaveric:</i> Plasma, Serum	Donor Screening: Qualitative detection of West Nile Virus (WNV) RNA	Gen-Probe, Inc., San Diego, CA US License 1592	12/1/2005	BL125121

Q&A-5

Q5: If an establishment performs HIV NAT testing, would antibody testing still be necessary?

Q&A-6

A6: Yes. NAT testing does not replace antibody testing. NAT and antibody assays test for different markers of disease – one may be nonreactive while the other is reactive (e.g., NAT negative, antibody reactive).

SPECIFIC DONOR TESTING – ADDITIONAL TISSUE TYPES

Viable, Leukocyte-Rich HCT/Ps

§ 1271.85(b), DE Guidance, VI.B.

For **viable, leukocyte-rich** HCT/Ps:

- Human T-lymphotropic virus, types I and II:
 - FDA-licensed screening test for anti-HTLV I/II
- Cytomegalovirus:
 - FDA-cleared screening test for anti-CMV (total IgG and IgM)

Examples of viable, leukocyte-rich HCT/Ps (based on their status at the time of recovery):

- Hematopoietic stem/progenitor cells (HPCs)
- Semen

Licensed Donor Screening Tests – Anti-HTLV-I/II Assays



Anti-HTLV-I and Anti-HTLV-II Assays (Detects antibodies to HTLV-I & II)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Licensure Date	STN
ABBOTT Alinity s HTLV-I/II Assay	HTLV-1, HTLV-2	CMIA	<i>Living:</i> Plasma, Serum <i>Cadaveric:</i> Serum	Donor Screening: Qualitative detection of antibodies to HTLV-I and HTLV II	Abbott GbmH & Co KG Wiesbaden, Germany US License 2095	6/27/2019	BL125675
Avioq HTLV-I/II Microelisa System	HTLV-1, HTLV-2	EIA	<i>Living:</i> Serum, Plasma <i>Cadaveric:</i> Serum, Plasma	In Vitro Diagnostic, Donor Screening: Qualitative detection of antibodies to HTLV-I and HTLV-II	Avioq, Inc. Research Triangle Park, NC US License 1856	03/26/2012	BL125394
ABBOTT PRISM HTLV-I/HTLV-II	HTLV-1, HTLV-2	ChLIA	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of antibodies to HTLV-I and HTLV-II	Abbott Laboratories Abbott Park, IL US License 0043	1/16/2008	BL103761

Viable, Leukocyte-Rich HCT/Ps


§ 1271.85(b), DE Guidance, VI.B.

Additional information about CMV:

- Not an RCDAD – must perform testing, but donors who test positive or reactive are not necessarily ineligible to donate
- Must establish and maintain an SOP regarding distribution of HCT/Ps when a test is positive
 - Must include how test result will be communicated to the physician responsible for accepting the HCT/P (i.e., summary of records)

Cleared Donor Screening Tests – anti-CMV Assays

Anti-CMV Assays (Detects antibodies to CMV)

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Clearance Date	STN
Immucor, Inc. Capture CMV	CMV	Solid phase red cell adherence	<i>Living:</i> Serum Plasma	Donor Screening: Qualitative detection of IgG and IgM antibodies to CMV	Immucor, Inc. Norcross, GA	11/20/2018 2/4/2019	BK180247 K183571
Olympus PK CMV-PA System 	CMV	Passive particle agglutination	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of IgG and IgM antibodies to CMV	Fujirebio Diagnostics, Inc. Malvern, PA	9/20/2007	BK070030
Abbott CMV Total AB EIA	CMV	EIA	<i>Living:</i> Serum, Plasma	Donor Screening: detection of antibodies to CMV	Abbott Laboratories Abbott Park, IL	03/24/1997	K954301
BD CMVscan Card Test	CMV	Latex Agglutination	<i>Living:</i> Serum, Plasma	Donor Screening: Qualitative detection of IgM and IgG antibodies to CMV	Becton, Dickinson & Company Franklin Lakes, NJ	12/22/1995	BK950068

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm#syp>

Reproductive HCT/Ps

§ 1271.85(c), DE Guidance, VII.C.

- Must test for evidence of infection due to *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, **unless**:
 - Excepted in § 1271.90 (e.g., SIP)
 - Gametes are recovered by a method that ensures freedom from contamination of the cells or tissue by infectious disease organisms that may be present in the genitourinary tract

Testing – Reproductive

§ 1271.80(c); DE Guidance, VII.C.-D.

- Currently, there are no FDA-licensed, cleared or approved donor screening tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*
 - Instead, must use FDA-licensed, approved, or cleared tests labeled for the detection of those organisms in an asymptomatic, low-prevalence population (§ 1271.80(c))
 - FDA recommends the use of FDA-cleared *Chlamydia trachomatis* and *Neisseria gonorrhoeae* diagnostic tests utilizing NAT technology (that are labeled for the detection in an asymptomatic, low-prevalence population)
 - If a repeat anonymous semen donor discontinues donations, then you may use the results for CT/NG obtained at the final donation, or any time later than that, as the test of record to qualify that final donation (i.e., not necessary to wait 6 months to retest)

Cleared Diagnostic Tests – Chlamydia Trachomatis



C. trachomatis NAT (Detects *C. trachomatis* DNA)

Note: This list may be incomplete.

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Clearance Date	STN
BD ProbeTec Chlamydia trachomatis (CT Q* amplified DNA assay)	<i>C. trachomatis</i>	SDA	<i>Living:</i> Endocervical and vaginal swabs, male urethral swabs, and male and female urine specimens	Direct qualitative detection of <i>C. trachomatis</i>	Becton, Dickinson & Co. Sparks, MD	5/20/2014	K140446
Aptima Assay for Chlamydia trachomatis	<i>C. trachomatis</i>	TMA	<i>Living:</i> Endocervical and vaginal swabs, male urethral swabs, and urine specimens	In vitro qualitative detection of <i>C. trachomatis</i> ribosomal RNA (rRNA) to aid in the diagnosis of chlamydial disease	Gen-Probe, Inc. San Diego, CA	1/22/2007	K063451
AMPLICOR CT/NG Test for Chlamydia trachomatis	<i>C. trachomatis</i>	PCR	<i>Living:</i> Endocervical swabs, male urethral swabs, urine specimens	In vitro qualitative in vitro test for the detection of <i>C. trachomatis</i> plasmid DNA to aid in the diagnosis of chlamydial disease	Roche Diagnostics Corporation Indianapolis, IN	4/16/2007	K070174

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm#syp>

Cleared Diagnostic Tests – Neisseria Gonorrhoeae

Neisseria gonorrhoeae

N. gonorrhoeae NAT (Detects *N. gonorrhoeae* DNA)

Note: This list may be incomplete.

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Clearance Date	STN
BD ProbeTec Neisseria gonorrhoeae (GC Q* amplified DNA assay)	<i>N. gonorrhoeae</i>	SDA	<i>Living:</i> Endocervical and vaginal swabs, male urethral swabs, and male and female urine specimens	Direct qualitative detection of <i>N. gonorrhoeae</i>	Becton, Dickinson & Co. Sparks, MD	5/20/2014	K140448
Aptima Assay for Neisseria gonorrhoeae	<i>N. gonorrhoeae</i>	TMA	<i>Living:</i> Endocervical and vaginal swabs, male urethral swabs, and urine specimens	In vitro qualitative detection of ribosomal RNA (rRNA) from <i>N. gonorrhoeae</i> to aid in the diagnosis of gonococcal urogenital disease	Gen-Probe, Inc. San Diego, CA	1/25/2007	K063664
COBAS AMPLICOR test for Neisseria gonorrhoeae	<i>N. gonorrhoeae</i>	PCR	<i>Living:</i> Endocervical swabs, male urethral swabs, urine specimens	In vitro qualitative detection of <i>N. gonorrhoeae</i> in clinical specimens. The test is intended for use with the COBAS AMPLICOR Analyzer (K964506)	Roche Molecular Systems Somerville, NJ	5/28/1999	K974342

Cleared Diagnostic Tests – Chlamydia & Gonorrhoeae



C. trachomatis and *N. gonorrhoeae* NAT (Detects *C. trachomatis* and *N. gonorrhoeae* DNA)

Note: This list may be incomplete.

Tradename	Infectious Agent	Format	Specimen	Use	Manufacturer	Clearance Date	STN
Aptima Combo 2 Assay	<i>C. trachomatis</i> , <i>N. gonorrhoeae</i>	TMA	<i>Living:</i> Endocervical and vaginal swabs, male urethral swabs, male and female and urine specimens, extragenital sites (i.e. throat, rectum)	In Vitro qualitative detection rRNA from <i>C. trachomatis</i> and/or <i>N. gonorrhoeae</i> to aid in the diagnosis of chlamydial and/or gonococcal disease using the Panther® System	Hologic Inc., San Diego, CA	6/13/2019	K180681
Xpert CT/NG Assay	<i>C. trachomatis</i> , <i>N. gonorrhoeae</i>	PCR	<i>Living:</i> Female and male urine, vaginal swab, endocervical, rectal, pharyngeal	In vitro qualitative detection and differentiation of DNA from <i>C. trachomatis</i> and/or <i>N. gonorrhoeae</i> to aid in the diagnosis of chlamydial and/or gonococcal disease using the GeneXpert Instrument System	Cepheid Sunnyvale, CA	5/23/2019	K190441
COBAS CT/NG Assay	<i>C. trachomatis</i> , <i>N. gonorrhoeae</i>	PCR	<i>Living:</i> Vaginal swabs, Endocervical swabs, male and female urine, cervical specimens	In vitro qualitative detection of <i>C. trachomatis</i> and/or <i>N. gonorrhoeae</i> DNA to aid in the diagnosis of chlamydial and/or gonococcal disease using the cobas® 6800/8800 system	Roche Molecular Systems Pleasanton, CA	3/21/2018	K173887
Amplicor CT/NG Test for Neisseria gonorrhoeae	<i>N. gonorrhoeae</i>	PCR	<i>Living:</i> Endocervical and urethral swab	In vitro qualitative in vitro test for the detection of <i>N. gonorrhoeae</i> DNA to aid in the diagnosis of chlamydial disease	Roche Diagnostics Corporation Indianapolis, IN	4/17/2007	K070172
Aptima Combo 2 Assay CDRH Summary	<i>C. trachomatis</i> , <i>N. gonorrhoeae</i>	TMA	<i>Living:</i> Endocervical and vaginal swabs, male urethral swabs, and urine specimens	In vitro qualitative assay for the detection and differentiation of ribosomal RNA (rRNA) from <i>C. trachomatis</i> and/or <i>N. gonorrhoeae</i> in specimens from symptomatic and asymptomatic individuals to aid in the diagnosis of gonococcal and/or chlamydial urogenital disease using the TIGRIS DTS Automated Analyzer or semi-automated instrumentation as specified	Gen-Probe, Inc. San Diego, CA	8/9/2005	K043224
BD ProbeTec ET Chlamydia trachomatis and Neisseria gonorrhoeae Amplified DNA Assays	<i>C. trachomatis</i> , <i>N. gonorrhoeae</i>	SDA	<i>Living:</i> Endocervical swabs, male urethral swabs, urine specimens	In Vitro qualitative detection of <i>C. trachomatis</i> and <i>N. gonorrhoeae</i> DNA in endocervical swabs, male urethral swabs, and in male and female urine specimens as evidence of infection with one or both organisms	Becton, Dickinson & Co., Sparks, MD	9/18/2001	K012351

Summary of Donor Testing

<p>HIV-1</p> <p>FDA licensed screening test:</p> <ul style="list-style-type: none"> • Anti-HIV-1 or combo test for anti-HIV-1 and anti-HIV-2, AND • NAT test for HIV-1 or combination NAT test 	<p>HIV-2</p> <p>FDA licensed screening test:</p> <ul style="list-style-type: none"> • Anti-HIV-2 or combo test for anti-HIV-1 and anti-HIV-2 • NAT test for HIV-2 or combination tests are now available 	<p>HBV</p> <p>FDA licensed screening test:</p> <ul style="list-style-type: none"> • Hepatitis B surface antigen (HBsAg), • Total antibody to Hepatitis B core antigen (IgG & IgM; anti-HBc), AND • NAT test for HBV 	<p>HCV</p> <p>FDA licensed screening test:</p> <ul style="list-style-type: none"> • Anti-HCV, AND • NAT test for HCV or combination test
<p><i>Treponema pallidum</i></p> <p>FDA cleared screening test:</p> <ul style="list-style-type: none"> • Nontreponemal or treponemal 	<p>WNV</p> <p>FDA licensed screening test:</p> <ul style="list-style-type: none"> • NAT test for WNV 	<p>HTLV-I/II</p> <p>FDA licensed screening test:</p> <ul style="list-style-type: none"> • Anti-HTLV-I/II 	<p>CMV</p> <p>FDA cleared screening test:</p> <ul style="list-style-type: none"> • Anti-CMV, total IgG and IgM
<p><i>Chlamydia trachomatis</i></p> <p>FDA cleared diagnostic test for detection of:</p> <ul style="list-style-type: none"> • NAT test for CT in an asymptomatic, low-prevalence population 	<p><i>Neisseria gonorrhoea</i></p> <p>FDA cleared diagnostic test for detection of:</p> <ul style="list-style-type: none"> • NAT test for NG in an asymptomatic, low-prevalence population 	<div style="border: 1px solid black; padding: 10px;"> <ul style="list-style-type: none"> • DE Guidance, sections VI.A-B. • Syphilis Guidance • WNV Guidance • HBV NAT Guidance </div>	

Q&A-7

Q7: If a semen donation is rendered leukocyte-poor by washing the semen, would the testing requirements be the same as for other leukocyte-poor tissues, or would the additional testing requirements for viable, leukocyte-rich HCT/Ps still apply?

Q&A-7

A7: The testing requirements for viable, leukocyte-rich HCT/Ps would still apply. The DE Guidance (section VI.B.2.) explains that you should consider cells and tissues to be viable and leukocyte-rich based on their status at the time of recovery, even if later processing might remove leukocytes. Therefore, semen is considered a viable, leukocyte-rich HCT/P regardless of any processing that occurs after recovery.

ADDITIONAL INFORMATION ABOUT DONOR SCREENING TESTS

Organ and “Other” Living Donors

NAME AND INTENDED USE

The ABBOTT PRISM HCV assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the qualitative detection of antibodies to hepatitis C virus (anti-HCV) in human serum and plasma specimens. The ABBOTT PRISM HCV (ChLIA) is intended to screen individual human donors, including volunteer donors of whole blood and blood components, and other living donors for the presence of anti-HCV. It is also intended for use in testing blood and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing blood specimens to screen cadaveric (non-heart beating) donors. It is not intended for use on cord blood specimens.

- Organ/other living donor indications do not require submission of additional data
 - Tests labeled for blood donor screening are acceptable for organ and other living donors

NAT: Individual Donation (ID) vs. Minipool (MP)

- ID testing only, unless data is submitted by test kit manufacturer to support pooling of plasma specimens from multiple donors
 - Read the intended use carefully
 - Some HIV/HBV/HCV NAT tests to allow pooling of specimens from donors of HPC and donor lymphocytes for infusion (DLI)
 - To date, no other test kits for HCT/P donors have a pooling claim for donor testing
 - **Note: This refers to “pooling of specimens (i.e. blood) for testing”, not pooling of HCT/Ps!**

Almost There

**THINGS TO CONSIDER WHEN INSPECTING
AN HCT/P MANUFACTURER OR TESTING
LABORATORY**

Points to Consider – Testing Laboratories

- Establishments should work with their testing laboratory to assure that the lab is using proper tests:
 - Is it FDA-licensed, cleared, or approved for donor screening purposes?
 - Is it approved for cadaveric specimens?
 - What kind of specimen (i.e., serum or plasma) does the test require?
If plasma, what type of anticoagulant?
 - Should the test be performed using individual donor (ID) specimens or is the use of pooled specimens acceptable?
 - What specimen storage/handling requirements should be considered? (shipping, how soon it should be tested?)
- Examples of each issue on the following slides

Is the Test Approved for Donor Screening Purposes?

Anti-HBc Reagent Pack (*Vitros* Immunodiagnostic Products)

Intended Use

For the *in vitro* qualitative detection of total antibody (IgG and IgM) to hepatitis B core antigen (total anti-HBc) in human adult and pediatric serum and plasma (EDTA and citrate) and neonate serum using the VITROS Eci Immunodiagnostic System.

Assay results, in conjunction with other serological and clinical information, may be used for the laboratory diagnosis of individuals with acute or chronic hepatitis B, or recovery from hepatitis B infection. The presence of anti-HBc may be used as an aid in the determination of exposure to HBV infection for individuals prior to HBV vaccination.

WARNING:

This assay has not been FDA cleared or approved for the screening of blood or plasma donors.

Is the Test Approved for Donor Screening Purposes?

COBAS AmpliScreen™ HIV-1 Test, version 1.5 (Roche Molecular Systems)

INTENDED USE

The COBAS® AmpliScreen HCV Test, version 2.0 (v2.0) is a qualitative *in vitro* test for the direct detection of Hepatitis C Virus (HCV) RNA in human plasma.

The COBAS® AmpliScreen HCV Test, v2.0 is intended to be used for the detection of HCV RNA in conjunction with licensed tests for detecting antibodies to HCV. This product is intended for use as a donor screening test to detect HCV in plasma specimens from individual human donors, including donors of whole blood and blood components, source plasma and other living donors. It is also intended for use to screen organ donors when specimens are obtained while the donor's heart is still beating and to detect HCV RNA in blood specimens from cadaveric (non-heart-beating) organ and tissue donors. This test is not intended for use on samples of cord blood.

Plasma from all donors may be screened as individual specimens. For donations of whole blood and blood components, plasma may be tested in pools comprised of equal aliquots of not more than 24 individual donations. For donations of hematopoietic stem/progenitor cells (HPCs) sourced from bone marrow, peripheral blood or cord blood, and donor lymphocytes for infusion (DLI), plasma may be tested in pools comprised of equal aliquots of not more than 24 individual donor specimens. For donations of source plasma, plasma may be tested in pools comprised of equal aliquots of not more than 96 individual donations.

The COBAS® AmpliScreen HCV Test, v2.0 can be considered a supplemental test that confirms HCV infection for specimens that are repeatedly reactive on a licensed donor screening test for antibodies to HCV, and reactive on the COBAS® AmpliScreen HCV Test, v2.0.

This test is not intended for use as an aid in diagnosis.

Is the Test Approved for Donor Screening Purposes?

- Generally, “newer” test kits are clearly labeled with (or without) the donor screening indication. This information can be found in the intended use section of the package insert
- Donor screening tests are regulated by CBER
 - Blood, general:
http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm080466.htm#anti_HIV12_HIV1Ag_CombosAssays
 - HCT/Ps:
<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm>
- Diagnostic tests are regulated by CDRH (except for retrovirus (HIV and HTLV) diagnostic tests, which are regulated by CBER)
 - <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfivd/index.cfm>
- If you are in doubt, ask CBERInspections@fda.hhs.gov

What Kind of Specimen Does the Test Require?

For living donors, this is often found in the Intended Use statement.

INTENDED USE

The PROCLEIX[®] WNV Assay is a qualitative *in vitro* nucleic acid assay system for the detection of West Nile Virus (WNV) RNA in plasma specimens from individual human donors, including volunteer donors of whole blood and blood components, and other living donors. It is also intended for use in testing plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing blood specimens to screen cadaveric (non-heart-beating) donors. It is not intended for use on cord blood specimens.

The assay is intended for use in testing individual donor samples. It is also intended for use in testing pools of human plasma comprised of equal aliquots of not more than 16 individual donations from volunteer donors of whole blood and blood components.

This assay is not intended for use as an aid in the diagnosis of West Nile Virus infection.

Plasma Sample vs. Serum Sample

Plasma samples

- From tubes w/anticoagulant
 - EDTA (cadaveric)
 - Others validated for living/blood donors
 - No heparin tubes for NAT
- Typically, centrifuge “as soon as possible”
- Separate plasma from cells and put plasma into new tube
- Timing described in PI

Serum samples

- Tubes without anticoagulant (“clot tubes”)
- Glass red-top tube; may be a different color
- Typically:
 - Allow specimen to clot at room temperature for 30 minutes to 1 hour
 - Centrifuge within a reasonable time period after collection, per PI instructions
 - Labs also generally follow standards from CLSI (Clinical Laboratories Standards Institute) – see GP44-A4



What Specimen Storage/handling Requirements Should be Considered?

- The test's PI has relevant information, including:
 - Shipping and storage temperatures
 - How soon the test must be performed after specimen collection
 - Proper specimen containers
- Requirements for cadaveric specimens often differ compared to those for living donor specimens
- Establishments should work with testing laboratories to develop SOPs to ensure proper collection, storage and shipment of specimens

Summary

In this course, you learned how to:

- Identify the testing requirements used by HCT/P establishments when determining donor eligibility
- Identify the criteria used to determine if an HCT/P poses a risk to public health
- Identify general donor testing requirements and recommendations

References

Tissue & Tissue Products Homepage

<http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm>

Code of Federal Regulations Title 21

http://www.ecfr.gov/cgi-bin/text-idx?SID=ae1deecc79a9f185d48af015ae277f5d&mc=true&tpl=/ecfrbrowse/Title21/21cfr1271_main_02.tpl

Test Kits for HCT/P Donors

<https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm>

Additional Test Kits for Living Donors (only consider the donor screening tests)

<https://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/ucm080466.htm>

Tissue Guidances – Complete Listing

<https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/tissue-guidances>

References

Searchable Guidances

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>

Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products

<https://www.fda.gov/media/73072/download>

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

<https://www.fda.gov/media/87143/download>

Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donor of Human Cells, Tissues, and Cellular and Tissue-Based Products

<https://www.fda.gov/media/99642/download>

Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

<https://www.fda.gov/media/87050/download>

Guidance for Industry: Recommendations for Obtaining a Labeling Claim for Communicable Disease Donor Screening Tests Using Cadaveric Blood Specimens from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

<https://www.fda.gov/media/73121/download>

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FDA Headquarters

- OTAT Learn Webinar Series:
<http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm>
- CBER website: www.fda.gov/BiologicsBloodVaccines/default.htm
- Phone: 1-800-835-4709 or 240-402-8010
- Consumer Affairs Branch: ocod@fda.hhs.gov
- Manufacturers Assistance and Technical Training Branch: industry.biologics@fda.hhs.gov
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