Update on FDA NAT Guidance: HIV-1, HCV, HBV, WNV

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XXII SoGAT meeting
HIV-1 and HCV NAT

1. FDA licensed HIV-1 and HCV NAT in 2001 for testing pools of plasma from Source Plasma donors and in 2002 for Whole Blood collections.

2. NAT is included in screening of all donations of Whole Blood and blood components (including Source Plasma and Source Leukocytes) in addition to an FDA licensed HIV antibody test and HCV antibody test.
HIV-1 and HCV NAT – cont.


4. NAT standard for licensure was 100 IU/ml for the pool test for both HIV-1 and HCV.

5. HIV-1 p24 antigen testing was discontinued on implementation of NAT approved to replace this test.
HIV-1/HCV NAT

- HIV-1/HCV NAT Final guidance on testing and re-entry issued May 2010

- NAT algorithms for testing, re-entry of 3 groups of donors deferred because of HIV test results
Testing, Product Disposition, Donor Mgmt., Lookback for **Multiplex** HIV-1/HCV MP-NAT Reactive or ID-NAT Reactive

**MP-NAT Reactive:**
Resolve by Testing Subpools

**TEST INDIVIDUAL REACTIVE DONOR SAMPLES USING SAME MULTIPLEX NAT METHOD**

**ID-NAT Reactive:**
- Reactive Donor Sample(s)
  - TEST USING DISCRIMINATORY NAT(s).
- Non- Reactive Donor Samples
  - RELEASE
TEST USING DISCRIMINATORY NAT(s).

Reactive for HIV-1 and/or HCV

DESTROY or RELABEL UNIT.
DEFER and NOTIFY DONOR.
PERFORM LOOKBACK for HIV-1 and/or HCV.
Donor Eligible for Reentry.

Non-Reactive for both HIV-1 and HCV (Non-Discriminated Reactives)

DESTROY or RELABEL UNIT.
DEFER DONOR for 6 MONTHS, REENTER without TESTING SAMPLE.
NOTIFY DONOR: “Likely FP, Not Infected.”
PERFORM LOOKBACK for HIV-1 and HCV.
(VARIANCES)
HIV-1 Group O Guidance

- HIV-1 Group O final guidance Issued August 2009 - New sub-Saharan countries added

- Recommendation –
  1) can discontinue questions if screening with a Group O sensitive test
  2) re-entry of donors deferred after one year following yes answer to a risk question
Advances in HIV Tests
Used as an Aid in Diagnosis

FDA has approved:

- Tests that use urine and oral fluid
- Automated assay platforms and NAT
- 2 Over-the-Counter Anti-HIV-1 Testing Services
  - Use dried blood spots / mail
- 8 Rapid HIV-1 Antibody Tests
  - 1 gives a result in 1 minute!
  - Use finger-stick blood, oral fluid, etc.
- An Antibody/Antigen “combo” assay
Advances in HIV Tests
Used for Monitoring Therapy

- FDA Approved Viral Load Assays
  - To measure HIV-1 virus in plasma of infected individuals

- FDA Approved HIV Drug Resistance Assays
  - To measure drug resistance in individuals undergoing antiretroviral therapy
Status of HIV Testing

- New FDA licensed / approved tests for blood screening, diagnosis, very rapid testing, and therapy monitoring

- Improved Prevention and Treatment: More people learning their HIV status

- Improvement in Blood Safety using NAT:
  - Window Period reduced to ~ 7 days, and
  - Residual risk of HIV transmission in transfused blood is 1 in ~ 3.1 million using NAT for individual donations
Estimated Residual Risk of Transmission of HBV, HCV, HIV by Blood Transfusion in the U.S.

HBV:  *1 per 269,000 transfusions
      (Tests: HBsAg and anti-HBc)

HCV:  *1 per 1,610,000 transfusions
      (Tests: Anti-HCV and MP HCV NAT)

HIV:   *1 per 1,780,000 transfusions
       (Tests: Anti-HIV and MP HIV NAT)

* Busch, MP. Transfusion 2006; 46:1624-1640
Testing Blood for Transfusion for HBV

- Consistent with current regulations and guidance documents, all blood and components for transfusion in the U.S. are tested for:
  - Hepatitis B surface antigen (HBsAg)
  - Antibody to hepatitis B core antigen (anti-HBc)
The Committee recognized the benefit of screening blood donations by sensitive HBV NAT.

The Committee agreed that donations from persons with HBV "breakthrough" infections (vaccinees who are HBV NAT (+) / HBsAg (-) / anti-HBc (-)) are potentially infectious.
Status of HBV NAT

- FDA is considering a Sensitivity Standard for screening of Whole Blood donations that is achievable by current HBV NAT assays and clearly shows utility.

- Issue of effectiveness of HBV NAT screening of Source Plasma to be considered at BPAC (April, 2011).

- Final Guidance issued May, 2010 for reentry of donors deferred because of anti-HBc test results after 8 weeks using NAT and serology.
Summer 1999: First outbreak of WNV in the US.

September 2002: Transmission of WNV by transplantation was confirmed, followed by the confirmation of transmission by transfusion (MMWR 2002; 51(35):790).

July 2003: Nationwide screening of blood donations for WNV RNA using NAT under IND on mini-pools (MP-NAT) of 6 or 16 donations, depending on the assay.
Background.....

**November 2003**: Evaluation of MP-NAT sensitivity to detect low viremia by retrospective studies using ID-NAT

- Identification of ID-NAT-positive and MP-NAT-negative units
- 6 confirmed cases of WNV transmission by transfusion of MP-NAT-negative units

**Summer 2004 and 2005**: Prospective testing by ID-NAT replaced MP-NAT in areas of high WNV activity during limited periods of time.
WNV Testing

• FDA licensed first WNV NAT for blood donor screening (Procleix® WNV Assay on eSAS) in December 2005.

• Draft guidance on WNV test implementation published in 2005 and final guidance Issued November 2009.

• Recommendation – Year round testing; Switching from MP-NAT to ID-NAT and back to MP-NAT.
WNV MP-NAT Unit/Donor Algorithm

1. Test each specimen in pool using ID-NAT
2. Reactive Master Pool with licensed MP-NAT for WNV
3. Reactive
   - Discard unit(s)
   - Defer donor for 120 days
   - Notify and counsel donor
   - Retrieve and quarantine in-date products from collections dating back 120 days
4. Non-reactive
   - If suitable, Unit Released
### Nucleic Acid Tests Licensed for Donor Screening in USA

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Test</th>
<th>Analyte</th>
<th>Donation tested</th>
<th>Date</th>
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<tbody>
<tr>
<td>NGI</td>
<td>UltraQual HIV-1 RT PCR</td>
<td>HIV-1 RNA</td>
<td>Source Plasma</td>
<td>9/18/2001</td>
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<tr>
<td>NGI</td>
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<td>Roche Molecular system</td>
<td>Cobas AmpliScreen HCV Test</td>
<td>HIV-1 RNA</td>
<td>Whole blood, Source Plasma, Cadaveric sample</td>
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<tr>
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<td>Roche Molecular system</td>
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<td>Roche Molecular system</td>
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<tr>
<td>Gen-Probe</td>
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<td>WNV RNA</td>
<td>Whole blood Cadaveric sample</td>
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<tr>
<td>Roche molecular System</td>
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</tr>
</tbody>
</table>
In the U.S. all blood donations are tested for HIV-1, HCV, and WNV by MP-NAT in pools of up to 24.

Source Plasma donations are also tested for HIV-1 and HCV by NAT.

Recommendations for HBV NAT for all Whole Blood and Source Plasma donations, are under consideration in the U.S.
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