Update on BPAC Discussion on WNV Testing

Maria Rios, Ph.D.
CBER/FDA

ACBSA DHHS
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BPAC 89th Meeting April 27, 2007: Issues Related to Implementation of WNV Testing

A. Update on WNV Epidemic 2006, Eileen Farnon, M.D., Centers for Disease Control and Prevention

B. Issues for Testing, Maria Rios, Ph.D., DETTD, OBRR, FDA
   i. Approaches to Confirmatory Testing
   ii. Donor and Unit Management
   iii. Approaches to ID-NAT Trigger

C. Data in Support of the Current ID-NAT Triggers, Susan Stramer, Ph.D., American Red Cross

Reported WNV Disease Cases in Humans – United States, 1999-2006*

Year	Total	**WNND**	WNF/other	**Deaths**
1999-2001	149	***142***	7	***18***
2002	4,156	***2,946***	1,210	***284***
2003	9,862	***2,866***	6,996	***264***
2004	2,539	***1,148***	1,391	***100***
2005	3,000	***1,309***	1,691	***119***
2006	4,261	***1,491***	2,770	***176***
Total	23,967	***9,902***	14,065	***961***

Since 2002: >1,000 cases of WNND and ≥100 fatalities / year

2003 – Nucleic acid amplification tests (NAT)
MP-NAT (6-16 units) → ID-NAT

PVDs Reported to ArboNET as of 4/12/2007

- Blood establishments:
  - Screen by WNV NAT and remove infectious blood products from circulation
  - Report presumptively viremic donors (PVDs) to local public health department
- Local public health departments report to ArboNET

Year	PVDs
2003	818
2004	224
2005	417
2006	361
Total	1820

- 2,000 WNV NAT reactive units interdicted
- Prevented 2,000 - 6,000 transfusion transmissions

Status of WNV Assays

- Dec 2005: FDA licensed the first WNV NAT for volunteer blood donor screening (Procleix® WNV Assay)
- Mar 2007: FDA licensed the first fully automated NAT for volunteer blood donor screening (Procleix® WNV Assay on Procleix® TIGRIS System)
- Other WNV NAT for donor screening are currently under IND

Issues Regarding Testing

- WNV is endemic in the US and is a reportable disease to the CDC
  - ✓ 1 in 150 to 1 in 350 infections are neuroinvasive, there have been ~1.5 to 3.5 Million infections
  - ✓ > 1,000 WNND cases and ≥ 100 fatalities / year since 2002
  - ✓ Human cases reported from January to December
- ➢ We are considering whether blood establishments should screen for WNV by MP-NAT year-round

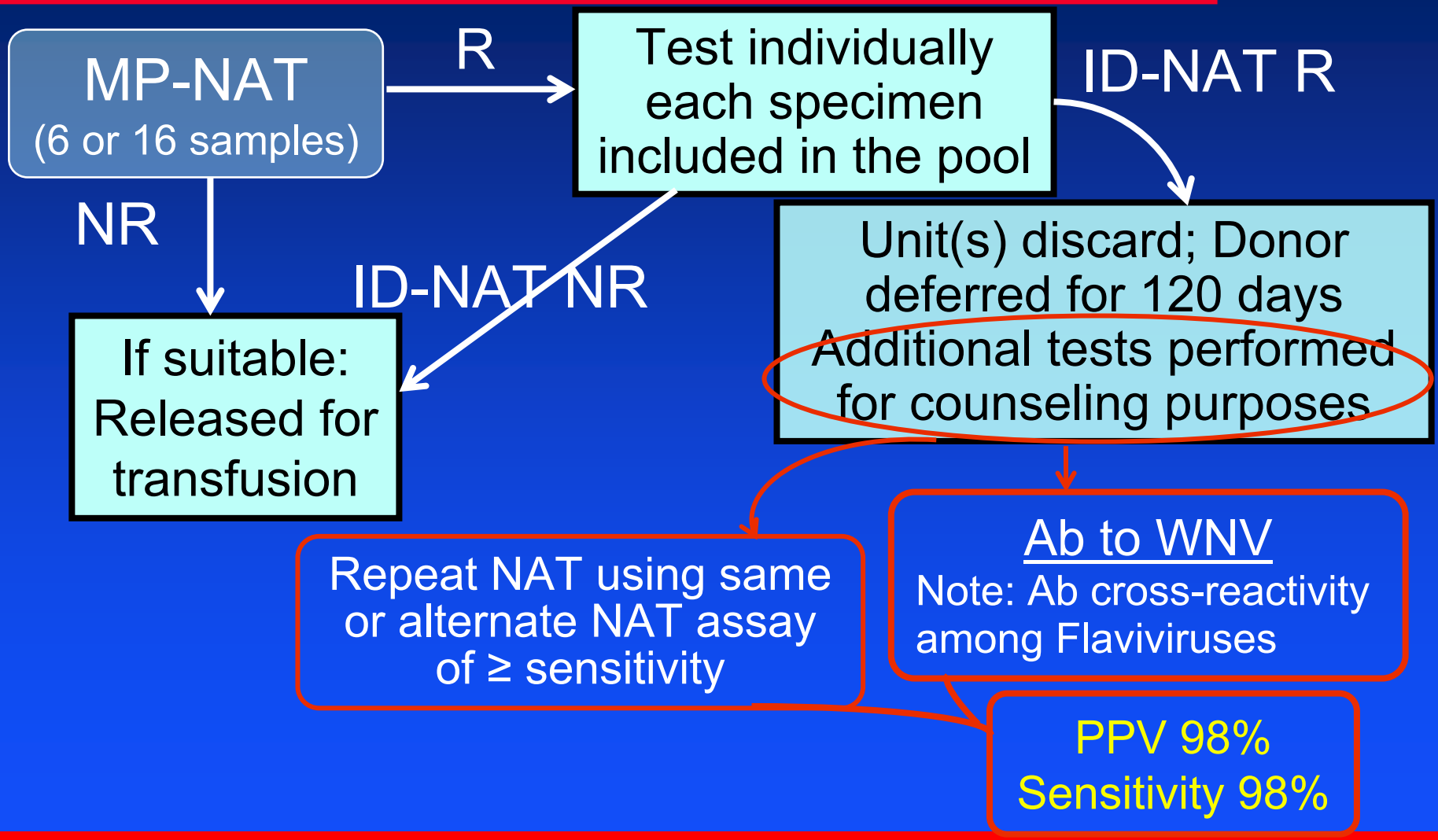
Issues Regarding Testing

- 2003: 6 cases of TT-WNV after MP-NAT implementation; MP-NAT detects 75% of WNV infected units (miss 25%)
- Conversion MP⇨ID NAT during epidemic periods based on: low WNV viral loads compared to HIV/HCV

  22% of WNV NAT (+) samples detected required ID NAT

  26% of detected samples were Ab positive of which majority (81%) required ID NAT
- 2004: ID-NAT used in high WNV activity regions
- Since selective ID-NAT: Three (3) confirmed cases of WNV transmission by transfusion
- ➢ FDA is considering whether blood establishments should implement ID-NAT in areas with high WNV activity

Additional Tests: Current Testing Algorithm



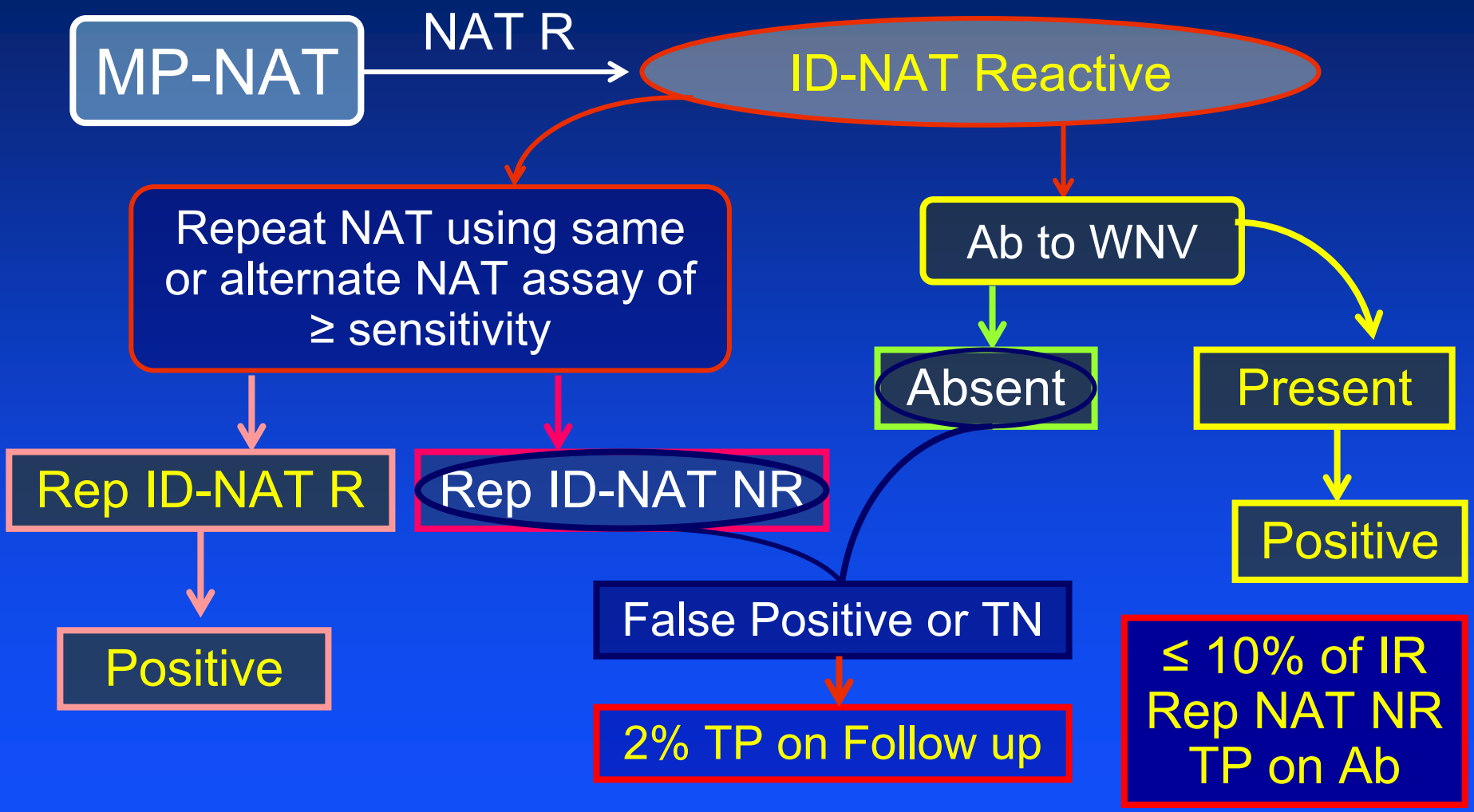
Issues Regarding Additional Testing

- FDA is considering whether blood establishments should:
  - ✓ Retest IR donations by ID-NAT using screening assay or alternate NAT of ≥ sensitivity
  - ✓ Test ID-NAT IR donations for Ab to WNV

If a NAT screening assay is specific for Flaviviruses but is not discriminatory for WNV:

- FDA is considering whether blood establishments should perform a WNV-specific discriminatory assay to determine WNV infection

Additional Testing Algorithm



Issues Regarding Donor Counseling

- FDA is considering whether it is appropriate for:
  - ✓ IR specimens not to be regarded as *False Positive* based solely on negative test results obtained on additional testing in the index donation
  - ✓ A donor to be considered *True Positive* based on RR by NAT or WNV Ab positive

Note: If NAT assay does not discriminate WNV from other viruses of the JE serogroup, it is not appropriate to consider *True Positive for WNV*

Antibody cross-reactivity among these viruses

Issues Regarding Donor Counseling

- Due to the potential for *False Negative* results, it is desirable to inform donors with IR ID-NAT about a possible infection with WNV
- Donors with IR ID-NAT may be counseled and invited for follow-up testing (ID-NAT and antibody) at least 30 days post IR donation
- IR ID-NAT donations may not be released for transfusion and donors be deferred for 120 days
- FDA is considering maintaining Donor Deferral and Reentry; Product Retrieval and Recipient Notification as stated in the June 2005 Guidance: www.fda.gov/cber/gdlns/wnvguid.htm

AABB ID-NAT Triggering Recommendations AB #07-02

- Minimum criteria based on IR donations; action within 24h
- Revert back to MP NAT following 7 days without a repeatable or Ab (+) ID-NAT reactive
- Missing link is communication between facilities
  - Communication plan based on the existing testing sites that have entered data into the AABB web site
  - Sites with adjacent/overlapping collections areas should communicate
  - Tools for tracking / planning within and between facilities:
    - » Site specific maps / location & donors residential zip code
    - » AABB WNV NAT-reactive donor website (Real time update)
    - » CDC/USGS maps for avian/mosquito and human WNV activity

Minimum Criteria proposed WNV TF

- Real time and Feasible, or it wont be done!
- 2 WNV NAT reactive donations and Rate of ≥1:1000

  < 1000 collections/week, use weekly collections; should combine with adjacent/overlapping facilities

  May have long intervals between 1st and 2nd reactive that may lead to false negative MP NAT results
- Defined geographic area to which the criteria are applied

  Most feasible/standardized method is based on number of collections

Committee Discussions/Comments

- Informational Topic. No specific question asked to the committee
- No objections to FDA considerations were raised
- The committee suggested ID-NAT to be used year-round instead of triggered by incidence in a region
- Blood establishments representatives argued that year-round use of ID-NAT would result in: increase false positive rates and donor deferral; incremental cost and exhaust the laboratory resources

Committee Discussions/Comments

- Importance of early and effective communication to facilitate quick & effective implementation of ID-NAT
- The committee stressed that early trigger of ID-NAT is extremely important
- The committee also alerted that compliance will be challenging without FDA Guidance
- Public discussions regarding rate of transmission, donor follow up and the need for data to evaluate the current criteria to implement ID-NAT