Evaluation of Strategies to Reduce the Risk of Zika Virus (ZIKV) Transmission by Blood and Blood Components

120th Meeting of the
Blood Products Advisory Committee
Silver Spring, MD

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Topic 1: Issue

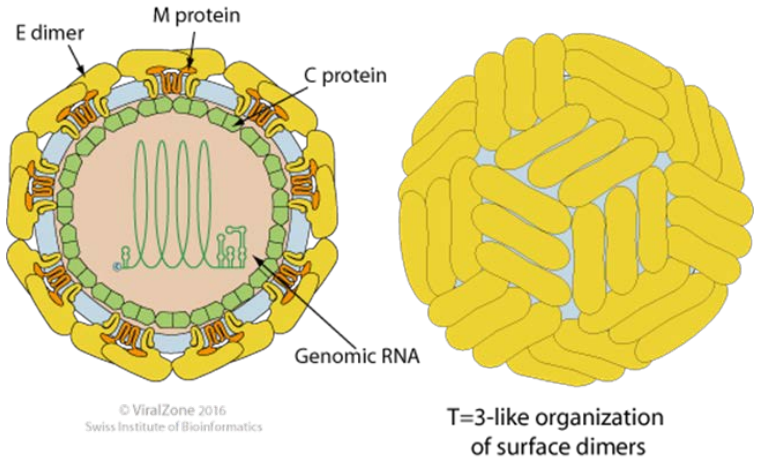
- Current FDA guidance (July 2018) recommends universal testing for U.S. blood donations by minipool nucleic acid testing (MP NAT) or individual donation NAT (ID NAT), with triggering to ID NAT when certain conditions are met indicating risk of ZIKV transmission.
- Available information indicates a decline in ZIKV transmission in the U.S. and Americas.
- Therefore, FDA is re-evaluating its July 2018 recommendations on testing blood donations for ZIKV using MP or ID NAT.

Topic 1: Discussion Outline

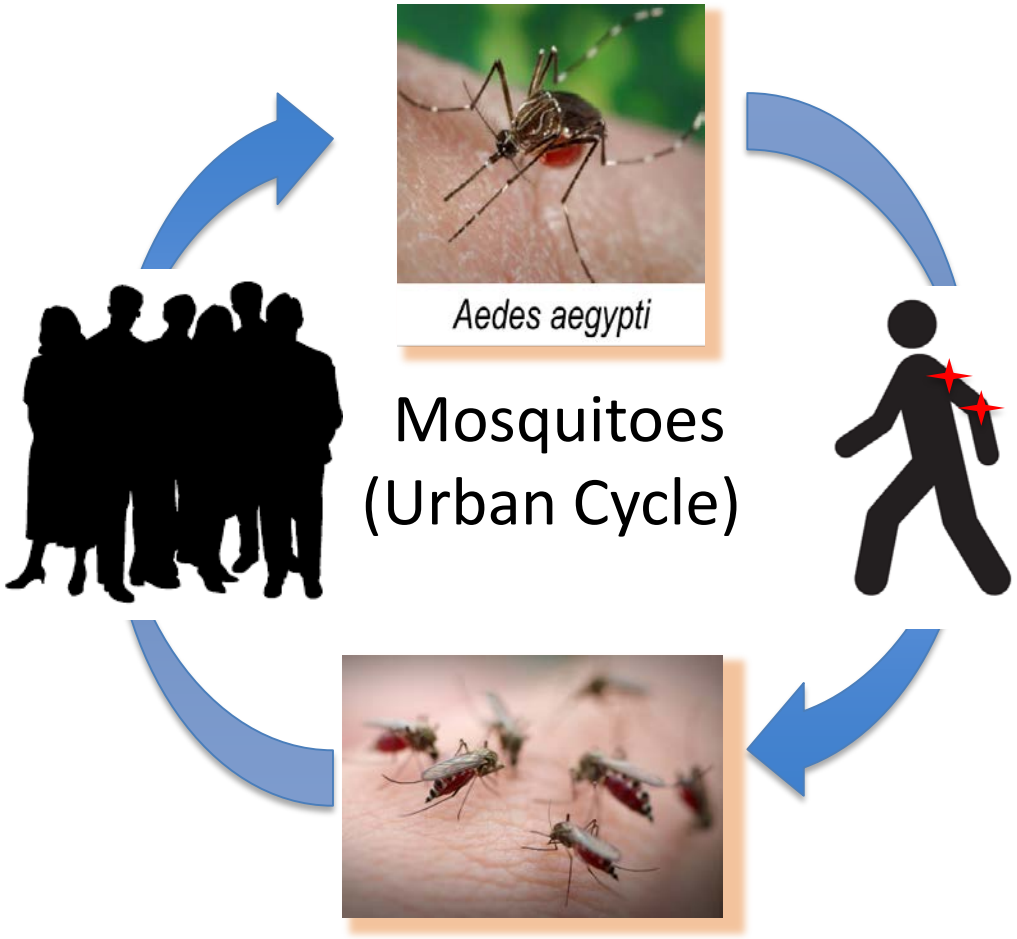
- Background
  - Zika virus
  - U.S. blood safety concerns
  - Screening of U.S. blood supply for Zika
- Introduction of speakers
- Consideration of blood safety options
- Questions for the Committee
- Discussion and voting

Zika Virus (ZIKV)

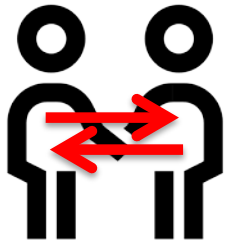
- Enveloped arbovirus, single stranded RNA genome
- *Flaviviridae* family, *Flavivirus* genus
  - Closely related to dengue virus (DENV), West Nile virus (WNV), yellow fever virus (YFV)
- Transmitted by *Aedes* mosquitoes
  - Also transmit DENV, YFV, chikungunya viruses
  - ZIKV most commonly by *Aedes aegypti*
- First identified in rhesus monkey, Zika forest, Uganda 1947
- First human infections, Nigeria 1953



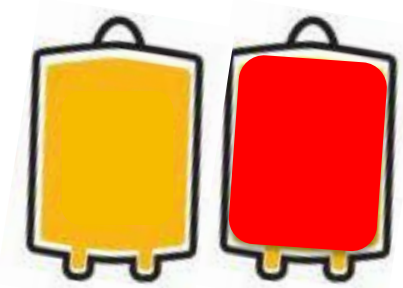
ZIKV Transmission Routes



During pregnancy



Sexual contact



Blood transfusion

Laboratory or
Other (rare)

Concerns at Outset of the ZIKV Epidemic in 2015

- Potential for ZIKV outbreak to spread to the U.S.
  - Increase in travel-associated ZIKV cases due to U.S. travelers returning from ZIKV-affected areas
  - Presence of competent mosquito vectors in the U.S.
- Significant potential morbidity of ZIKV infections, including congenital microcephaly, Guillain-Barré syndrome
- Demonstrated sexual transmission
- Probable transfusion-transmission

Risk of Transfusion-Transmitted ZIKV

- Known transfusion-transmission of other flaviviruses
- Most (~80%) infected individuals remain asymptomatic
- Viremia may begin 1-2 days prior to symptom onset and persists 1-2 weeks; longer in some individuals
- Viral RNA typically can be detected for longer in whole blood/RBCs relative to serum/plasma

Paz-Bailey et al. New Eng J Med 2017;379(13):1234-1243; Lessler et al. Bull World Health Organ 2016;94(11): 841-9; Lustig et al. Euro Surveill 2016;21(26)

Risk of Transfusion-Transmitted ZIKV

- Asymptomatic blood donors were ZIKV RNA-positive in outbreaks in French Polynesia (2.8%) and the Americas (Puerto Rico-1.8%, Brazil-2.7%, and Martinique-3.0%)
- Probable transfusion-transmitted ZIKV cases reported in Brazil (3 in peer-reviewed journals)
- Retrospective study in French Polynesian outbreak
  - 30 ZIKV RNA-reactive units transfused to 26 patients; follow-up on 12 patients, none had ZIKV symptoms after transfusion

Barjas-Castro ML et al. Transfusion 2016;56:1684-8; Motta et al. N Engl J Med 2016;375:1101-3; Bierlaire MJ et al. Transfusion 2017;57:729-733; Musso et al. Euro Surveill 2014;19(14):pii=20761; Slavov et al. Transfusion 2017; 57:2897-2901; Gallian et al. Blood 2017;129:263-6; Adams et al. MMWR 2016;65:774-9.

FDA Guidance on Zika and Transfusion-Transmission

- *Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus* – February 2016
- *Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components* – August 2016
- *Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components* – July 2018

https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM518213.pdf

Initial Guidance--February 2016

- Areas with active ZIKV transmission: **Obtain** blood and blood components from unaffected areas until pathogen reduction technology (PRT) and/or testing available
  - Puerto Rico – All blood components obtained from continental U.S. from March 5, 2016-April 2, 2016. ZIKV NAT implemented under IND April 3, 2016.
- Areas without active ZIKV transmission: **Screen** donors; deferrals for ZIKV infection or risk associated with travel or sexual transmission

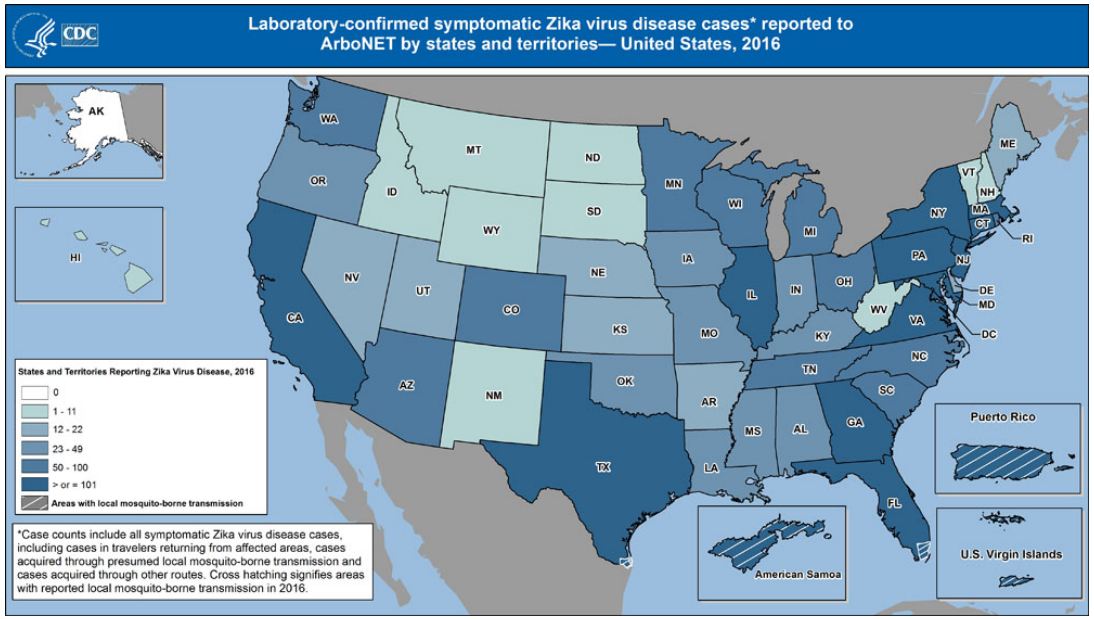
Basis for Revision, August 2016

- Two ZIKV NAT-based assays were developed
  - Testing began under IND in April 2016 (Roche) and June 2016 (Grifols)
- First reports of local mosquito-borne transmission in Florida
  - Significant lag time between recognition and confirmation of local mosquito-borne transmission
- Increased concern about sexual transmission as a mode of spread of epidemic
- Logistic complexity and challenges of donor screening for risk factors, especially with local transmission
- Potential effect of travel-based deferrals on adequacy of blood supply in some areas

Revised Guidance --August 2016

- **All** donations collected in U.S. and its territories must be:
  - **Tested** by investigational or licensed ID-NAT *or*
  - **Pathogen reduced** using FDA-approved PRT device for plasma/apheresis platelets.
- ID-NAT phased in through December 2016
- Donor screening and deferral based on travel and sexual contact discontinued
- Maintained deferral for recent history of ZIKV for 120 days after positive viral test or resolution of symptoms, whichever is longer

ZIKV Disease 2016 - CDC ArboNet



U.S. STATES	**5,168**
Travelers	4,897
Local, Mosquito	224 (FL, 218; TX, 6)
Sexual/Lab/Other	45/1/1
U.S.TERRITORIES	**36,512**
Travelers	145
Local, Mosquito	36,367

https://www.cdc.gov/zika/reporting/case-counts.html

U.S. Blood Donations tested by ZIKV ID NAT under IND

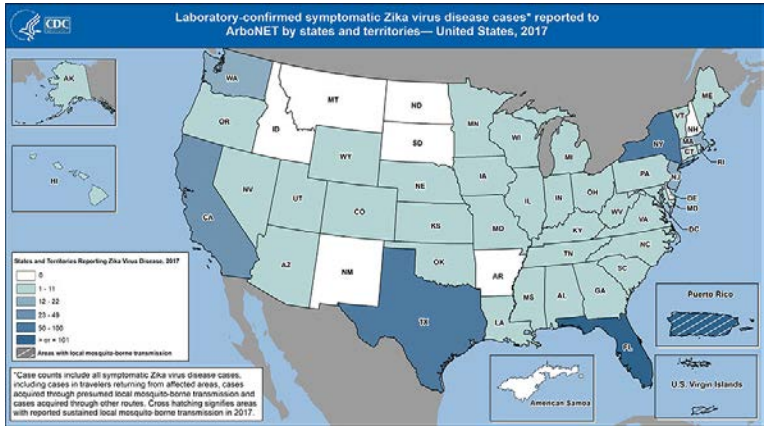
	U.S. states [1,2]	Puerto Rico [1]
Donations Tested	11,540,307	111,842
Initial Reactive	398 (0.0034%)	369 (0.32%)
Confirmed positive	50	356

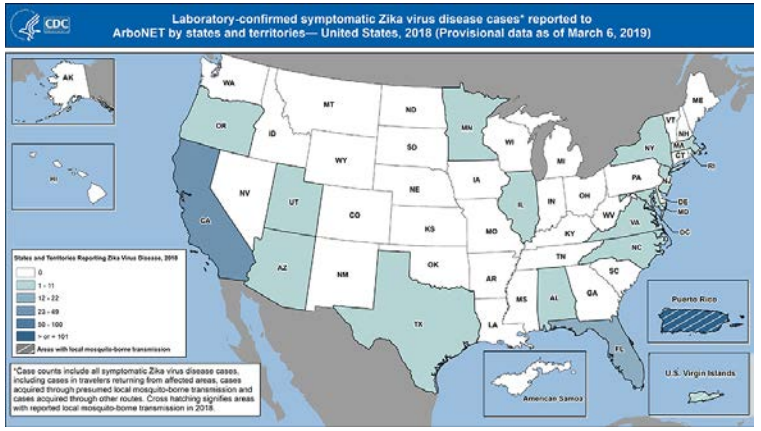
From beginning of testing through September 23, 2017

[1] Investigational cobas® Zika test (Roche Molecular Systems, Inc, Pleasanton, CA)
Licensed by FDA on October 5, 2017

[2] Investigational Procleix® Zika assay (Grifols, San Diego CA)
Licensed by FDA on July 5, 2018

ZIKV Disease 2017-2018 - CDC ArboNet





	2017	2018*
U.S. STATES	452	72
Travelers	437	72
Local, Mosquito	7 (FL, 2; TX, 5)	0
Sexual/Lab/Other	7/1/0	0
U.S.TERRITORIES	666	148
Travelers	1	1
Local, Mosquito	665	147

https://www.cdc.gov/zika/reporting/case-counts.html *data as of March 6, 2019

Reevaluating risk, 2017-2018

- Decrease in ZIKV cases reported in U.S. and worldwide 2017-2018
- December 2017, BPAC provided advice on screening blood donors for ZIKV:
  - Incidence of ZIKV in U.S. did not warrant continued universal blood testing by ID NAT
  - Blood establishments should not stop testing donations for ZIKV in the U.S. and its territories
  - Majority of committee supported use of MP NAT with ID NAT trigger

Revised Guidance -- July 2018

- All donations collected in U.S. and its territories must be:
  - Tested by either **MP NAT <u>or</u> ID-NAT** *or*
  - Pathogen reduced using FDA-approved PRT device for plasma/apheresis platelets.
- **ID NAT recommended** when certain conditions met which indicate increased risk of suspected mosquito-borne transmission in a defined geographic area
  - If ZIKV-reactive donation identified and local transmission is possible (immediate trigger if in prior areas of increased risk; investigation if not)
  - If CDC announces increased risk in an area
  - MP NAT may resume if reactive donation not due to local mosquito-borne transmission, or no cases in 14 days and CDC removes risk designation

Proposals for the Committee

- FDA seeks advice from the Committee on three proposed testing strategies to be presented today.
  1. No policy change; continue universal testing for ZIKV by MP or ID NAT
  2. Regional testing for ZIKV with MP or ID NAT; with considerations for regional options
  3. Eliminate all testing for ZIKV

Today's Topics and Speakers

- Update on the Current Status of the ZIKV Epidemic
  - Marc Fischer, MD, MPH -- CDC
- AABB Biovigilance Network
  - Srijana Rajbhandary, MPH -- AABB
- Questions for the Committee
  - David A. Leiby, PhD -- CBER, FDA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