Impact of ZIKA virus (ZIKV) risk on public Cord Blood Banking

NATIONAL CORD BLOOD PROGRAM

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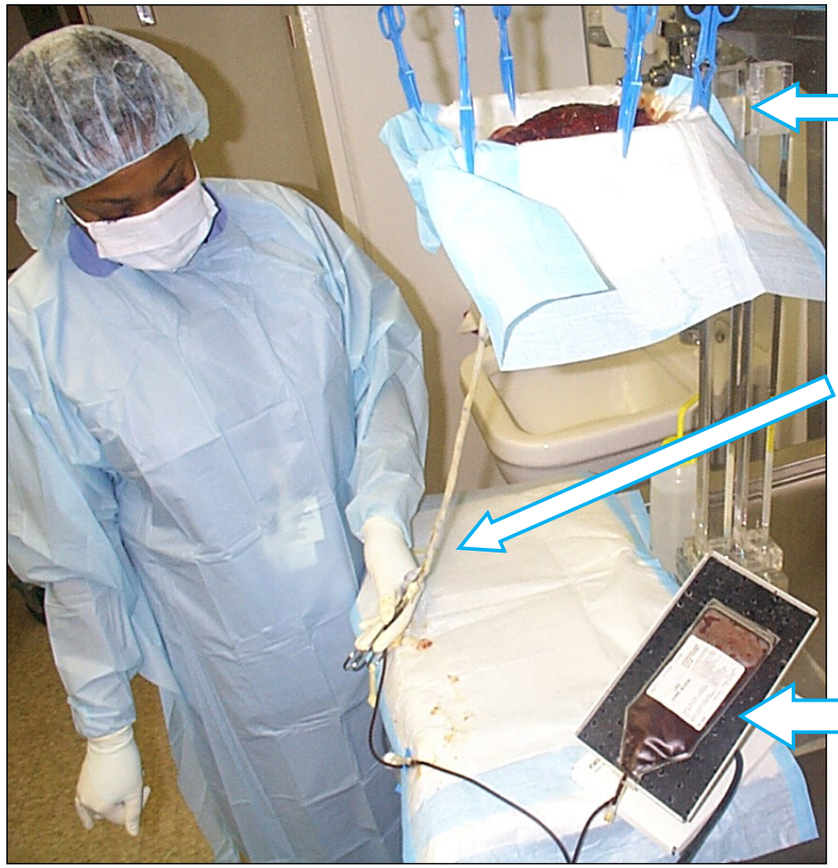
NCBP Procedures: Cord Blood Collection and Evaluation of Mother



Placenta

Umbilical Cord

Cord Blood Unit (CBU)

Time from collection to completion of processing: maximum 36 hours

Two-part Informed Consent at collection

Part I: Permission to review maternal record and collect CB

Harvest CB → TNC → clinical CBU

Total Nucleated Cell Count

Part II: Donation Informed Consent, and

- Maternal blood sample
- Maternal Questionnaire (details on risk factors)
- Detailed Review of Medical Records (mother and infant)

NCBP Procedures: Donor Eligibility Assignment and Medical Evaluation

CBU considered for evaluation are from asymptomatic mothers and newborns with no findings associated with ZIKV

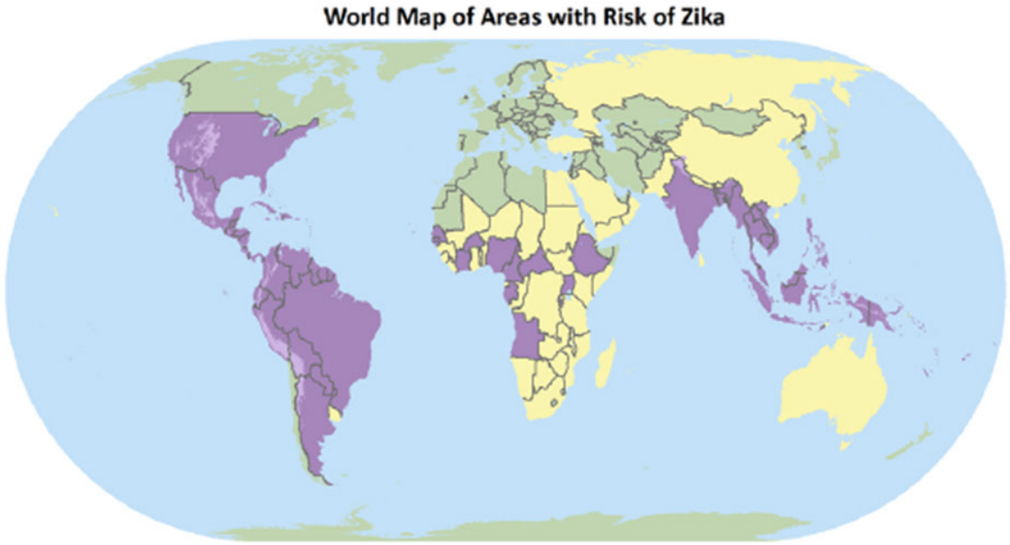
- Maternal information is evaluated by electronic script to identify risk factors
- Maternal information and IDMs are reviewed by medical staff (2 separate reviews) for risk assessment and eligibility assignment (FDA Guidance)
- Donor infant follow-up questionnaire is sent to mother (1 year) - review

CBU from ineligible donors:

- cannot be licensed
- cannot be included in the NCBI
- can be used for transplantation under Urgent Medical Need

Questions to capture risk for ZIKV
~~Positive ZIKV test~~
~~Mother with Diagnosis of ZIKV~~
Travel history (MOB alone or with FOB)
Contact with person at risk
Domestic travel one parent or both

CDC map: Geographic areas at increased risk for Zika virus transmission through blood or tissue donation



Map Legend

- Country or territory with current Zika outbreak[1]
- Country or territory that has ever reported Zika cases[2] (past or current)
- Areas with low likelihood of Zika infection because of high elevation (above 6,500 feet/2,000 meters)
- Country or territory with mosquito[3] but no reported Zika cases[2]
- Country or territory with no mosquitoes[3] that spread Zika

[1] No areas are currently reporting Zika outbreaks

[2] Locally acquired, mosquito-borne Zika cases

Areas with Risk of Zika

Africa: Angola, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Ethiopia, Gabon, Guinea-Bissau, Ivory Coast, Nigeria, Senegal, Uganda

Asia: Bangladesh, Burma, Cambodia, India, Indonesia, Laos, Malaysia, Maldives, Philippines, Singapore, Thailand, Vietnam

The Caribbean: Anguilla, Antigua and Barbuda, Aruba, Bahamas, Barbados, Bonaire, British Virgin Islands, Cayman Islands, Cuba, Curacao, Dominica, Dominican Republic, Grenada, Guadeloupe, Haiti, Jamaica, Martinique, Montserrat, Puerto Rico, Saba, Saint Barthelemy, Saint Kitts and Nevis, Saint Lucia, Saint Martin, Saint Vincent and the Grenadines, Sint Eustatius, Sint Maarten, Trinidad and Tobago, Turks and Caicos, United States Virgin Islands

Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama

North America: Mexico, United States (Continental US)

The Pacific Islands: American Samoa, Cook Islands, Easter Island, Federated States of Micronesia, Fiji, French Polynesia, Marshall Islands, New Caledonia, Palau, Papua New Guinea, Samoa, Solomon Islands, Tonga, Vanuatu,

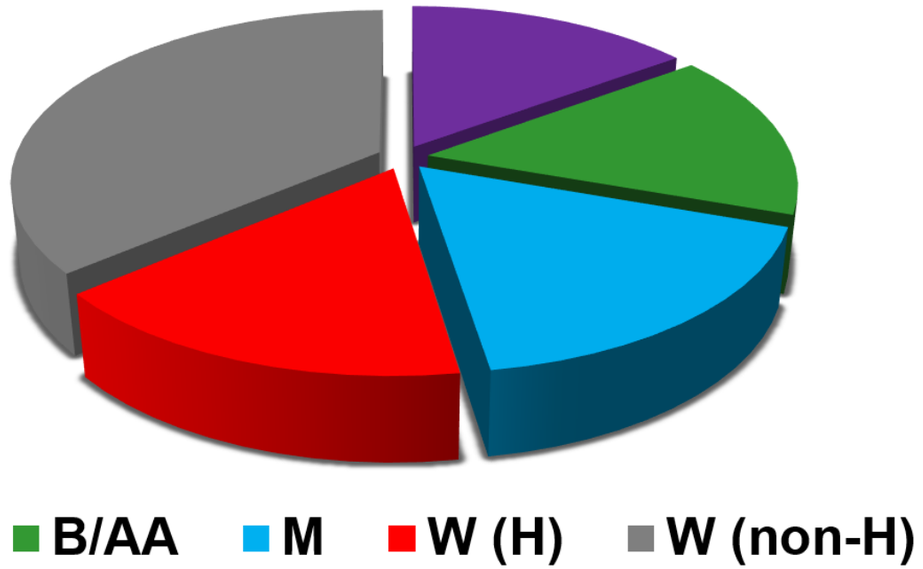
South America: Argentina, Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Peru, Suriname, Venezuela

Technical note: Because of variations in laboratory and surveillance capacity internationally, data are not available to define ...els of risk. CDC, the World Health Organization, and the European CDC have jointly reviewed the scientific literature.

Current as of: March 27, 2019

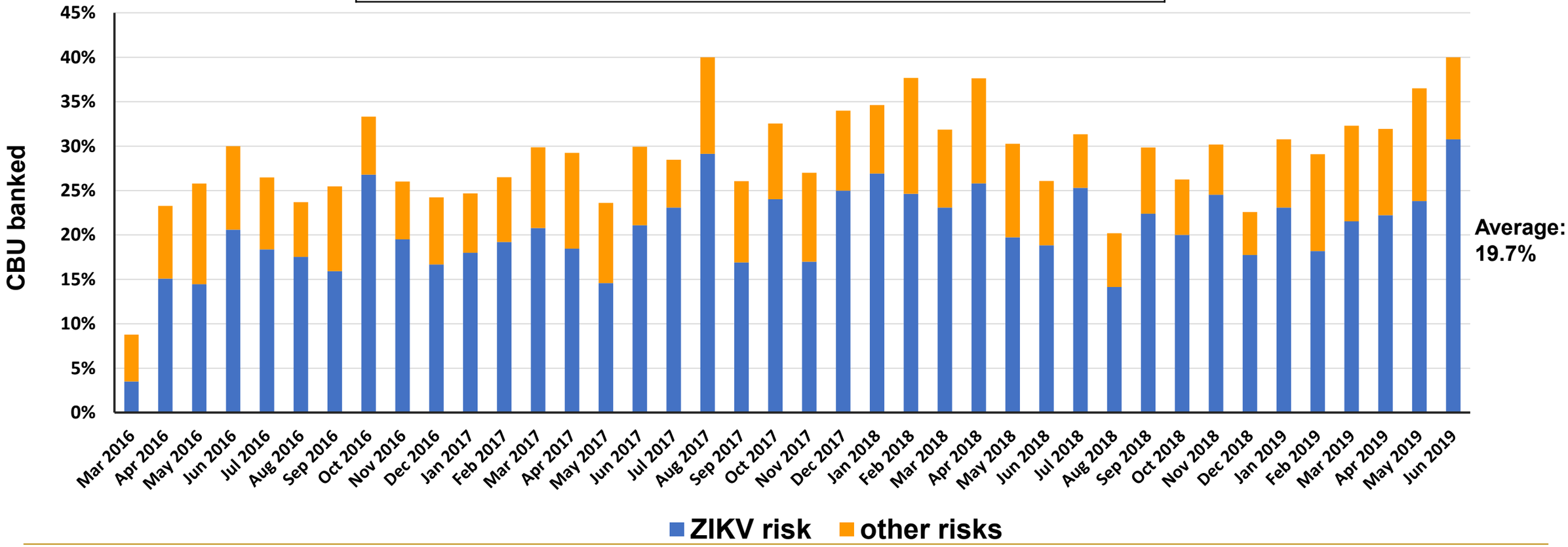
Race Diversity of banked CBU

Banking period March 2016 - June 2019						
CBU	**Asian**	**B/AA**	**Mix**	**W (H)**	**W (non-H)**	**All**
N	671	702	772	738	1636	4519
%	**15%**	**16%**	**17%**	**16%**	**36%**	



Incidence of ZIKV-risk on banked CBU for Period March 2016 - June 2019

CBU	2016	2017	2018	2019	Total	%
All banked CBU	1575	1652	920	372	**4519**	
Eligible/Licensed CBU	1190	1166	645	247	3248	71.9%
All ineligible CBU	385	486	275	125	1271	28.1%
ZIKV-ineligible CBU	262	342	201	87	**892**	**19.7%**



Race/Ethnicity Distribution of donors at risk for ZIKV

ZIKV risk - Donor Race	Asian	B/AA	Mix	W (H)	W (non-H)	All
ZIKV (% of total CBU banked)	19.4%	20.1%	22.2%	23.5%	17.0%	19.7%
ZIKV (% of ineligible CBU)	**63.1%**	**64.4%**	**74.7%**	**94.0%**	**65.1%**	**70.2%**

ZIKV risk - Collection site	VA	NY1	NY2	NY3	GA
Eligible/Licensed (% of total)	73.2%	67.2%	67.9%	71.5%	80.0%
ZIKV risk (% of total)	18.3%	21.6%	25.2%	19.0%	**5.3%**
other risk (% of total)	2.5%	**6.2%**	2.2%	1.5%	3.4%
other risk (% of total)	2.9%	1.3%	1.7%	3.1%	**9.2%**

Variability based on the target population served by the collection sites

Previous reports from our CB Bank on risk factors for donors of ethnic minorities:

- R. Ciubotariu et al, ZIKV Impact on Eligibility Determination of HCT/P Donors-Cord Blood (CB). **Transfusion 2017** (AABB meeting 2017).
- R. Ciubotariu et al, History of Hepatitis B infection is the most common risk factor impacting eligibility in minority donors for cord blood. **Blood** 2014 (ASH meeting 2014).

CBU donor status and potency evaluation

Donor status	CBU Potency Evaluation	
	TNC< 150x10^7	TNC> 150x10^7
Eligible/Licensed	1277 (42.8%)	1702 (57.1%)
ZIKV ineligible	402 (47.2%)	419 (52.7%)
Other risks - ineligible	128 (44.1%)	162 (55.9%)

No difference in post-processing TNC (p: 0.33); post-processing CFU (p: 0.33); trend for post-processing CD34+ counts (p: 0.03); no difference in CD34+/CD45+ viability, among eligible/licensed CBU, those with ZIKV-risk and those ineligible for other risks.

CBU released for Transplant

CBU released for transplant (of those banked: 03/2016-06/2019)	N
All CBU released	**57**
Eligible/Licensed CBU	**49**
Ineligible (all risks)	9
ZIKV risk	**5**
Anti-hepatitis B core Ab positive (HBV PCR and HbsAg negative	3
Mother's residency in Europe	1

International (N=3) and US (N=2) centers

Bank-initiated donor follow-up:

Of 715 infants with ZIKV-risk, 1-year follow-up response was received on 235 (33%).
All infants were reported healthy.

In summary…..

Our primary aim has always been the quality and safety of the CBU for clinical use

ZIKV risk, as assigned by current procedures, has:

- negative impact on donors of ethic minorities: **high**
- negative impact on CBU clinical use: ineligible donors, “uncertainty” regarding the risk
- negative impact on growth of the NCBI: these CBU are not included
- negative impact on public CB banking: increases indirectly banking costs and operational challenges
- negative impact on the social value of CB particularly for ethnic minorities
- no FDA-approved test for ZIKV for HCT/P donors

Is it time to reconsider the regulatory framework?

- **What is the risk of exposure now?**
  Countries at risk as per CDC data are those that had outbreaks at any time
- **How can we evaluate accurately the risk of transmission to the newborn?**
  Other testing options? test with assays under IND?
  Infant donor follow-up; “retrospective clearance” of the infant donor?
- **How do the changes in the overall incidence/prevalence of ZIKV and experience from blood donors help evaluate the risks?**