



VACCINE DEVELOPMENT FOR ZIKA VIRUS

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Resilient People. Healthy Communities. A Nation Prepared.
PR: Resilient People. Healthy Communities. A Nation Prep

Photo credit: CDC/James Gathany

Zika virus

- Zika virus belongs to the family Flaviviridae
- Other flaviviruses include:
 - Dengue, West Nile, yellow fever, Japanese encephalitis
- Enveloped viruses containing positive-strand RNA genome
- First isolated in Zika forest in 1947 with limited human infections in Africa and SE Asia through 2006
- 2007 emerged in Micronesia
- 2013-14 emerged in French Polynesia (>30,000)



Spread of Zika virus in 2015-2016

Countries and territories with confirmed cases of Zika virus (autochthonous transmission) in the Americas, 2015-2016.



Updated as of
Epidemiological Week 4
(Jan 24-30, 2016)

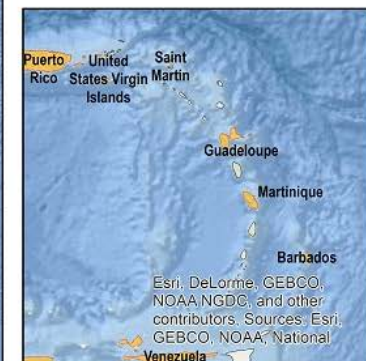


Legend

Countries with confirmed cases of Zika virus

Orange box: Countries with confirmed cases

White box: Country limits



Data Source:
Reported from the IHR National Focal Points
and through the Ministry of Health websites.

Map Production:
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Travellers from Brazil



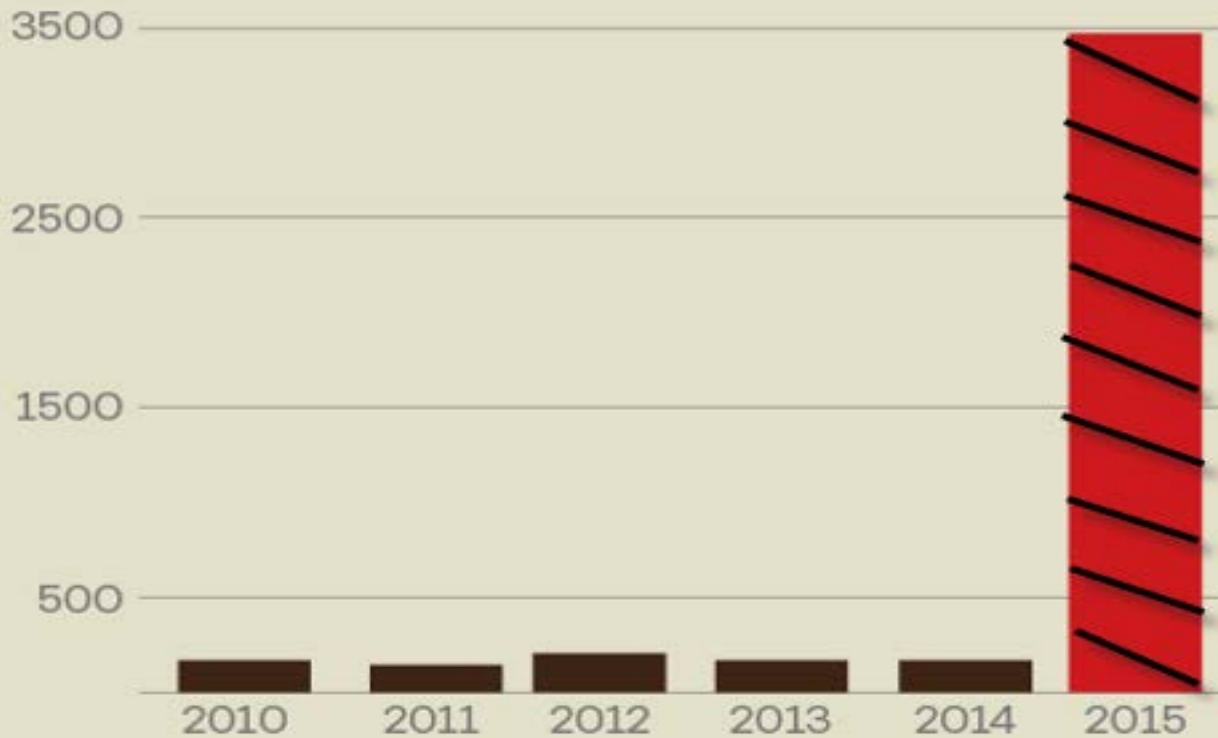
Clinical symptoms of Zika virus

- ~80% of cases could be asymptomatic
- Disease symptoms are similar to dengue and chikungunya including a fever, rash, conjunctivitis, and joint pain
- Severe disease outcomes requiring hospitalization and fatalities are rare
- Duration is ~4-7 days



Microcephaly in Brazil

Brazil saw 20 times more microcephaly cases in 2015 than normal



SOURCE: Brazil Ministry of Health

Vox

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Zika vaccine need

- There is evidence suggesting Zika virus causal association with GBS in adults, microcephaly, and other central nervous system malformations in fetuses
- There is growing evidence of potential complications attributable to Zika virus infection in pregnant woman
 - Cases of miscarriage and stillbirth with evidence of Zika virus infection in the fetus and newborn
 - Evidence of Zika virus passing the placenta to infect the fetus
- There is evidence of Zika virus in donated blood
- This is potential for sexual transmission of Zika
- Zika virus has demonstrated high attack rates and rapid global spread

There is currently no vaccine available to prevent infection from Zika virus



Zika vaccine development

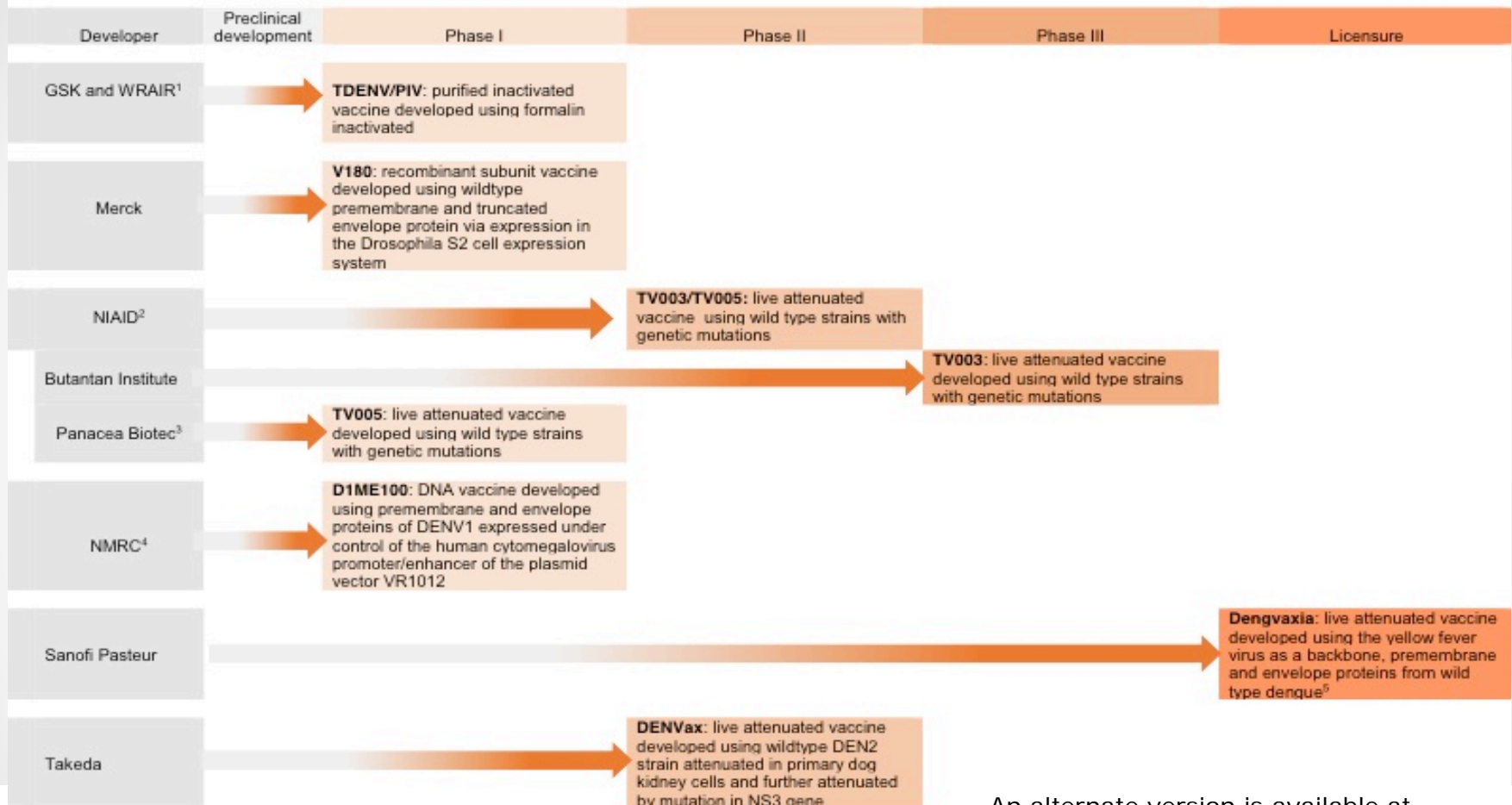
There is currently no vaccine available to prevent infection from Zika virus, however,

- Vaccine for other flaviviruses have been developed and used for over 70 years
 - Japanese encephalitis vaccine have been available since 1930s and have been made in numerous forms, including live attenuated virus, whole inactivated virus, recombinant and chimeric viruses
 - Yellow fever vaccine was licensed over 60 years ago – 17D live attenuated virus that is still in use today
- Active development programs for dengue and West Nile vaccines have been ongoing for over 30 years, exploring a variety of vaccine platforms to develop vaccines for these flaviviruses
- Experiences gained and vaccine platforms developed for other flaviviruses could be leveraged for Zika vaccine development



Dengue vaccine development

Dengue Vaccine Candidates in Clinical Development*



*Table last updated January 4, 2016

¹ GlaxoSmithKline and Walter Reed Army Institute Research.

² National Institute of Allergy and Infectious Diseases, US NIH: National Institutes of Health. NIAID licensed its strains to several [developing country manufacturers](http://www.denguevaccines.org/sites/default/files/Dengue%20Vaccine%20Candidates%20-%203316%20-%20DVI.pdf) on a non-exclusive basis.

³ Both Butantan Institute and Panacea Biotech use NIAID vaccine formulation.

⁴ US Navy Medical Research and Development.

⁵ Dengvaxia has been approved by Mexico, the Philippines and Brazil for 9 to 45 year olds living in dengue endemic areas.

An alternate version is available at <http://www.denguevaccines.org/sites/default/files/Dengue%20Vaccine%20Candidates%20-%203316%20-%20DVI.pdf>

Zika Virus Vaccine Landscape

Vaccine Platform

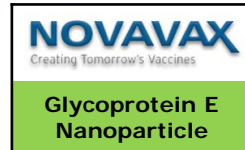
Discovery/*in vitro*

Pre-Clinical

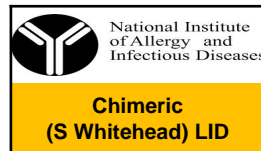
Clinical

Non-Clinical Studies

Recombinant Subunit



Live Attenuated



Plasmid DNA



Viral Vector

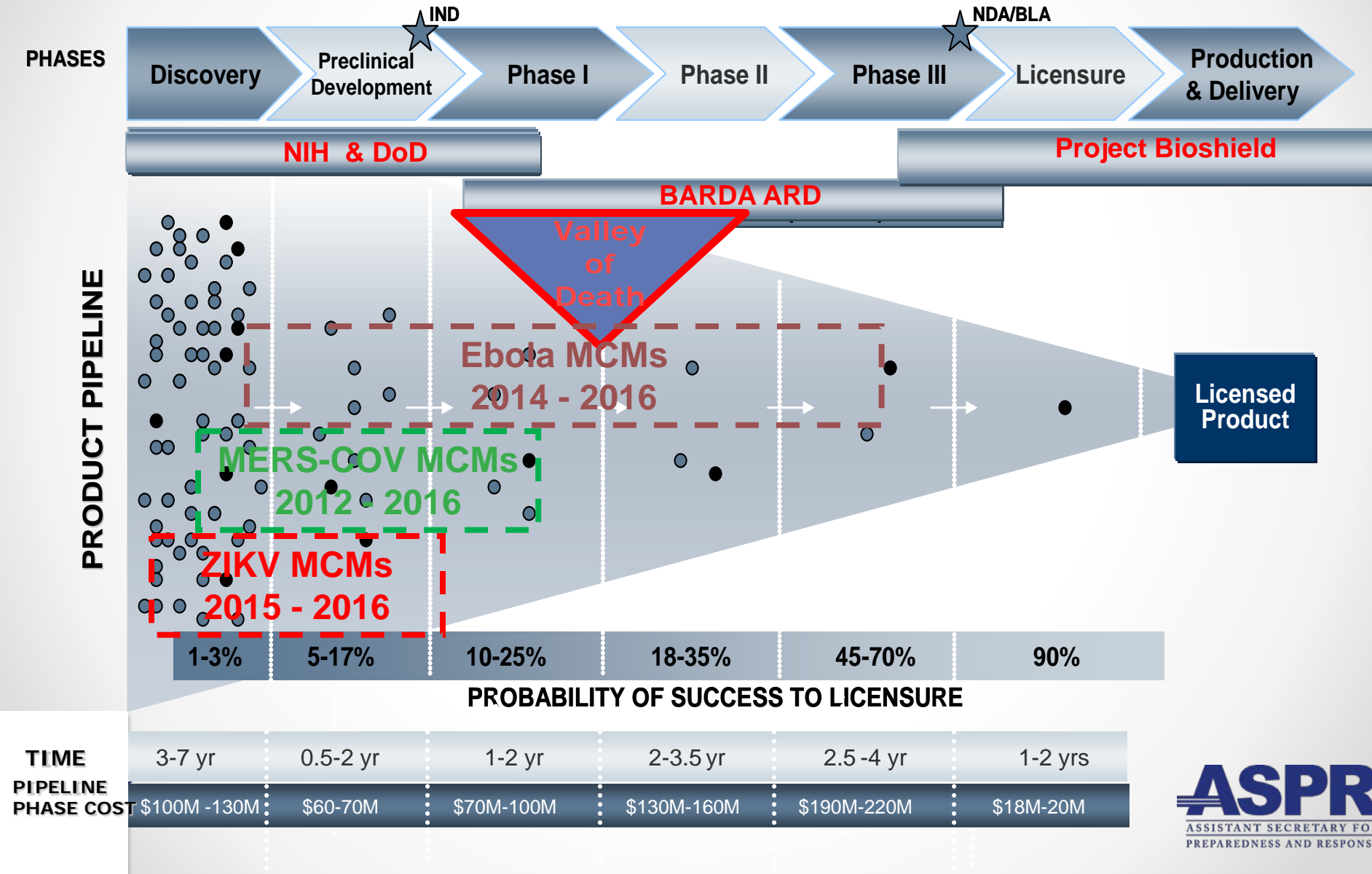


An accessible version can be found on page 17

February 01, 2016



Vaccine & Drug Development is still Expensive, Risky and Lengthy



Zika virus vaccines R&D

Key Questions/Concerns

- Safety Concerns
 - Pre-existing immunity to Zika, Yellow Fever, Dengue, and vaccine platforms
 - Is there a potential for antibody dependent enhancement?
- Intended Usage
 - General usage (GUP) and post-exposure (PEP) prophylaxis
 - Special populations – Pregnant women, WoCBA, infants, children
- Vaccine Properties
 - Vaccine components (e.g. E protein, whole virus, adjuvants, other viruses)
 - Level and type of elicited immunity
 - Kinetics of vaccine immunity
 - Duration of immunity (Heterologous Prime/Boost Approach)
 - Routes of administration
 - Platform technology maturity
 - Manufacturing process maturity (potency assays, vaccine stability)
- Zika virus natural and adaptive immunity in animals and humans
 - Correlates of protective immunity
 - Immunogenicity and protection study design

Assays & reagents



Upcoming workshops

- 2-5 February 2016, Nicaragua: Sub-regional Laboratory Training Workshop for Zika detection and sub-regional training workshop on *Aedes aegypti* control
- 15 February 2016, Puerto Rico: Experts Meeting on Zika regional laboratory surveillance
- 16-17 February 2016, Puerto Rico: WHO Dengue Collaborating Centers Meeting
- 18-19 February 2016, Puerto Rico: Meeting of the Latin American Network on Arboviruses Diagnostic (RELDA)
- 1-2 March 2016, Washington DC: PAHO Meeting on the Zika virus research agenda and its public health implications in the Americas
- 28-29 March 2016, Washington DC: HHS Stakeholders meeting on Zika virus and Medical Countermeasures



Summary

- We are at the forefront of this outbreak situation and many questions remain unanswered
 - Careful prioritization and coordination is needed to address these questions
 - International collaborations will be critical to accelerating the response
- Zika viruses will continue to spread throughout the Americas and remain a human health threat
- WHO declared a Public Health Emergency of International Concern on February 1, 2016
 - Urgent Priority must be considered to better understand the potential link between Zika virus and congenital malformations and other neurological disorders
 - Diagnostics must be developed to be able to detect Zika virus infection to contribute to surveillance and disease mitigation
 - Systems must be developed and validated to ensure safety of blood supply
 - Risk communications must be developed and disseminated
- There are currently no commercially approved vaccines or therapeutics for Zika
- Vaccines development for other flaviviruses should be leveraged to potentially accelerate the Zika virus vaccine
 - Caution should be given to safety concerns observed from other flavivirus vaccine efforts
 - Careful consideration should be given to the development of vaccines indicated for pregnant women, women of childbearing age, neonates and children



Contact us

- Request a Tech Watch meeting through www.medicalcountermeasures.gov
 - Contact Jonathan Seals, Director Strategic Science and Technology Division, jonathan.seals@hhs.gov
- BARDA Broad Agency Announcement
 - [BAA-16-100-SOL-00003](#) will support innovation through development of platform technologies that enhance capabilities for development and manufacturing of MCMs.
 - Technical Point of Contact: Mark Craven; mark.craven@hhs.gov
- NIH Federal Funding Opportunity
 - [NOT-AI-16-026](#) will support high-priority Zika virus research areas detailed in the solicitation





Boston Globe
Silvia Izquierdo/AP

Zika Virus Vaccine Landscape

Vaccine Platform	Discovery / in vitro		Pre-Clinical	Clinical	Non-Clinical
Recombinant Subunit	GlycoproteinE Nanoparticle				
Live Attenuated	Chimeric (S Whitehead) LID				
Plasmid DNA	DNA	DNAVRC			
Viral Vector	VSV				