OVERVIEW OF CHIKUNGUNYA AND CHIKUNGUNYA VACCINES

Susan Hills, MBBS, MTH
CDC Lead, Chikungunya Vaccines Work Group
Arboviral Diseases Branch
Division of Vector-Borne Diseases
Fort Collins, Colorado

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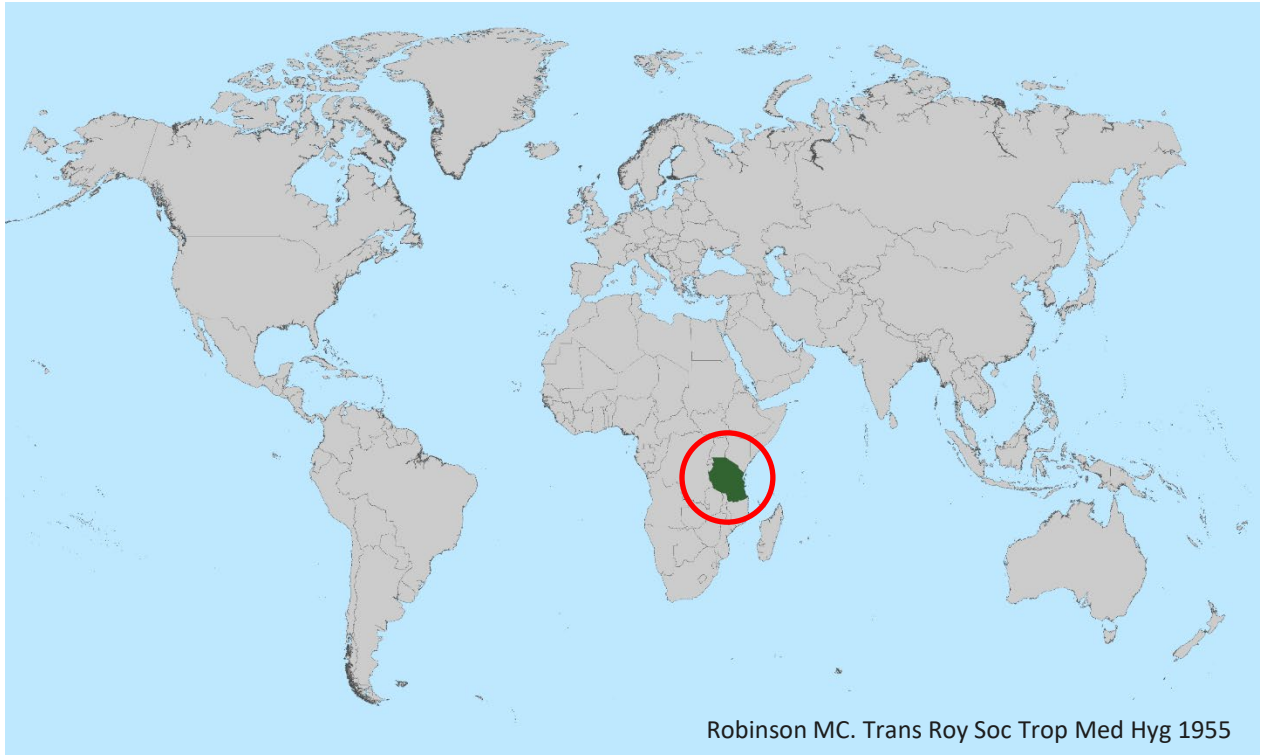
Chikungunya virus disease

- Mosquito-borne disease caused by an alphavirus
- Clinically characterized by acute onset of fever and often severe polyarthralgia
- Has caused large outbreaks with high attack rates
- Outbreaks have occurred in Africa, Asia, Europe, Americas, and islands in the Indian and Pacific Oceans

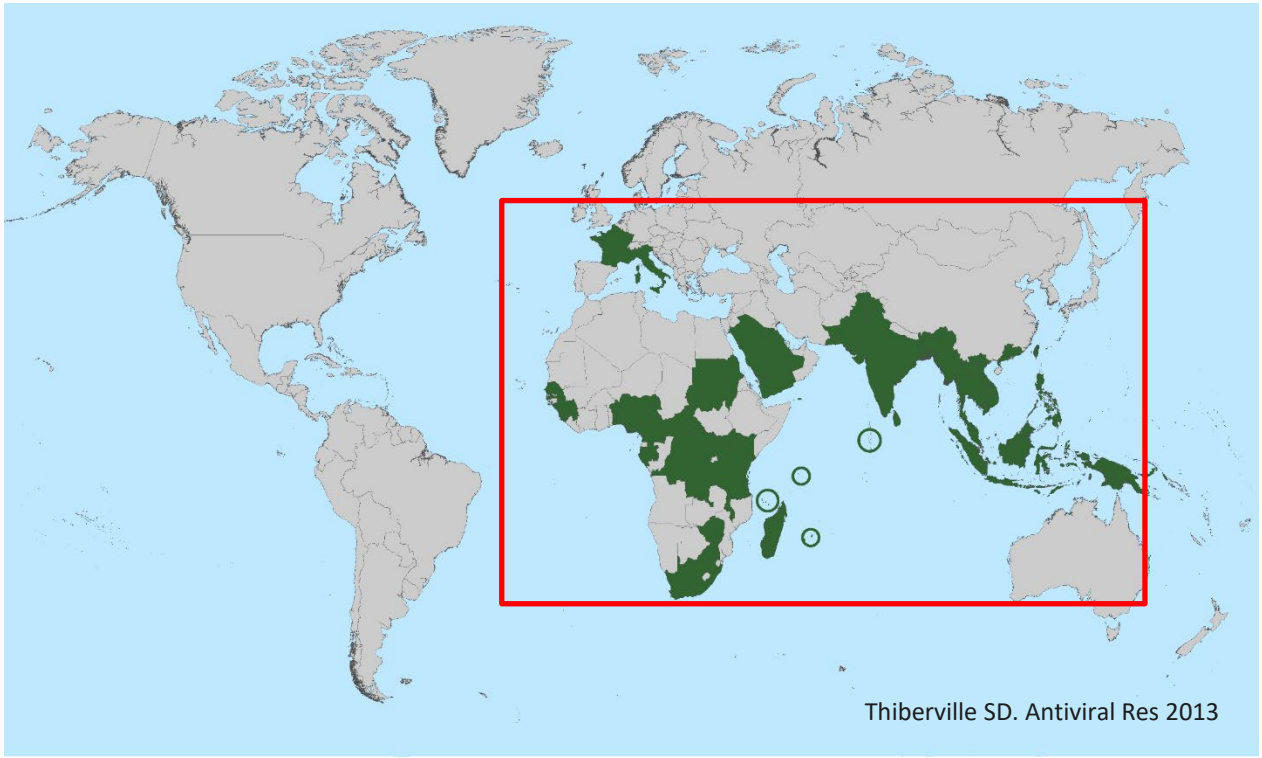
Source: PAHO, 2011. www.paho.org

Chikungunya virus first identified during outbreak of fever and joint pain in Tanzania, 1952–1953



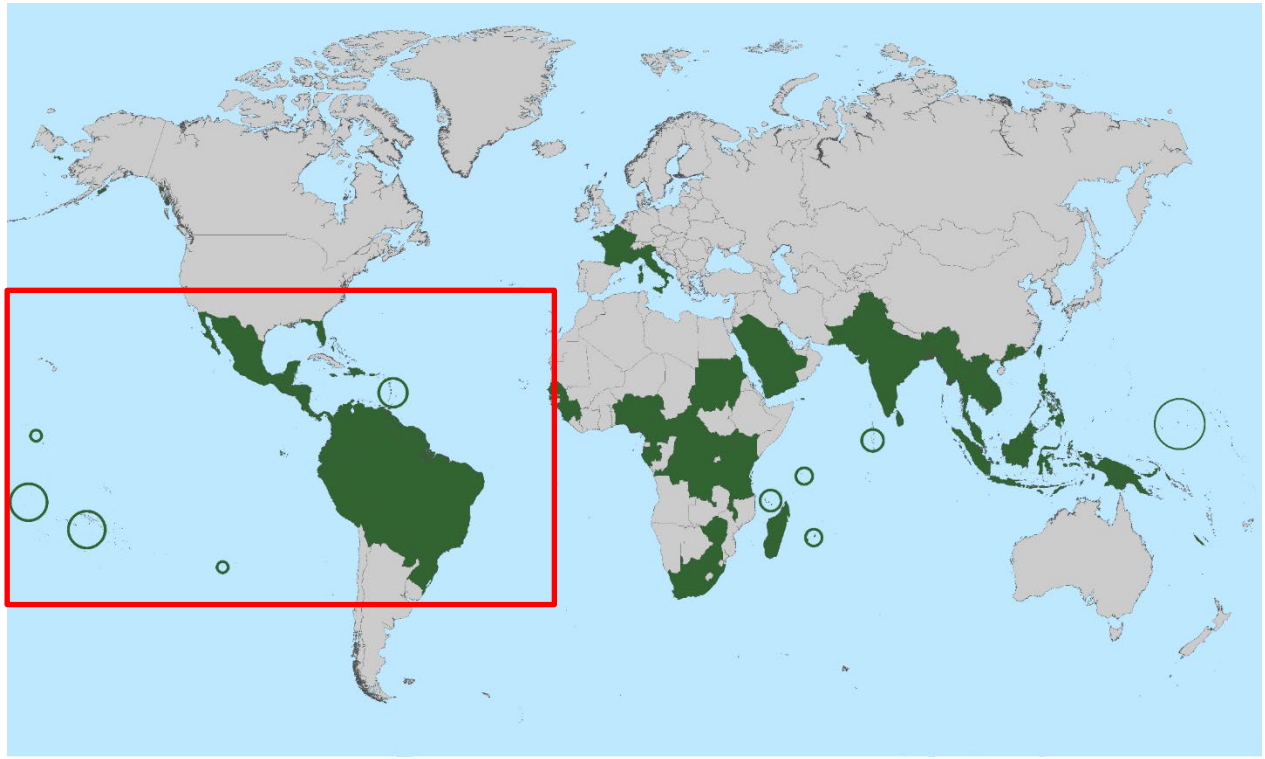
Robinson MC. Trans Roy Soc Trop Med Hyg 1955

Expansion in area of transmission in Africa, Asia and the Indian Ocean, 1953–2012



Thiberville SD. Antiviral Res 2013

Chikungunya virus introduction and spread in the Americas, 2013–2015



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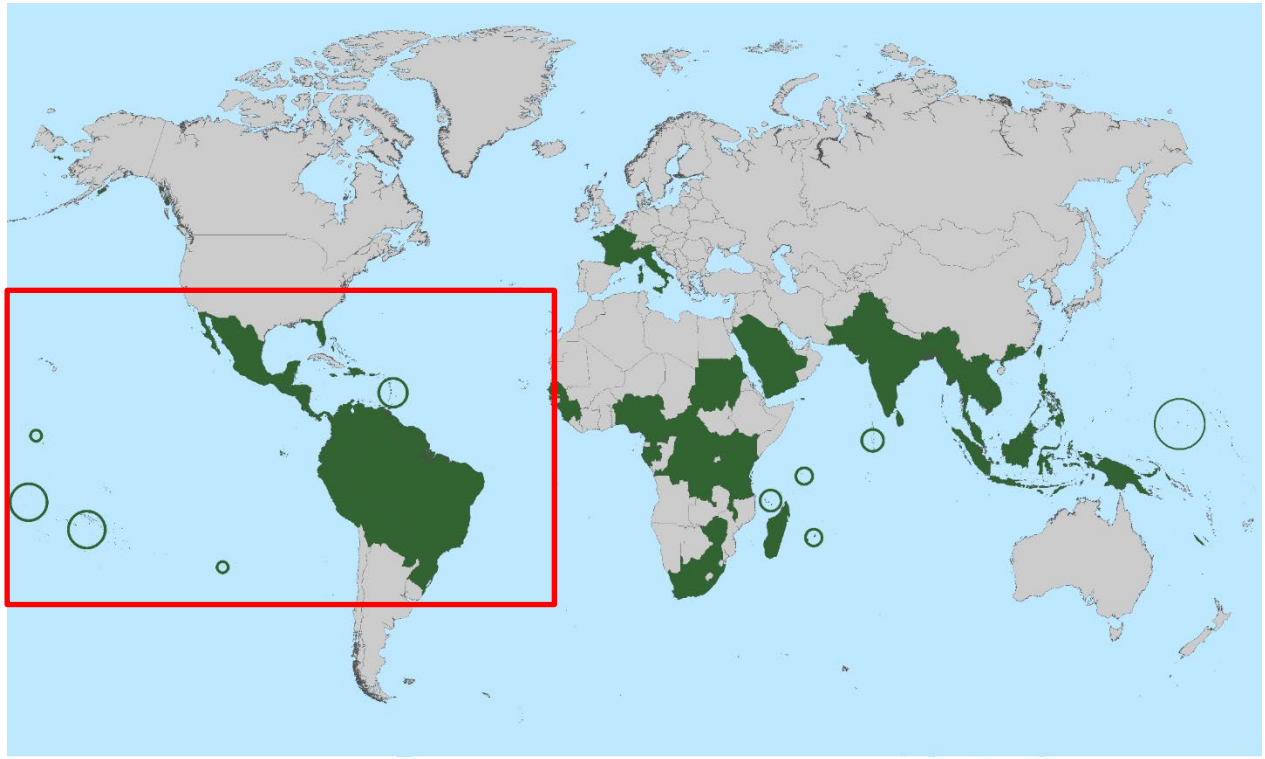
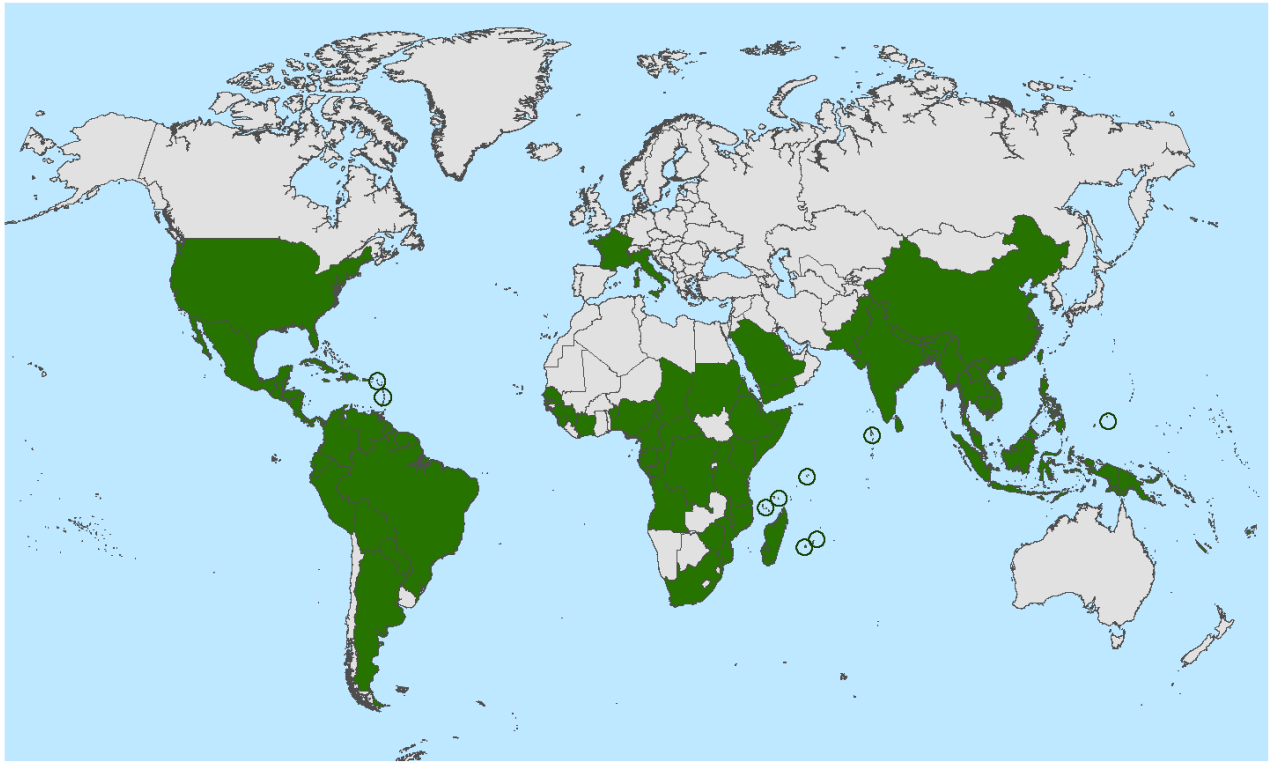


Outbreaks in US territories

Limited local transmission in Florida and Texas

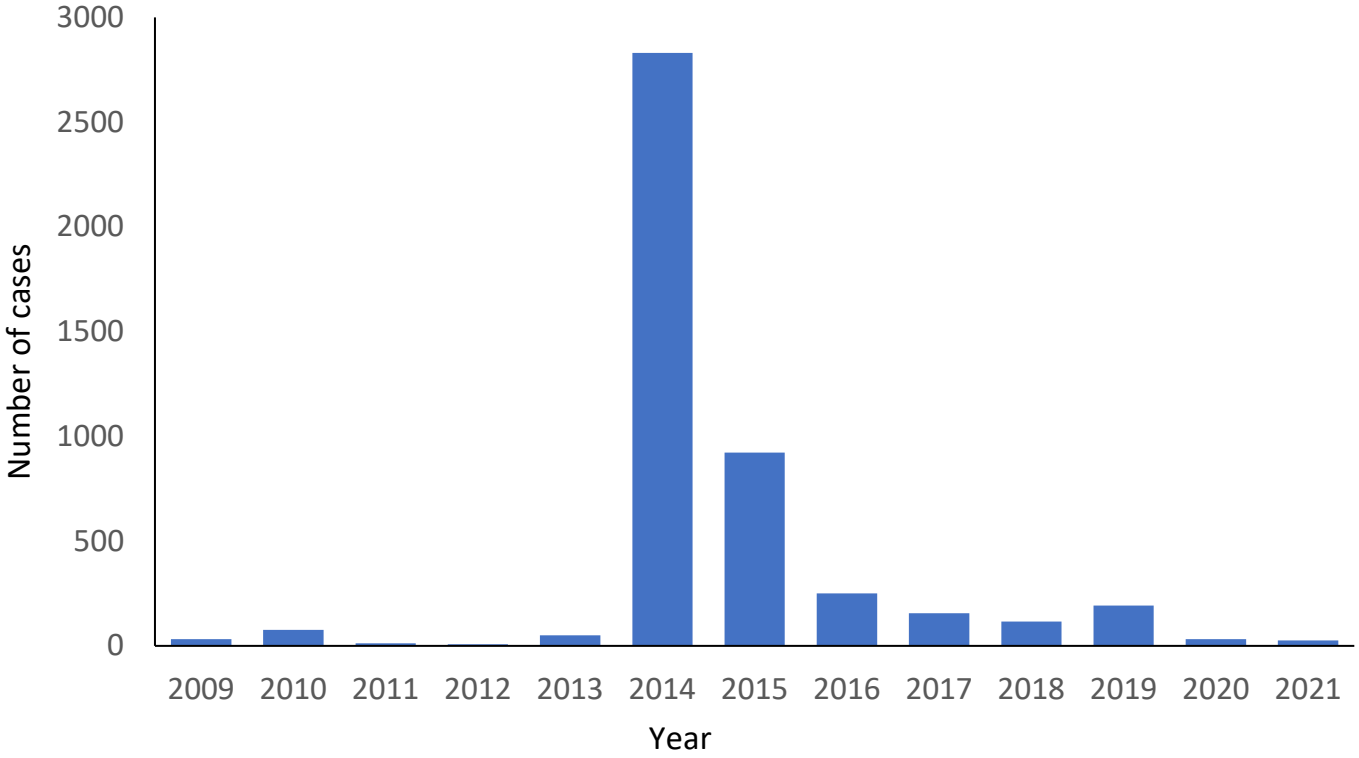
https://www.cdc.gov/chikungunya/geo/index.html

Countries and territories with past or current transmission of chikungunya virus, 2022



https://www.cdc.gov/chikungunya/geo/index.html

Chikungunya cases in US travelers, 2009–2021*



*Based on CDC laboratory and surveillance data

Mosquito vectors

Aedes aegypti

Aedes albopictus

- Daytime biters with peak activity dawn and dusk
- Lay eggs in containers that hold water

Other uncommon chikungunya virus transmission modes

Intrauterine

Intrapartum

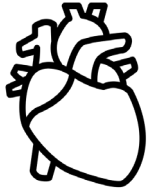
Needlestick injury

Laboratory exposure

Clinical features of chikungunya

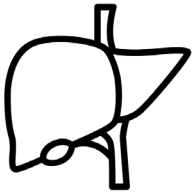
- Incubation period: 3–7 days
- Febrile illness with often severe arthralgia
- Multiple joints involved, typically bilaterally and symmetrically
- Arthralgia most common in hands and feet, can involve more proximal joints
- No specific antiviral treatment

Rare complications

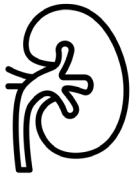


Myocarditis

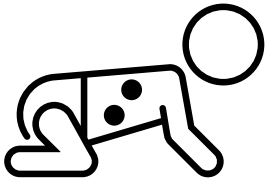
Ocular disease



Hepatitis



Acute renal disease



Severe bullous lesions

Neurologic disease

Risk factors for severe disease

- Age >65 years
- Underlying medical conditions (e.g., hypertension, diabetes, heart disease)
- Intrapartum transmission
  - Neonatal complications can include neurologic, myocardial, hemorrhagic symptoms

Outcomes

- For many, symptoms resolve in 7–10 days
- Some have ongoing joint pain and prolonged fatigue for months or years
- > 50 studies with variability in results based on
  - Study methodology
  - Duration of follow up
  - Symptom ascertainment
  - Type of cohort
  - Demographics

Risk factors for prolonged symptoms

- Older age
- Severity of acute illness
- Pre-existing joint disease

Prevention of chikungunya

No vaccine currently licensed

Chikungunya vaccines (Phase III clinical trials)

Manufacturer	Type	Schedule and administration	Status	Notes
Valneva	Live attenuated	1 dose IM	- Phase III in adults ≥18 years completed - Phase III in adolescents (12–17 years) commenced January 2022 - Lot-to-lot consistency completed	CEPI co-funding
Emergent BioSolutions	Virus-like particle	1 dose IM	- Phase III in 12–65 years commenced October 2021 - Phase III in ≥65 years commenced May 2022	

Abbreviations: IM-Intramuscular; BLA-Biologics License Application; FDA-Food & Drug Administration; CEPI-Coalition for Epidemic Preparedness Innovations

Other chikungunya vaccines with support from CEPI

Manufacturer	Type	Schedule and admin		Status	Notes
Merck	Live attenuated measles-vectored	1 dose + booster	-	Phase ll completed	CEPI co-funding
International Vaccine Institute/ Bharat Biotech	Inactivated whole virus	2-dose	-	Phase ll/lll commenced August 2021	CEPI co-funding

Abbreviations: CEPI - Coalition for Epidemic Preparedness Innovations

Valneva's chikungunya vaccine

- Rolling BLA submission to FDA initiated August 2022
- FDA has given Breakthrough Therapy designation which allows request for priority review
- Licensure expected during 2023
  - Initial indication for ages ≥18 years

Summary of chikungunya and chikungunya vaccine

- Mosquito-borne disease that can cause large outbreaks
  - In United States, previous outbreaks in territories and limited local transmission in states (i.e., Florida, Texas)
  - For travelers, greatest risk during outbreak periods
- Clinical presentation with fever and severe polyarthralgia with risk for long-term joint symptoms
- No chikungunya vaccine previously licensed and no existing ACIP chikungunya vaccine recommendation
  - Work Group discussing potential recommendations for travelers and residents of U.S. territories and states with, or at risk of, transmission

Accelerated Approval Pathway for Chikungunya Vaccines

FDA approval pathways

- Traditional approval
- Accelerated approval
- Animal rule

Traditional approval: Is it possible for chikungunya vaccine?

- Efficacy study?
  - Outbreaks are unpredictable and duration can be short so logistically challenging
- Human challenge study?
  - Some chikungunya patients get persistent arthralgia and no treatment available
- Immunogenicity study?
  - Animal and human studies have suggested protection mediated by chikungunya virus neutralizing antibodies, but no established protective antibody titer

Yang et al. Vaccine 2017. Regulatory considerations in development of vaccines to prevent disease caused by chikungunya virus

Accelerated approval

- Used for products for serious conditions and that fill unmet medical need
- Effectiveness demonstrated by clinical trials showing vaccine has effect on surrogate endpoint reasonably likely to predict clinical benefit
- Post-licensure requirement for controlled trials to confirm clinical benefit

Accelerated approval for chikungunya vaccine

- Approach for accelerated approval of chikungunya vaccines endorsed at FDA Vaccines and Related Biological Products Advisory Committee (VRBAC) meeting, November 2019[1]

- Marker of protection being used for accelerated approval based on neutralizing antibody titer estimated from validated non-human primate model

- Vaccine effectiveness will need to be confirmed in post-licensure field study

1. Vaccines and Related Biological Products Advisory Committee (VRBAC) meeting, November 8, 2019 (https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-november-8-2019-meeting-announcement)

Thank you