Journey Into the Tropics:

The BIOFIRE® FILMARRAY® Tropical Fever Panel and BIOFIRE® Global Fever Special Pathogens Panel in Focus

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AGENDA

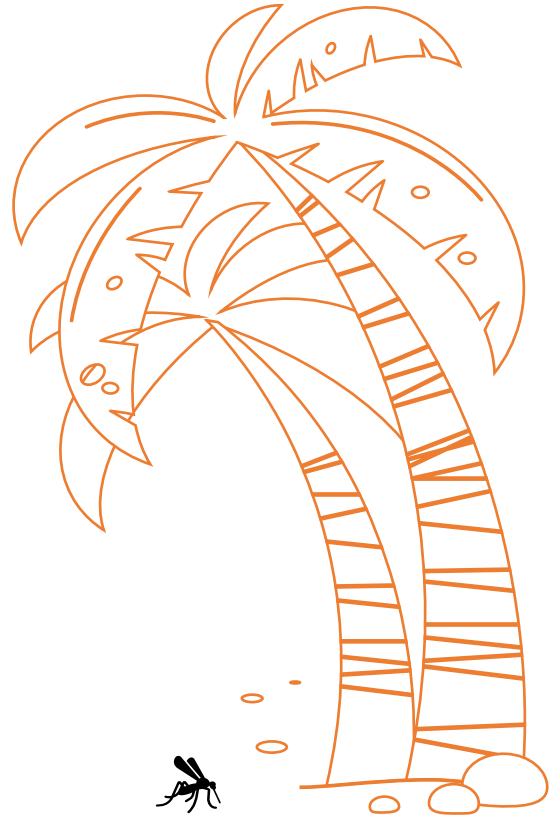
- What is a Tropical Fever?
- BIOFIRE® Tropical Fever Panel and BIOFIRE® Global Fever Special Pathogens Panel Overview
- Pathogen Specific Information
  - Chikungunya
  - Dengue
  - Leptospirosis
  - Malaria

WHAT IS A TROPICAL FEVER?

TROPICAL FEVER

Febrile infections prevalent or unique to tropical and subtropical regions. May overlap with multiple clinical syndromes.

Causes	**Multiple different bacteria, parasites, and viruses**
Transmission	**Insect vectors, contaminated water/food**
Common Types	**Dengue, malaria, chikungunya, leptospirosis**
Symptoms	**Range from mild/asymptomatic to severe with high risk of fatality**



Centers for Disease Control and Prevention. *Yellow Book: Health Information for International Travel*. Atlanta, GA: US Dept of Health and Human Services; 2024

CHALLENGES IN TROPICAL FEVER DIAGNOSIS

Laboratory

- Time Consuming
- Limited Testing Options
- Limited Resources
- Complex Test
- Batch Testing

Clinician

- Overlapping Symptoms
- Interpretation of Results
- Selection of Appropriate Test
- Time to Results

Patient

- Inappropriate Treatment
- Unnecessary Isolation
- More Invasive Procedures
- Longer Length of Stay

1. Guerrant RL *et al*. *Clin Infect Dis.* 2001;32(3):331–351.
2. LaFond LF *et al*. *Am J Trop Med Hyg.* 2013;89(5):892–896.
3. Riddle MS *et al*. *Am J Gastroenterol.* 2016;111(5):602.

GLOBAL BURDEN OF TROPICAL FEVER

Tropical Fever, including Malaria, Chikungunya, Dengue, and Leptospirosis:

Affect over 100 countries worldwide

Cause over 316 million infections annually

Result in more than 500,000 unnecessary deaths annually

Approximately **76% of all malaria deaths** are in children under 5 years old

World Health Organization. *A Global Brief on Vector-Borne Diseases*. Geneva, Switzerland: WHO Press; 2014

BIOFIRE® FILMARRAY ® TROPICAL FEVER PANEL

BIOFIRE® FILMARRAY® TROPICAL FEVER PANEL

BIOFIRE® TROPICAL FEVER PANEL
1 PCR TEST. 6 TARGETS. ~50 MIN

VIRUSES
Chikungunya
Dengue (serotypes 1,2,3 and 4)

BACTERIA
Leptospira spp.

PROTOZOA
Plasmodium spp.
P. falciparum
P. vivax/ovale

SUPPORTED BIOFIRE SYSTEMS

BIOFIRE® FILMARRAY® TORCH

BIOFIRE® FILMARRAY® 2.0

NOT AVAILABLE ON BIOFIRE® SPOTFIRE®

OVERALL TROPICAL FEVER PANEL PERFORMANCE
(EDTA whole blood specimens)[1]

95.1%
PPA
(Positive Percent Agreement)

99.8%
NPA
Negative Percent Agreement)

SAMPLE REQUIREMENTS

Human Whole Blood collected in EDTA tubes

Minimum Sample Volume: **~0.2 mL (200 µL) of whole blood**

[1] The performance of the BIOFIRE FILMARRAY GF Panel was evaluated only with human whole blood collected in EDTA

BioFire® FilmArray® Tropical Fever Panel – Instructions for Use. Salt Lake City, UT: April 2025.

BIOFIRE® FILMARRAY® TROPICAL FEVER PANEL

Organism	No. of Assays	Assay Interpretation Rules
Bacteria		
Leptospira spp.	1	Positive = Detected
Viruses		
Chikungunya virus	2	Any Positive = Detected
Dengue virus	5	Any Positive = Detected
Protozoan		
Plasmodium spp.	1	Positive = Detected
Plasmodium falciparum	1	Positive = Detected
Plasmodium vivax/ovale	1	Positive = Detected

See Instructions for Use for additional information about assays and *Plasmodium* reporting

BIOFIRE®
GLOBAL FEVER SPECIAL PATHOGENS PANEL

BIOFIRE® GLOBAL FEVER SPECIAL PATHOGENS PANEL

1 Test, 16 Pathogens, FDA Cleared

Pathogens Presumptively Identified

- *Bacillus anthracis*
- Crimean-Congo hemorrhagic fever virus
- *Ebolavirus* spp. (5 Species)
- *Francisella tularensis*
- Lassa virus
- *Marburgvirus*
- Yellow fever virus
- *Yersinia pestis*

Pathogens Identified

- Chikungunya virus
- Dengue virus (serotypes 1, 2, 3 and 4)
- *Leishmania* spp. that cause visceral leishmaniasis
- *Leptospira* spp.
- *Plasmodium* spp.
  - *Plasmodium falciparum*
  - *Plasmodium vivax/ovale*
- West Nile virus

Specimen(s)

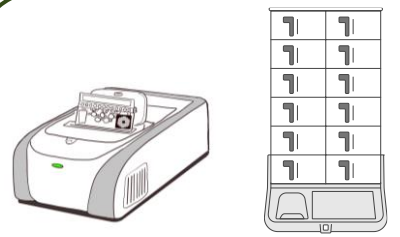
Whole Blood

Hands-on Time

2 minutes

Results

~ 50 Minutes



Instrument

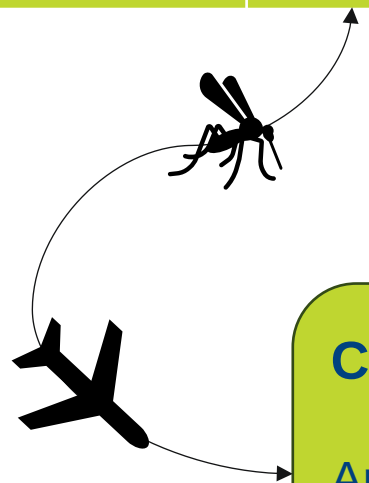
FilmArray 2.0 or Torch

CHIKUNGUNYA

CHIKUNGUNYA VIRUS IN THE UNITED STATES

- **Chikungunya virus disease cases reported to ArboNET- United States 2024**

Year	US States Locally Acquired	US States Travel-associated	US Territories Locally acquired	US Territories Travel-associated
2024	0	199	0	0



Cases in U.S travelers returning from India

Among the cases reported in 2024, CDC identified a higher-than-expected number of CHIKV cases among returning U.S. travelers from India

CDC. Chikungunya virus in the United States. 2025

CHIKUNGUNYA CLINICAL BACKGROUND

- Mosquito-borne viral disease
  - *Aedes aegypti & albopictus*
    - Same for dengue & zika
  - ssRNA virus (alphavirus genus)
- Africa, Asia, Americas, Europe, islands in Indian & Pacific oceans
  - 2014 outbreak in Florida & 2015 in Texas
  - No US acquired cases reported since 2019
- 1st approved vaccine (2023) IXCHIQ®
- Fun facts
  - First discovered in Tanzania in 1952
  - “to become contorted” in Kimakonde
  - “bent over in pain” in Makonde

(Ueslei Marcelino/Reuters)

Centers for Disease Control and Prevention. *Leptospirosis: Epidemiology and Clinical Presentation*. Atlanta, GA: US Dept of Health and Human Services; 2024.

CHIKUNGUNYA- SYMPTOMS & TREATMENT

- **Onset**:
  - Symptoms typically begin **4-8 days after exposure**
- **Most common symptoms**: Fever & severe joint pain
  - Joint pain usually lasts several days
  - Can persist for months or years
- May also have
  - Joint swelling, myalgias, headache, nausea, fatigue, rash
- Symptoms like dengue & zika
  - Easy to misdiagnose and likely under reported & diagnosed
- Severe symptoms & death rare
  - Most fully recover
  - Mortality 1 in 1000
- Infection = lifelong immunity
- **Treatment is supportive care**

Chikungunya rash., PAHO / Flickr cc

CLINICAL TESTING AND DIAGNOSIS OF CHIKUNGUNYA

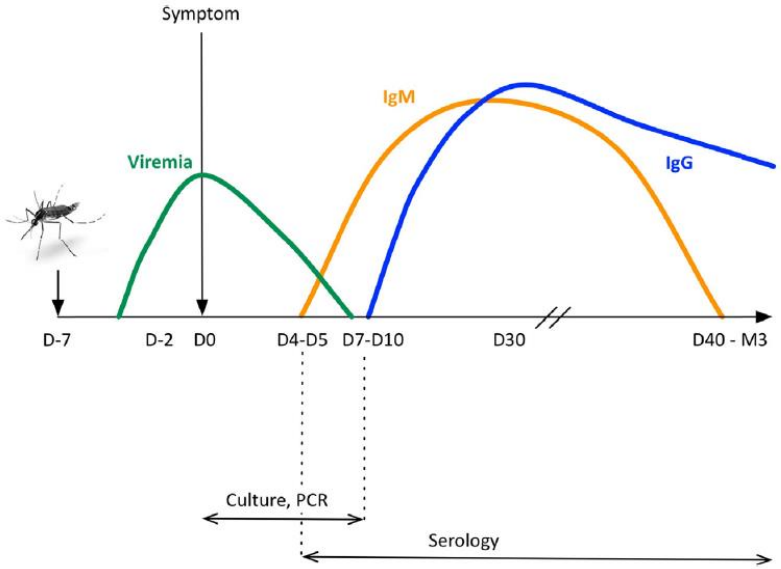
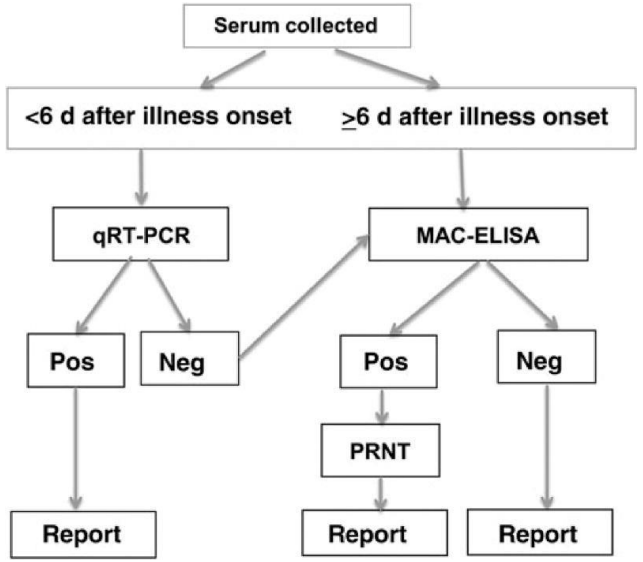


Fig. 2. Contribution of PCR and blood tests for the diagnosis of chikungunya, according to delay after infection (1).
Place de la PCR et de la sérologie dans le diagnostic du chikungunya en fonction du temps après l'infection.



PRNT = Plaque Reduction Neutralization Test

- **RT-PCR**: capable of detecting viral RNA during first 8 days of illness (acute phase)
- **IgM serology**: Useful after day 7; confirm positives via neutralizing Ab test (CDC/State lab)
- **Viral Culture**: Possible within 3 days, but requires BSL-3 precautions
- **Serologic confirmation**: needed if acute sample negative; collect convalescent-phase sample

1. Simon et al. 2015, French guidelines for the management of chikungunya
2. Johnson *et al*. 2016, J. Infect. Dis
3. Staples JE, et al. Chikungunya CDC Yellow Book 2024

DENGUE

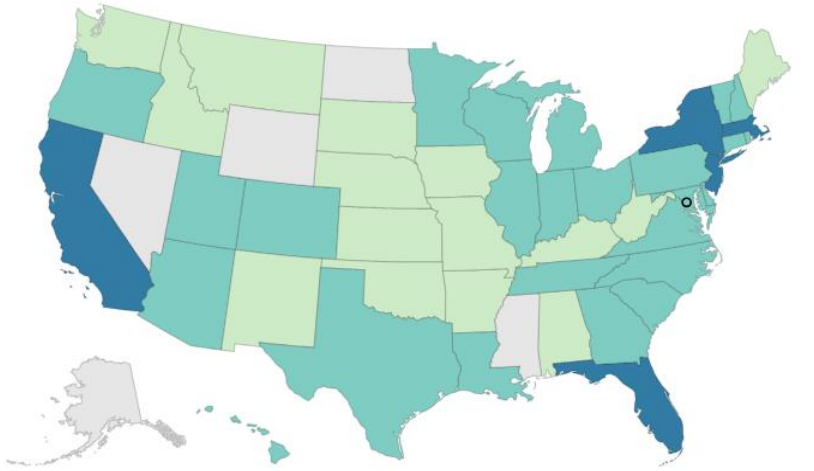
IN THE NEWS

[Counties warn of post-Debby mosquito invasion | Fox Weather]

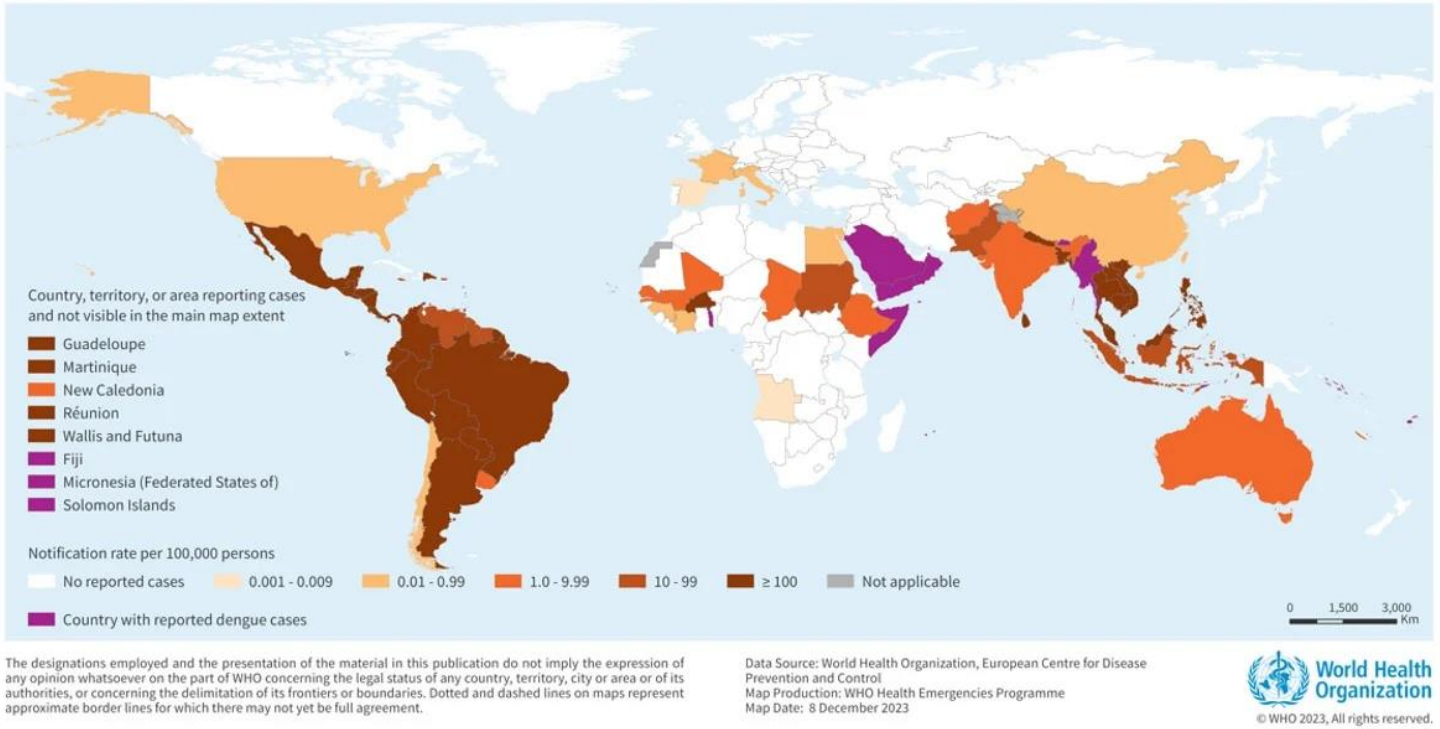
Specialists are concerned about the potential spread of dengue fever, an illness for which the Centers for Disease Control and Prevention has sent out health alerts. More than 10 million people around the globe have reportedly been infected with the virus, which has already surpassed last year's entire count.

"There have been 13 cases of locally acquired Dengue in the US so far."

[Current Year Data (2024) | Dengue | CDC]



DENGUE OVERVIEW



> 12 million cases reported in North, Central, and South America & Caribbean.

Secondary infection with another serotype represents **the highest risk of severe clinical evolution**.

Dengue (DENV) Virus

Single-stranded RNA

Flaviviridae

4 serotypes (1,2,3,4)

Frequent viral infection

Transmitted by Aedes mosquitoes
(tropical and subtropical climates)

Induced lifetime protection against the infecting serotype

Only short-term cross-protection immunity is built up against other serotypes.

OMS. Guide pour la prise en charge clinique de la dengue [Internet]. 2013, Dengue Around the World | Dengue | CDC

WHY IS IT IMPORTANT TO DIAGNOSE DENGUE?

Dengue diagnosis

Complications can occur

No prediction factor

to identify who will evolve to severe dengue

Severe dengue is a **medical emergency** and requires immediate attention or hospitalization

Appropriate and timely management of severe dengue decreases the fatality rate

Differential diagnosis

Dengue can look like many other severe febrile infections

- Malaria
- Other arboviruses: chikungunya, Zika, yellow fever, etc.
- Exanthematous infections (measles, rubella)
- Influenza
- Severe bacterial infections including meningococcemia, typhoid fever, leptospirosis, and bacterial sepsis
- COVID-19

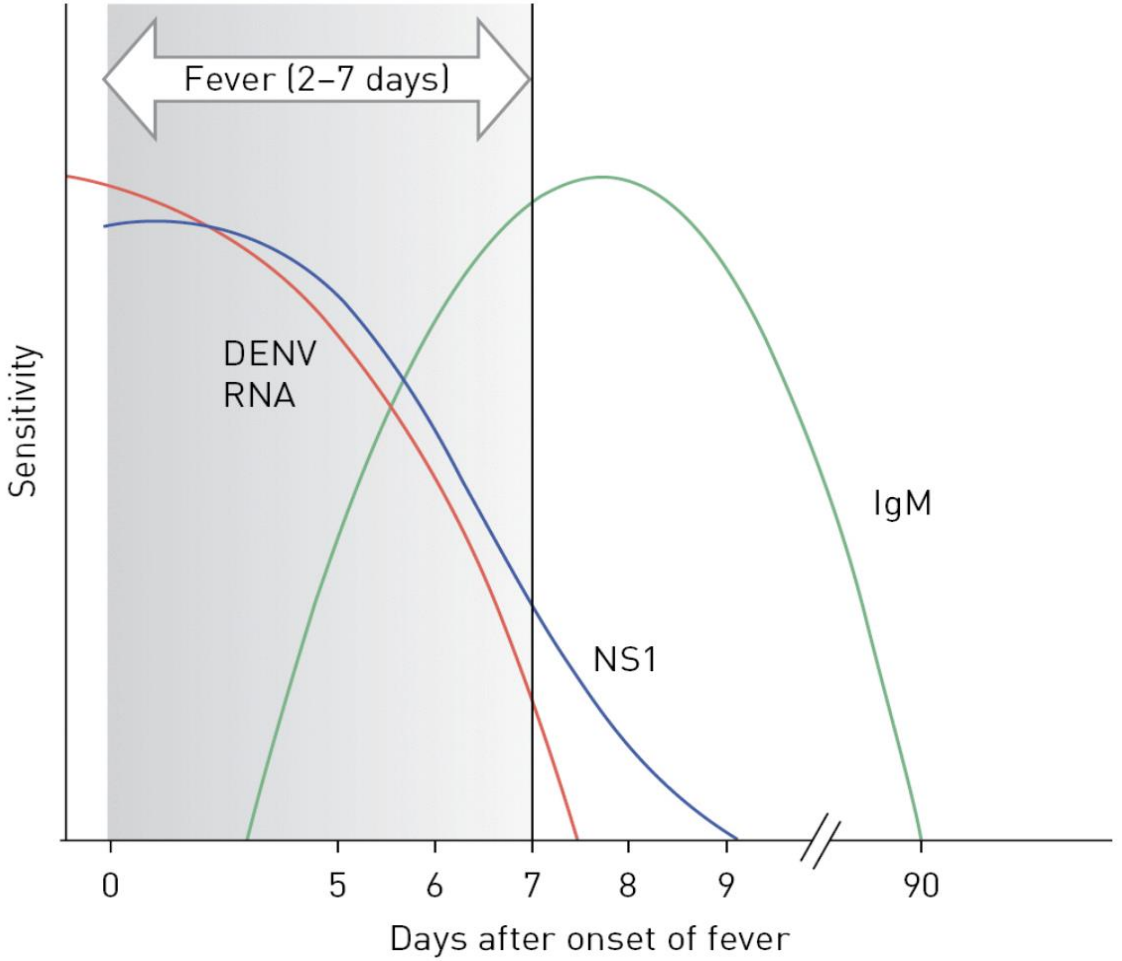
Dengue might **co-exist** with **many tropical infections**

E.M.Torres, estudos avançados 22 (64), 2008

CDC YELLOW BOOK- 2024

- Nationally notifiable disease in the US
  - All suspected cases to the state or local health department
- Patients presenting ≤ 7 days after fever onset testing should include nucleic acid amplification test for DENV and IgM
- Patients presenting ≥ 7 days after fever onset, IgM testing is recommended
- Presence of virus RT-PCR or DENV nonstructural protein 1 (NS1) antigen in a single diagnostic specimen is considered laboratory confirmation

Figure 5-01 Relative sensitivity of detection of dengue virus nucleic acid, antigen, and IgM



Sanchez-Gonzalez L, et al. Dengue CDC Yellow Book 2024

TREATMENT

- No targeted antiviral agents
- Supportive care only
  - Proper fluid management is associated with a decrease in disease mortality
  - Pain/fever management
- Avoid mosquito exposure while viremic
- Dengvaxia® vaccine by Sanofi-Pasteur (discontinued)
  - Indicated for ages 9-16 years of age
  - Prior laboratory confirmed dengue infection
  - Must live in endemic area
  - Lack of demand in the global market led to discontinuation

LEPTOSPIRA

LEPTOSPIROSIS OUTBREAK- VENTURA COUNTY, CALIFORNIA

Photo credit: PrimaryMedical.net

Photo credit: Brian van der Brug/Los Angeles Times

- 18 cases among berry farm workers
- Severe cases included meningitis
- Linked to rodent-contaminated water/soil
- Most worked in hoop-house farming structures

Ventura County Public Health. *Update on Locally Acquired Leptospirosis Infections in Ventura County*. February 2025.

NEW YORK CITY- RISING URBAN CASES (2023-2024)

- New York City reported **24 human leptospirosis cases** in 2023**, highest annual number to date**
- Common clinical presentations included **acute renal** and **hepatic failure**
- Most infections were linked to **exposure to environments contaminated with rat urine**

New York City Department of Health and Mental Hygiene. Health Advisory #10: Increase in Leptospirosis Cases—New York City, 2024. April 16, 2024.

PUERTO RICO-POST-HURRICANE FIONA OUTBREAK (2022)

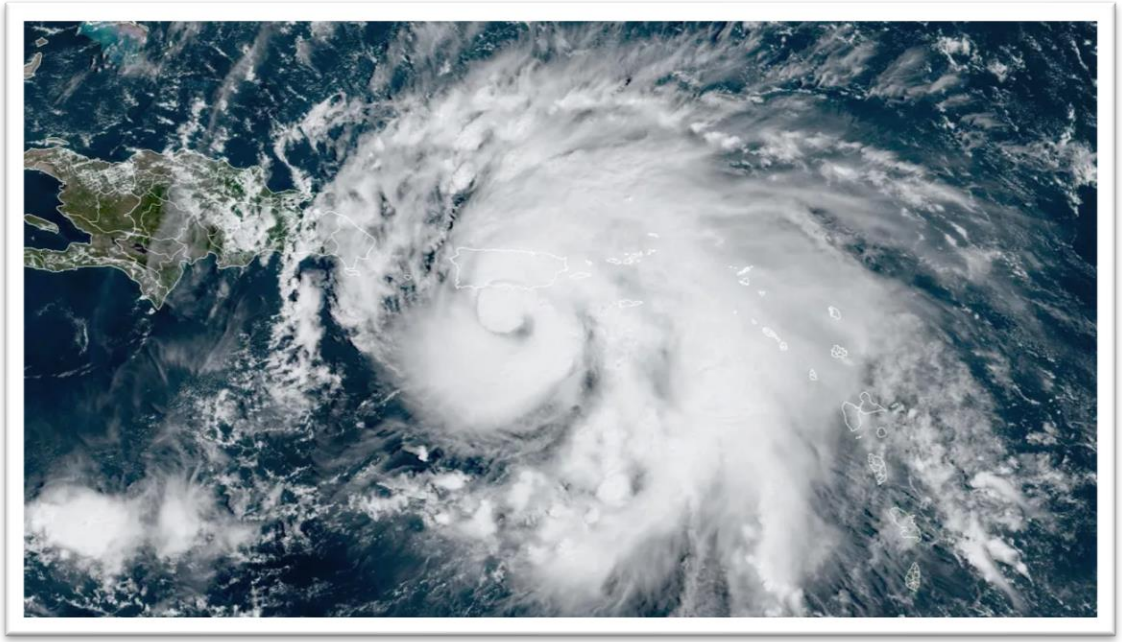


Image credit: NOAA/RAMMB/Colorado State University

Image credit: Erika P. Rodriguez for The New York Times

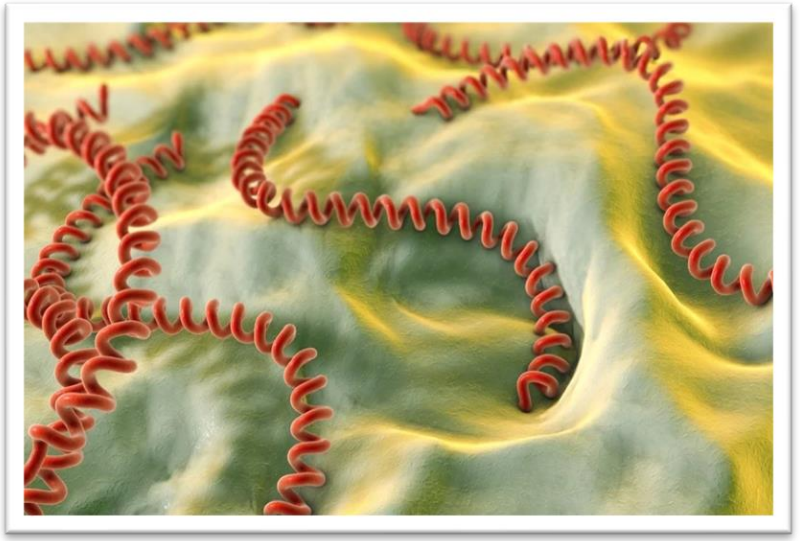
- In Puerto Rico**, 156 cases of leptospirosis reported** post-Hurricane Fiona
- Approximately**, 72% of cases required hospitalization, and 10 fatalities reported**
- Majority of cases linked to exposure to floodwaters contaminated with animal urine

CDC. Leptospirosis after Hurricane Fiona—Puerto Rico. *MMWR*. 2024;73(35):747–751

LEPTOSPIROSIS- CLINICAL BACKGROUND

- **Pathogen**: *Leptospira* (spirochete)
  - Group 1: **pathogenic** (fastidious, slow-growing)
  - Group 2: Intermediate
  - Group:3 Saprophytic (non-pathogenic)
- **Epidemiology**
  - 1 million cases/year worldwide
  - 60,000 deaths/year
- **Transmission**:
  - Urine or tissue from infected animals
  - Contaminated soil or water
  - ↑ Risk after flooding or hurricanes
- **Note:** Vaccine for dogs

Image Credit: Kateryna Kon / Shutterstock.com



Centers for Disease Control and Prevention. *Leptospirosis: Epidemiology and Clinical Presentation*. Atlanta, GA: US Dept of Health and Human Services; 2024.

LEPTOSPIROSIS- CLINICAL PRESENTATION & MANAGEMENT

Figure 1: Conjunctival suffusion. Source: American Journal of Tropical Medicine and Hygiene, 2012.

- **Onset & Incubation**
  - Onset: 2-30 days after exposure
  - Incubation period: Typically, 5-14 days
- **Clinical Spectrum**
  - Symptoms can range from subclinical to severe
    - Most common: fever, headache, myalgias, conjunctival suffusion (redness & edema), jaundice, fatigue
    - Weil's syndrome: jaundice, renal failure, hemorrhage, myocarditis, arrythmias
    - Meningitis/encephalitis
    - Pulmonary hemorrhage with respiratory failure
- **Treatment**: Doxycycline or Penicillin
- **If untreated**
  - Kidney damage, meningitis, liver failure, respiratory failure, death

Centers for Disease Control and Prevention. *Leptospirosis: Epidemiology and Clinical Presentation*. Atlanta, GA: US Dept of Health and Human Services; 2024.

LEPTOSPIROSIS- CLINICAL PRESENTATION & MANAGEMENT

Serology

- MAT (Microscopic Agglutination Test)
  - *Gold standard*
  - Requires 2 serum samples (≥10 days apart)
  - Positive = ≥ 4 fold increase in Ab titer
- ELISA
  - Supports diagnosis, often used in early disease

Direct Detection

- PCR / Culture / Immunostaining
  - Detect or isolate Leptospira organisms
  - Sample types: blood, urine, or tissue

MALARIA

MALARIA IN THE UNITED STATES: A REEMERGING THREAT (2023)

- First locally acquired cases in the U.S. since 2003
- Total of **10 cases** reported in 2023:
  - **Florida**: 7 cases (*Plasmodium vivax*)
  - **Texas**: 1 cases (P. *vivax*)
  - **Maryland:** 1 case (P. *falciparum*)
- Cases **not linked to international travel**, transmission via **local Anopheles mosquitoes**

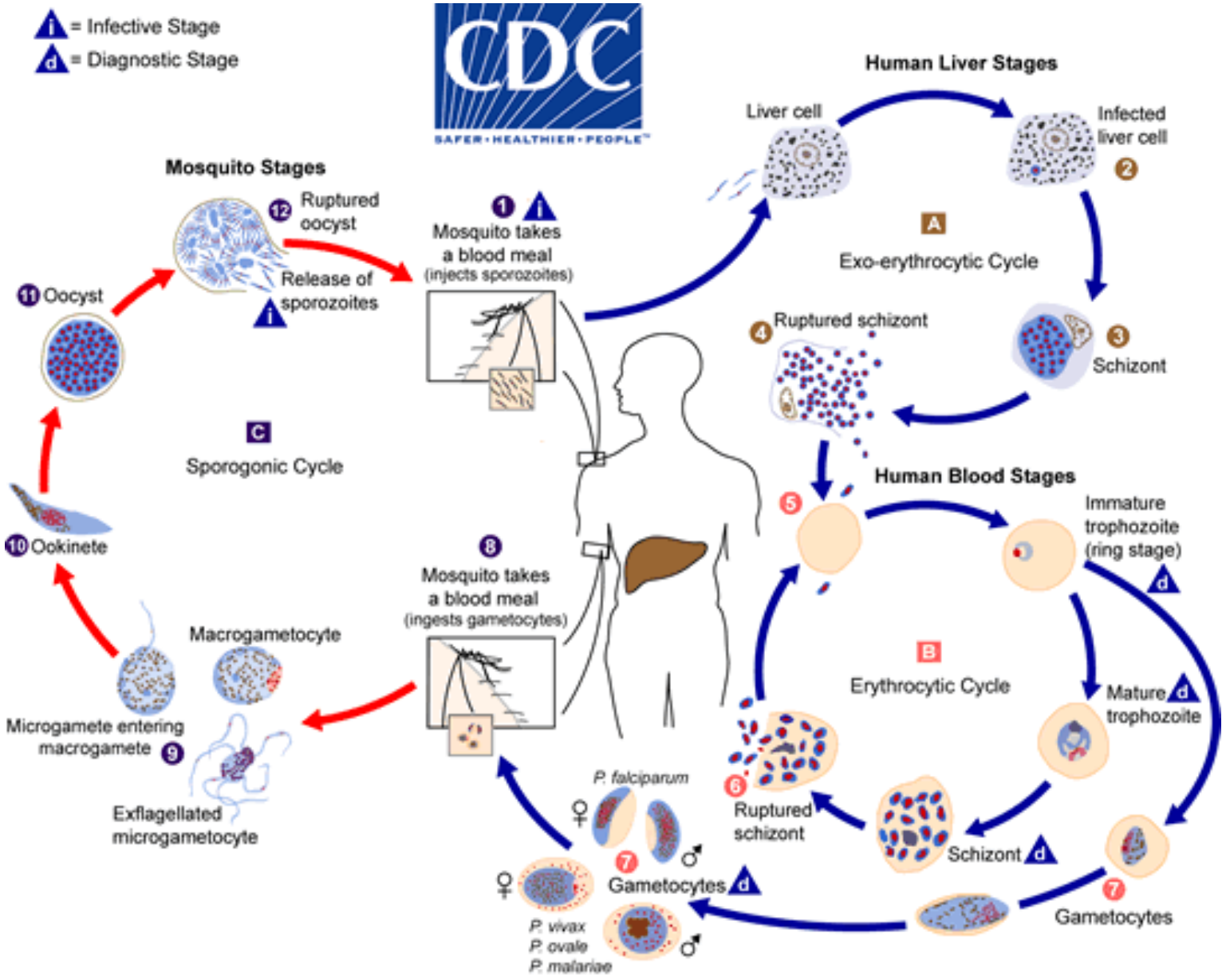
Joe Raedle / Getty Images file

1. Chuck E. New malaria case in Florida brings national total to 8, first US cases in 20 years. *NBC News*. Published June 27, 2023.
2. Lovelace B. Maryland reports first locally acquired malaria case in 40 years. *NBC News*. Published August 19, 2023.
3. Centers for Disease Control and Prevention (CDC). Locally acquired malaria cases—Florida, Texas, and Maryland, 2023. *Health Alert Network*. Published August 18, 2023.
4. Centers for Disease Control and Prevention (CDC). Locally acquired mosquito-transmitted malaria—Florida and Texas, May–July 2023. *MMWR Morb Mortal Wkly Rep.* 2023;72(36):961-965.

MALARIA OVERVIEW

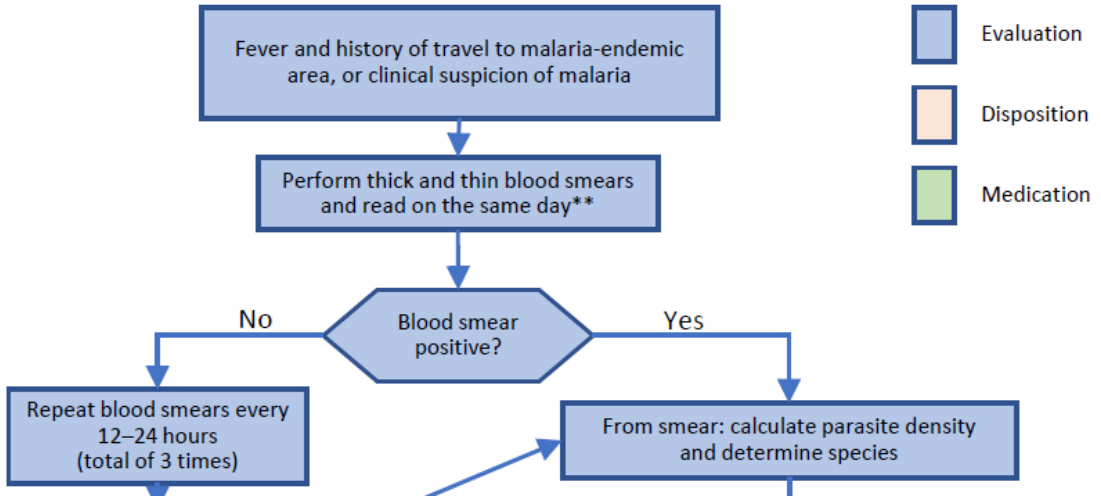
- Malaria is primarily caused by five species of Plasmodium:
  - P. falciparum, P. vivax, P. ovale, P. knowlesi and P. malariae
  - Transmission of these parasitic protozoans occurs through bites from female mosquitoes of the Anopheles genus.
- The five species are found in various geographical locations, and treatments vary depending on the species and drug resistance in the region of infection
- Co-infection with multiple Plasmodium species is possible and should always be considered
- Malaria in the U.S. is almost entirely from travelers from endemic countries

MALARIA LIFECYCLE

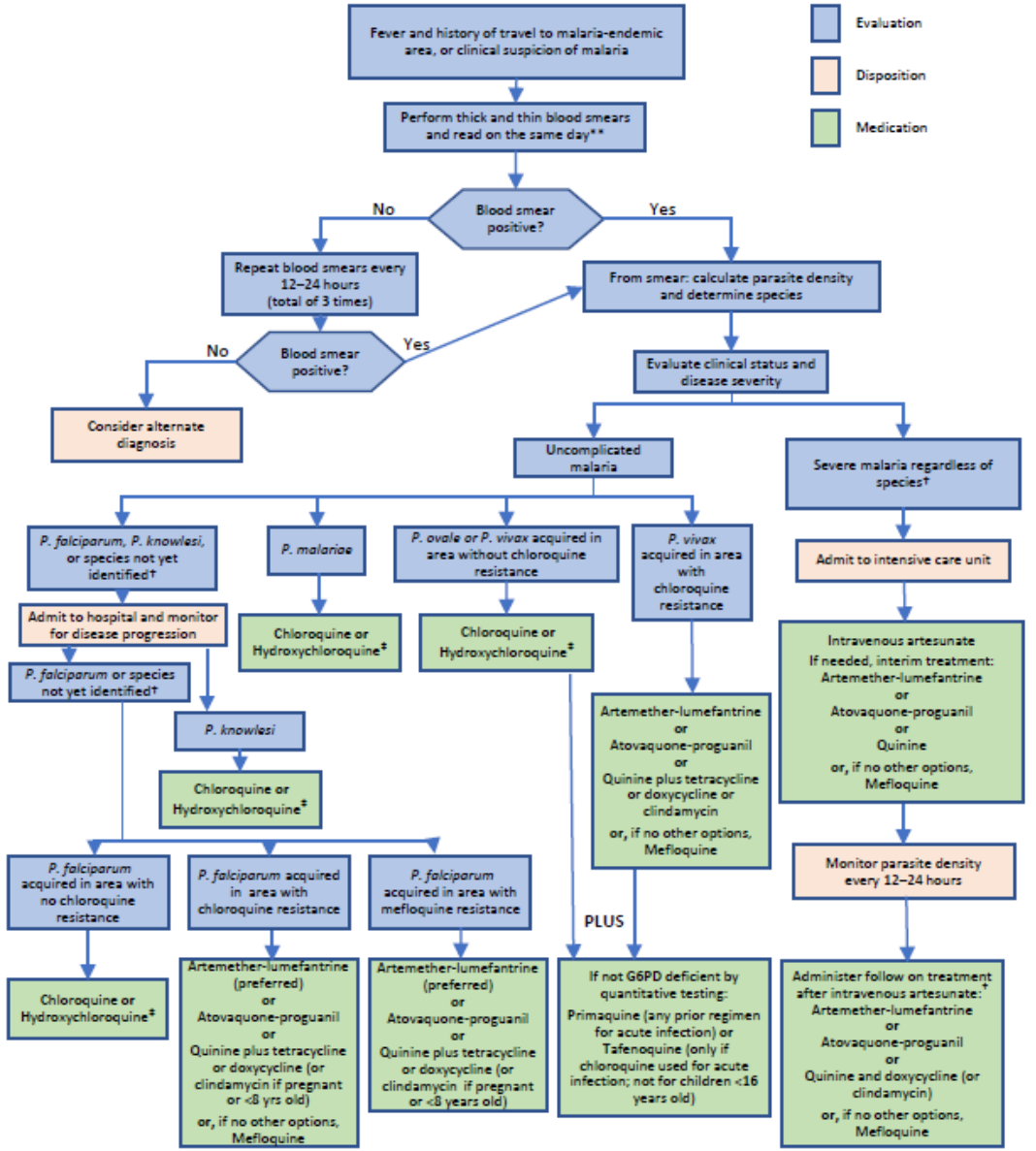


CDC MALARIA ALGORITHM

- PowerPoint Presentation (cdc.gov)



Footnotes:
* Treatment for special populations (children and pregnant women) can be found in the CDC Treatment Guidelines and Treatment Table.
** If rapid diagnostic test performed, smear should also be performed with results available as soon as possible.
† If species later identified as *P. vivax* or *P. ovale*, add primaquine if not G6PD deficient by quantitative testing. Tafenoquine can only be used if concurrently given with chloroquine or hydroxychloroquine.
‡Drug options for chloroquine-resistant *P. falciparum* may be used.



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‡Drug options for chloroquine-resistant *P. falciparum* may be used.

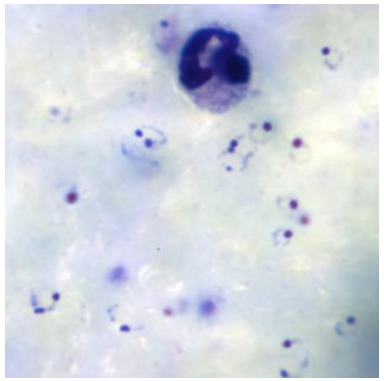
CLINICAL PRESENTATION

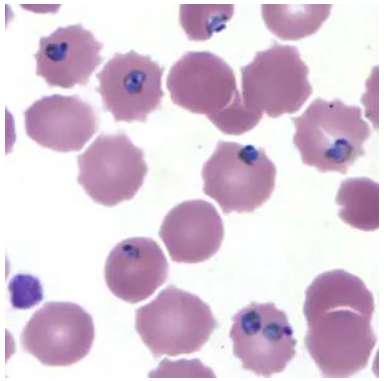
- Symptoms of uncomplicated malaria are often non-specific
- Most Common Symptoms:
  - Fever and chills, headache, myalgias, arthralgias, weakness, vomiting, and diarrhea
- Other clinical features:
  - Splenomegaly, anemia, thrombocytopenia, hypoglycemia, pulmonary or renal dysfunction, and neurologic changes.
- Presentation may vary depending on the infecting species, the level of parasitemia, and the immune status of the patient
- Untreated malaria can progress to severe and may be rapidly fatal
- *P. falciparum* is the most likely to progress to severe with potential for; central nervous system involvement, acute renal failure, severe anemia, or acute respiratory distress syndrome

https://www.cdc.gov/dpdx/malaria/index.html

TRADITIONAL MALARIA DIAGNOSIS

- The CDC recommends considering malaria in any febrile person who has traveled to a malaria-endemic area in the weeks to months preceding symptom onset
- Laboratory diagnosis is traditionally through microscopic examination of thick blood smears to detect presence of parasites and thin smears for species identification.
- Microscopists aren’t always able to differentiate between species when morphologic characteristics overlap
  - Parasite morphology can be altered by drug treatment or improper sample storage
- Molecular diagnostics can detect parasites in specimens where the species is indistinguishable on smear or the parasitemia is below the level detectable by blood film examination.





https://www.cdc.gov/malaria/hcp/clinical-guidance/evaluation-diagnosis.html
https://www.cdc.gov/dpdx/malaria/index.html

MEDICAL VALUE OF TESTING FOR TROPICAL FEVER

Malaria

- Artemisinin-based combination therapy (ACT)

Rapid antigen | Microscopy | Molecular | IA

Dengue

- IV Fluids
- Transfusion for overt bleeding if needed
- Avoid aspirin and NSAIDs

IA | Molecular | Culture

Chikungunya

- Hydration
- Acetaminophen
- NSAIDs are not recommended until dengue infections are ruled out

IA | Molecular | Culture

Leptospira

- Antibiotics

IA | Molecular | Culture

Centers for Disease Control and Prevention. Malaria, dengue, chikungunya, and leptospirosis: diagnosis and treatment guidelines. CDC.gov.

BIOFIRE DEFENSE

BIOMÉRIEUX

PIONEERING DIAGNOSTICS

CLINICAL EVALUATION OF THE BIOFIRE GLOBAL FEVER PANEL FOR THE IDENTIFICATION OF MALARIA, LEPTOSPIROSIS, CHIKUNGUNYA, AND DENGUE FROM WHOLE BLOOD: A PROSPECTIVE, MULTICENTRE, CROSS-SECTIONAL DIAGNOSTIC ACCURACY STUDY

A prospective, multicenter, cross-sectional diagnostic accuracy study on whole blood samples collected in EDTA tubes between March 2018 – September 2019 from 10 different sites from rural to urban in tropical and sub-tropical settings enrolling 1975 adult and pediatric patients, and 1875 were included in the final analysis. The accuracy of the BioFire® Global Fever Panel[1] was evaluated and compared to PCR assays for each of the 6 analytes using different primers.

At least one analyte was detected in 35.0% (657/1,875) of specimens

- Dengue (1-4 serotypes) was detected in 266/1,875 (14.2%) by the BioFire Global Fever Panel vs 283/1,875 (15.1%) by the comparator assay
- Chikungunya was detected in 27 of 1,875 (1.4%) in which 25 of 27 (92.6%) were confirmed by the comparator assay
- *Leptospira* detections were 19 of 1,875 (1.0%); of these, 15 of 19 (78.9%) the comparator confirmed
- *Plasmodium* spp (*P. falciparum*; *P. vivax/ovale*) detections in 351 of 1,875 (18.7%) and 339 (96.6%) were confirmed by comparator PCR

Overall, 28 (1.5%) of 1,875 specimens had multiple analytes detected; including 28 of 657 (4.3%) positive specimens. Two co-detections of dengue and chikungunya virus were found.

PPA & NPA

PPA for the six analytes evaluated as follows:

- **Chikungunya virus 100% (95% CI 86.3–100)**
- **Dengue virus 94.0% (90.6–96.5)**
- ***Leptospira* spp 93.8% (69.8–99.8)**
- ***Plasmodium* spp 98.3% (96.3–99.4)**
- ***P. falciparum* 92.7% (88.8–95.6), and *P. vivax* or *P. ovale* 92.7% (86.7–96.6)**

NPA equal to or greater than 99.2% for all analytes.

PPA = Positive Percent Agreement

NPA = Negative Percent agreement

[1] bioMérieux provides a product identical to BioFire Defense's BioFire® Global Fever Panel called the BIOFIRE® FILMARRAY® Tropical Fever (TF) Panel. All product names and trademarks are property of their respective owners.

Manabe, Y.C. et al. *Lancet Infect Dis*. 2022 Sep;22(9):1356-1364