

Zika Virus in Brazil

January 2016



Photo: Ministry of Health

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INTRODUCTION

Zika virus, an acute viral disease still little known worldwide, was first identified in Brazil in 2015. This virus is endemic to the East and West of the African continent, with sporadic circulation reports in Africa, Asia and Oceania. In the Americas, Zika virus was only identified in early 2014 on Easter Island, part of the Chilean territory in the Pacific Ocean, 3,500 kilometers from the mainland. Imported cases of Zika virus have been reported in Canada, Germany, Italy, Japan, United States and Australia.

The disease caused by this virus - transmitted by the *Aedes aegypti* mosquito, the same vector of dengue and chikungunya - was quickly characterized as epidemic by Brazilian public authorities following an outbreak of exanthem (itchy rashes on the skin), especially in the Northeast.

The disease initially seemed to be only a milder form of dengue, without major consequences or after-effects, and asymptomatic in 80% of cases. The disease became a bigger concern at the end of 2015, when Brazilian public health authorities discovered a possible association between the contagion of women by Zika virus during pregnancy and the birth of babies with microcephaly, a severe congenital malformation in which the fetus' brain does not develop properly. From October 22, 2015, until January 23, 2016, 4,180 suspected cases of microcephalic babies were reported in 830 municipalities in 24 Brazilian states. Of this total, 460 cases have been ruled out and 270 have been confirmed as microcephaly, 6 of them related to Zika virus. Up until 2014, less than 200 cases of newborns with microcephaly were reported in the country every year.

With a universal and integrated public healthcare system, Brazil reacted swiftly in face of the epidemic, from the determination of the virus's behavior to identification of the pathogenesis of the disease (how it arises and evolves) and associated risk factors. As a result, Brazil was able to quickly associate microcephaly and Zika virus.

The Brazilian government has set up an unprecedented task force, with ample financial, technological and scientific resources, to prevent and combat the mosquito and the disease in the short, medium and long terms.

This is a completely new scenario in terms of global public health and for the international scientific community. Up until 2014, there were only sporadic circulation reports of Zika virus in Africa, Asia and Oceania. But since last year, in addition to

Brazil, 18 other Latin American countries have confirmed autochthonous circulation (local contamination) of the virus.

Brazil is combining efforts of specialists from different areas of medicine around the world to conduct investigations in the country. There is constant dialogue with international entities such as the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC). The issue is a national priority, treated with transparency and agility.

ZIKA VIRUS INFECTION

ZIKA VIRUS INFECTION	
Forms of transmission	<ul style="list-style-type: none"> • Through the bite of a contaminated female <i>Aedes aegypti</i> mosquito • There is no evidence so far of Zika virus transmissions through breast milk, nor through urine, saliva or semen.
Main symptoms	<ul style="list-style-type: none"> • Itchy skin rashes. • Intermittent fever. • Conjunctival hyperemia (red eyes) without secretion and itching. • Joint pain. • Periarticular edema (accumulation of liquid around joints). <p>*Asymptomatic in 80% of cases</p>
Diagnosis	<ul style="list-style-type: none"> • Blood test (PCR) during the period in which the patient presents symptoms. • 3-in-1 molecular biology test (national production of the test forecast to begin in February).
Treatment	<ul style="list-style-type: none"> • Acetaminophen (paracetamol) or dipyron to control fever and pain. • Antihistamines in the case of itching eruptions. <p><i>*It is inadvisable to use or indicate acetylsalicylic acid and other anti-inflammatory drugs. Every suspected</i></p>

	<i>case should seek a health service unit.</i>
<p>Prevention and control</p>	<ul style="list-style-type: none"> • Remove all standing water from containers indoors and brush them to eliminate the eggs. • Before traveling, carefully check for any mosquito breeding areas and dispose of existing ones. • Ensure reservoirs and any places that can hold water are fully covered. • Apply larvicides to tanks, water tanks, swimming pools and other areas where it is necessary to hold water. • Apply fogging in the event of an epidemic. • Use mosquito repellent and reapply it throughout the day as directed on the label. Repellents based on DEET, picaridin or icaridin and IR3535 or EBAAP are considered safe for use during pregnancy. • Prefer to wear light-colored clothes, pants and long-sleeved blouses. • Appropriate garbage collection and disposal. • Use mosquito nets to sleep, especially in the morning and late afternoon. • Place mosquito screens in apartments and favor accommodations that have window screens. • Call the municipality if you suspect there are mosquito breeding areas near where you live.

What it is

Zika virus is an RNA virus of the Flavivirus genus, the same as the dengue virus. It is known that the main form of transmission of Zika virus in Brazil is through the *Aedes aegypti*, the same vector that transmits dengue fever and chikungunya. Those infected by Zika virus usually have milder symptoms than those infected by these two diseases, characterized by itchy skin rashes, intermittent fever, conjunctival hyperemia (red

eyes), muscle ache, joint pain, headache and periarticular edema (accumulation of liquid around joints).

Usually there are no serious complications, and no reports of deaths have been registered. The hospitalization rate is potentially low and the symptoms usually disappear spontaneously between 3 and 7 days after exposure. However, even after this period the virus has been found in the amniotic fluid in the uterus of women who had been infected. In addition, there are reports, though unproven, of neurological consequences (such as the Guillain-Barre syndrome) possibly associated with Zika virus. It is estimated that 80% of cases are asymptomatic.

What remains to be discovered about Zika virus
Presence in the body after the symptomatic period
The probability of a woman who has been infected before pregnancy transmitting the virus to the fetus while pregnant
The probability of a woman who has been infected during pregnancy transmitting the virus to the fetus
Possible sequels for children and adults
Transmission routes other than via the <i>Aedes aegypti</i> mosquito

How it emerged

Zika virus was first isolated in non-human primates in 1947, in the Zika forest (Uganda). Between 1951 and 2013, serologic evidence in humans was reported in countries in Africa (Uganda, Tanzania, Egypt, Central African Republic, Sierra Leone, and Gabon), Asia (India, Malaysia, Philippines, Thailand, Vietnam, and Indonesia) and Oceania (Micronesia and French Polynesia).

In the Americas, Zika virus was first identified in early 2014 on Easter Island, a Chilean territory in the Pacific Ocean, 3,500 kilometers from the mainland.

Zika virus is considered endemic (i.e. it is an infectious disease that occurs habitually and has significant impact on a given population and/or region) in East and West Africa. Serological evidence in humans suggests that the virus has spread to Asia beginning in 1966.

Up until 2014, sporadic circulation reports had only been seen in Africa (Nigeria, Tanzania, Egypt, Central Africa, Sierra Leone, Gabon, Senegal, Ivory Coast, Cameroon,

Ethiopia, Kenya, Somalia, and Burkina Faso), Asia (Malaysia, India, Pakistan, Philippines, Thailand, Vietnam, Cambodia, India, and Indonesia) and Oceania (Micronesia, French Polynesia, New Caledonia/France and Cook Islands). Imported cases of Zika virus have been reported in Canada, Germany, Italy, Japan, United States, and Australia.

Since November last year, 18 countries and territories have confirmed circulation of the autochthonous Zika virus in addition to Brazil: Barbados, Bolivia, Colombia, Ecuador, El Salvador, Guatemala, Guyana, French Guyana, Haiti, Honduras, Martinique, Mexico, Panama, Paraguay, Puerto Rico, St. Martin, Suriname, and Venezuela.

The Pan American Health Organization (PAHO), which is part of the World Health Organization (WHO), recommended that these countries take a host of measures, including: establishing and maintaining the ability to detect and confirm cases of infection by the disease; preparing health services to respond to a possible increase in demand for care of specialized neurological syndromes; and strengthening prenatal consults and care. The organization considers it essential that countries continue their efforts to reduce the presence of the mosquito through an effective strategy that includes vector control and communication with the population.

Timeline of the disease in Brazil

May/2015 - A researcher from the Federal University of Bahia performs the first PCR blood test to identify the presence of Zika virus.

July/2015 - Increased cases of neurological manifestations, especially in some states in the Northeast.

October/2015 - Pediatricians of the public healthcare system observe an increase in cases of children born with microcephaly in the same states where there were reports of Zika virus infections.

- ✓ The Pernambuco State Health Department notifies the Ministry of Health on the increase of microcephaly cases in the state.
- ✓ The Ministry of Health sends a team to monitor the investigation of cases in the state of Pernambuco.
- ✓ The situation is reported to PAHO and WHO.

November/2015 - The Healthcare Emergency Operations Center (COES) is established in Brasilia, with staff prepared to work 24/7. Experts from various sectors of society (universities, research institutes, public officials) meet weekly to discuss actions based on outstanding demands.

- ✓ The Ministry of Health declares a Public Health Emergency of National Importance.
- ✓ A Microcephaly Epidemiological Bulletin is published weekly by the Ministry of Health.
- ✓ A Strategic Interministerial Group for Public Health Emergencies of National and International Importance is created to define cross-ministerial actions.
- ✓ The first death of a baby due to Zika virus is confirmed.
- ✓ The Brazilian Ministry of Health confirms the relationship between Zika virus and microcephaly in the country, a result of the work done by the group of experts from different areas set up to investigate and study the case.

December/2015 - The Armed Forces are employed to provide support to the state of Pernambuco.

- ✓ President Dilma Rousseff launches the Plan to Combat Aedes and Microcephaly, involving 19 ministries and other federal agencies.
- ✓ The Surveillance and Response Protocol for Zika-related Microcephaly is launched, including guidelines and technical guidance for health and surveillance professionals.
- ✓ Beginning of activities of the National Coordination and Control Room, an information center that coordinates, consolidates and directs the demands of states and municipalities.
- ✓ Launch of the Protocol for Care and Response to Occurrences of Microcephaly, which guides health professionals and managers regarding Zika virus infections.

January/2016 - Launch of the Early Stimulation Guidelines, aimed at children under 3 years of age with developmental delays due to microcephaly. The Guidelines include professional guidance to Primary Care and Specialized Care teams for early stimulation.

Diagnosis, prognosis and treatment

The symptoms of Zika virus appear within three to 7 days after exposure. Diagnosis can be clinical or based on laboratory tests. Since the Zika epidemic was detected in Brazil in 2015, the Brazilian Unified Healthcare System (SUS) began performing PCR blood tests to identify the presence of genetic material of Zika virus in the sample while the patient presents symptoms. Initially, the test was conducted free of charge by five public reference laboratories.

Since August 2015 the total capacity has been, on average, 1,000 PCR tests per month to identify Zika virus. The Brazilian government will increase the supply of this test to all 27 states of the country, providing reagents for 20,000 tests/month. According to the Ministry of Health, this amount is sufficient for a reliable monitoring of the disease.

Each PCR test currently costs R\$ 2,000 to the government. In order to expand the supply of diagnosis to the population at a lower cost, the Oswaldo Cruz Foundation (Fiocruz) - the most important healthcare science and technology institution in Latin America and a reference in public health research - is developing a 3-in-1 molecular biology test capable of simultaneously diagnosing suspected cases of the three diseases transmitted by the *Aedes aegypti* mosquito (Zika virus, dengue fever and chikungunya) during the onset of clinical symptoms of these infections. At a cost of US\$ 20 a unit, the test, called NAT Discriminatory Test Kit for Dengue Fever, Zika and Chikungunya, begins production in the country in February, with initial supply capacity of 50,000 units, expected to reach 500,000 units by the end of the year.

In case of suspected infection by Zika virus, treatment is administered based on the symptoms, with acetaminophen (paracetamol) or dipyron used to control fever and manage pain. In case of itchy rashes, antihistamines may be considered. It is inadvisable to use or indicate acetylsalicylic acid and other anti-inflammatory drugs, since they increase the risk of bleeding complications.

Profile of the *Aedes aegypti* mosquito

- Fostering environments
 - ✓ The larvae of the *Aedes aegypti* mosquito (transmission vector of Zika virus) will preferably develop in clean, standing water, usually in dark places and in different types of containers.
 - ✓ From egg to adult form, the life cycle of the *Aedes* varies with the temperature, availability of food and amount of larvae breeding in the same place. In favorable environmental conditions, the cycle from egg hatching to development into an adult mosquito can take an average of 7 to 10 days. The elimination of breeding sites must be a priority to stop the mosquito's life cycle, an action that must involve effective participation of the population over time and in a sustained manner.
 - ✓ The eggs can withstand up to 450 days in dry areas, allowing them to survive until the next rainy and warm season before they can outbreak.
- Lifetime of adult mosquitoes: on average up to 50 days.
- Habits and living location

- ✓ The *Aedes aegypti* has preferably diurnal habits, and usually bites more frequently in the early morning and late afternoon.
- ✓ It lives in urban areas, usually around homes or other places with people circulation, such as shops, schools or churches.
- ✓ In Brazil, about 80% of the larva breeding sites are in homes, with only about 20% outdoors.

- Reproduction
 - ✓ Only the female bites humans to suck blood.
 - ✓ A female may breed 1,500 mosquitoes during its lifetime.
 - ✓ Eggs are spread over several breeding grounds - a strategy that ensures dispersion and preservation of the species. If the female has been infected by Zika virus, there is the possibility that the larvae are already born with the virus, in a process called vertical transmission.

- Period of higher infestation
 - ✓ Infestation is more intense in the summer, due to temperature rise and the intensification of rains - factors that favor the emergence of mosquito eggs.
 - ✓ Peak infestation in Brazil takes place between February and May, with a significant decline between July and September, when rainfall is lower and temperatures are milder. This movement is easily detectable by the monthly incidence of dengue (diseases transmitted by the *Aedes*).

According to the 2015 *Aedes aegypti* Rapid Infestation Index Assessment (LIRAA), which is prepared annually to measure the number of sources of infestation by mosquitoes in the country, 199 municipalities were at risk of dengue fever, chikungunya and Zika outbreaks in 2015. "Risk of outbreak" means that over 4% of the houses visited in these towns contained mosquito larvae.

Microcephaly

Microcephaly is a congenital malformation in which the brain does not develop properly. Babies with the condition are born with head circumference equal to or less than 32 centimeters, according to a standard diagnostic established by the World

Health Organization (WHO) to point out that these newborns have measures below the reference for their sex, age or gestation time. Microcephaly cases already existed in Brazil prior to the identification of Zika virus, the result of a number of factors from different sources, including chemicals, radiation, bacteria and toxoplasmosis, rubella and other infectious agents acting during pregnancy. However, less than 200 cases of newborns with microcephaly had been reported in the country per year until 2014. In 2015, about 3,600 suspected cases of the disease were reported (total cases reported minus cases ruled out, as per the table below). The increase in the number of cases of microcephaly is unprecedented, and the evidence available to date indicates that this is related to Zika virus.

Region/State	Total cases reported (2015/2016)	Reported cases under investigation	Cases of microcephaly and/or malformation suggestive of congenital infection	
			Confirmed	Ruled out
NORTHEAST	3,607	2,984	268	355
Alagoas	158	158	0	0
Bahia	533	471	35	27
Ceará	229	218	4	7
Maranhão	134	119	0	15
Paraíba	709	497	31	181
Pernambuco	1,373	1,125	138	110
Piauí	91	91	0	0
Rio Grande do Norte	208	133	60	15
Sergipe	172	172	0	0
SOUTHEAST	240	200	1	39
Espírito Santo	52	52	0	0
Minas Gerais	48	8	1	39
Rio de Janeiro	122	122	0	0
São Paulo	18	18	0	0
NORTH	94	82	0	12
Pará	6	6	0	0

Rondônia	1	1	0	0
Roraima	5	5	0	0
Tocantins	82	70	0	12
MIDWEST	227	180	0	47
Federal District	14	5	0	9
Goiás	62	62	0	0
Mato Grosso	147	110	0	37
Mato Grosso do Sul	4	3	0	1
SOUTH	12	2	1	9
Paraná	10	2	0	8
Santa Catarina	1	0	0	1
Rio Grande do Sul	1	0	1	0
Brazil	4,180	3,448	270	462

MICROCEPHALY CASES REPORTED IN BRAZIL PER YEAR BEFORE 2015

	2010	2011	2012	2013	2014
Brazil	153	139	175	167	147

BRAZIL: PREVENTION AND COMBAT TASK FORCE

In December 2015, the Brazilian government created the National Plan to Combat *Aedes* and Microcephaly (PNEM), with actions on several fronts in order to reduce the rate of infestation by *Aedes aegypti* to less than 1% in Brazilian municipalities and reduce the number of cases of diseases transmitted by the mosquito. The Armed Forces will support the health workers and other entities involved in the fight against the epidemic with 220,000 troops, in four phases: collective effort inside military premises, mobilization of the population, direct participation in the fight against the mosquito and raising awareness in educational facilities. Below are the main actions of the Plan:

- **Surveillance and monitoring**

- ✓ Increase in the number of laboratories performing PCR blood tests – The number of laboratories performing PCR bloods test to detect the presence of Zika virus will more than triple in February. The Brazilian Unified Healthcare

System (SUS) will increase the supply of PCR reagents to increase the number of possible tests from 1,000 to 20,000 per month.

- ✓ Development of the 3-in-1 rapid test by Fiocruz – In order to expand the supply of diagnosis to the population at a lower cost, the Oswaldo Cruz Foundation (Fiocruz) research institute has developed a 3-in-1 quick test that can detect Zika virus, dengue fever and chikungunya infections at the same time at a cost of US\$ 20 per test. Production is expected to begin in February with about 50,000 units, reaching 500,000 by the end of 2016.
- ✓ Setting up of the National Coordination and Control Room – Already operating, it monitors actions developed in states and municipalities on a daily basis and records new cases of the disease.
- ✓ Creation of State and Municipal Control and Coordination Rooms – 26 already in operation.
- ✓ Integrated actions involving Healthcare, Education, Social Welfare, Civil Defense and Armed Forces departments, other invited bodies, and civil society. Already in operation.

- **Prevention and control**

- ✓ Increase in the number of health workers – expansion (from 43,900 to 309,900) of the number of health professionals going into houses and buildings in the country as part of rounds to identify potential *Aedes aegypti* breeding sites, apply larvicide in containers such as cisterns, pools and water tanks and inform residents about ways to prevent breeding of the mosquito. The goal is to have 100% of households and public and private facilities inspected.
- ✓ Intensification of mosquito control visits with monthly visits until February and bimonthly visits beginning in March.
- ✓ First phase of deployment of Armed Forces agents – Cleaning effort in 1,200 military premises scattered throughout Brazil. The goal of this measure is to raise awareness of the needed prevention measures against the mosquito, as well as eliminate potential breeding spots in these locations.
- ✓ The second phase of the plan for the Armed Forces is the deployment of 220,000 men and women (160,000 from the Army, 30,000 from the Navy and 30,000 from the Air Force) in the efforts to raise the awareness of the population. These troops will be deployed in 356 municipalities, including all state capitals and the 115 cities considered epidemic by the Ministry of Health.
- ✓ In the third phase of the Armed Forces' deployment, 50,000 troops will get on the ground to support agents directly involved in the fight against the mosquito.

- ✓ Purchase of larvicides – Purchase of 100 tons of larvicides for use until June 2016. A total 114.4 tons were distributed throughout 2015.
- ✓ Communication with hotels – The Brazilian Ministry of Tourism has sent a statement to 56,000 hotels, inns and hostels in the country with a recommendation to install mosquito screens on windows, clean their land and premises, in addition to general measures aimed at the entire population (see box on p. 4).
- **Financial investment**
 - ✓ An additional R\$ 500 million to combat the disease – Brazil has earmarked an additional R\$ 500 million to strengthen the fight against *Aedes aegypti* in 2016, besides the R\$ 1.87 billion budget allocated to health and surveillance promotion as a tool to combat diseases.
- **Assistance**
 - ✓ Planned expansion of SUS Rehabilitation Centers.
 - ✓ Offer of 10 million rapid pregnancy tests.
 - ✓ Plans to extend the offer of CATscans using the installed capacity in public and private healthcare units.
- **Information, awareness and mobilization of society at large**
 - ✓ A [Travelers' Health](#) website has been created with general guidelines on protection against insect bites in English, Portuguese and Spanish.
 - ✓ Intensification of mass campaigns in radio, television, newspapers, billboards and social networks from December 2015 to June 2016.
 - ✓ Campaign focused on pregnant women and women of childbearing age. It is being broadcast in the media since December 2015.
 - ✓ The last phase of military deployment, still under discussion with the Ministry of Education, will involve the visit of troops in schools. The goal is to reinforce the work of raising awareness of children and teenagers on how to avoid the proliferation of the vector mosquito.
 - ✓ Specific website to be completed by February 2016 and development of an app for health professionals with information about microcephaly and Zika virus, available for free.
 - ✓ Sending of SMS messages to the population with information about the campaign for mosquito prevention and control. Over 200,000 messages have already been sent in the Northeast to residents of areas with high infestation

rates. Audios and videos to be sent by WhatsApp to 750,000 residents of the most affected regions by February.

- ✓ Mobilization of State Departments of Health, Education, Civil Defense and Social Welfare. In progress.
 - ✓ Mobilization among trade union, employers, educational, religious, social, industry, commerce, social networking and communication movements. In progress.
 - ✓ Under the coordination of the Ministry of Education, there will be three weeks of mobilization in schools, starting the week after Carnival. For the younger students, brochures and fliers will be distributed, and there will be lectures on the importance of helping parents in the fight against the mosquitoes. In high school, students will make visits to houses near schools to encourage people to watch out for potential mosquito breeding areas.
 - ✓ The Ministry of Education will produce publicity material and promote actions on social networks, encouraging people to send photos or videos with activities such as cleaning water tanks and cisterns or a simply cleaning the house to prevent the accumulation of water.
 - ✓ MEC will also create a hot site for the schools to download educational and informative games on the mosquito and diseases, particularly Zika virus.
 - ✓ In higher education, deans in charge of the universities' relationship with the community will promote actions in the most vulnerable areas and on campuses.
- **Capacity building**
 - ✓ Launch (in January 2016) of the Early Stimulation Guidelines, directed to children under 3 years of age with developmental delays due to microcephaly. The Guidelines include professional guidance for Basic Care and Specialized Care teams for early stimulation.
 - ✓ Launch of clinical protocol in December 2015 for healthcare professionals for early stimulation of babies with microcephaly.
 - ✓ Online training of 737 maternity ward professionals on neonatal screening for babies with microcephaly, beginning in March 2015.
 - **Research**
 - ✓ **Zika virus vaccine**

Several vaccines that immunize against viruses transmitted by *Aedes aegypti* are being developed and are at different production stages. Three public national institutes are ahead of such projects - the Butantan Institute in São Paulo, the Evandro Chagas Institute in Pará, and the Institute of Technology in Immunobiologicals (Bio-Manguinhos) in Rio de Janeiro. In addition, three international private laboratories are well advanced in the development of the vaccine as well: French Sanofi Pasteur, British company GlaxoSmithKline (GSK) - in partnership with Biomanguinhos - and Japanese pharmaceutical company Takeda.

The vaccine being developed by Sanofi is the one at the most advanced stage: the product has already been certified by ANVISA (Brazil's health surveillance authority), and is currently at the stage of defining the price ceiling for Brazil, a decision which should be presented within three months. It will consist in the application of 3 doses over a one-year period, with an efficiency rate of 60%.

GSK has held technical meetings with ANVISA but has not yet requested formal authorization to conduct research. Takeda is in the last phase of its research, Phase 3, which consists in applying the vaccine in a significant number of volunteers to prove the safety and efficacy of the product. The previous stages were held outside the country.

The Butantan Institute has already received approval by ANVISA to begin Phase 3 of its research, and is now completing the results of Phase 2, which evaluates the response of the vaccine applied to volunteers. A total of 17,000 volunteers from 13 cities in five regions of Brazil will participate in the clinical trials, which are about to begin and should last a year. The research results will depend on how the virus circulates, but Butantan estimates that it will have its dengue fever vaccine available in 2018. Butantan's vaccine has the potential to protect against all four dengue fever viruses with a single dose, and is produced with live but genetically attenuated (i.e. weakened) viruses. The Brazilian Ministry of Health is discussing international partnerships with Butantan for production of the vaccine. The institute is a national reference in the production of vaccines and serums.

The Evandro Chagas and Bio-Manguinhos Institutes are seeking partnerships with scientific institutions for future production of other vaccines in the country.

✓ **Introduction of bacteria in the *Aedes aegypti* that prevents the development of larvae**

This study proposes the use of a bacterium found naturally in the environment (the *Wolbachia*), which, when present in the *Aedes*, is capable of preventing transmission of the disease by the mosquito. The characteristic is also passed on to its larvae.

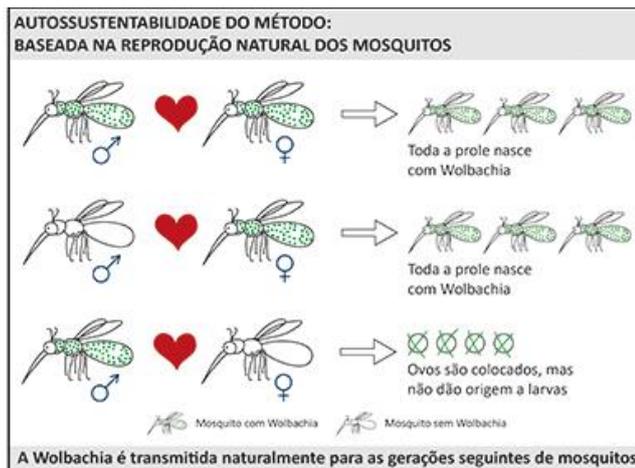
This is the first time a country in the Americas receives the project, which has already been successfully conducted in Australia, Vietnam and Indonesia. In Brazil, it is being led by Fiocruz, with the participation of the Oswaldo Cruz Institute, the René Rachou Research Center (Fiocruz/Minas) and the Scientific Computing Program.

The first place to participate is Tubiacanga, a district on the Ilha do Governador neighborhood in the city of Rio de Janeiro, which has been studied by the project team since 2012.

Approximately 10,000 *Aedes aegypti* mosquitoes with *Wolbachia* will be released weekly by researchers for about four months.

Initially, researchers will evaluate the ability of mosquitoes with *Wolbachia* to establish themselves in the environment and reproduce with mosquitoes that already exist on site.

Large-scale studies planned for 2016 in other parts of Rio de Janeiro will evaluate the effect of this strategy.



✓ Production of transgenic mosquitoes

Moscamed, a bio-factory established in 2005 and subsidized by the Ministry of Agriculture and the state government of Bahia, is specialized in producing transgenic insects for biological control of pests. It produces genetically modified *Aedes aegypti* males on a large scale.

The technology is innovative and created in-country as an option for mosquito control. Modified mosquitoes are released into the environment in an amount two times higher than non-modified ones and attract females for mating. Their offspring is not able to reach adult stage, which should reduce the population of *Aedes*.

The pilot project has already achieved successful results in two districts of the city of Juazeiro (Bahia) - Mandacaru and Itaberaba - both with a population of around 3,000 and high mosquito proliferation rates. The use of this technique led to a 95% reduction in the mosquito population in these districts after six months. Suppression reached satisfactory levels which, according to mathematical models, would render dengue epidemic transmission impossible.

Based on these results, the government will expand the strategy nationwide and, within a few years, incorporate it into the Unified Healthcare System (SUS) as one of the mechanisms to combat the disease. Studies to measure the impact in terms of reducing dengue rates take at least five years to complete, according to the *National Institute of Health* (US equivalent of the Brazilian Ministry of Health). For the technology to be incorporated into SUS and commercially

reproduced by private companies, it must have the approval of the National Biosafety Technical Commission (CTNBio), the Ministry of Health, Anvisa, IBAMA (Brazil's National Environmental Institute), and the Ministry of Agriculture.

BRAZIL ERADICATED THE Aedes Aegypti IN THE 1950s

In the early twentieth century, the identification of *Aedes aegypti* as the transmitter of urban yellow fever prompted the enactment of strict control measures, which led to the eradication of the mosquito in the country in 1955. In 1958 the country was declared free of the vector by the Pan American Health Organization (PAHO)/WHO). However, eradication did not reach the entirety of the American continent, and the vector remained in places such as Venezuela, southern United States, Guyana and Suriname, as well as the entire insular extension that includes the Caribbean and Cuba.

The most likely hypothesis for the reintroduction of the mosquito in Brazil in the 1960s is the so-called "passive dispersal" of the vectors, caused by marine or terrestrial human displacement - a dynamic facilitated by the high resistance to dryness of the vector's eggs.

FIOCRUZ

Brazil, through the Oswaldo Cruz Foundation (Fiocruz), is recognized by Brazilian society and other countries alike for its ability to put science, technology, innovation, education and the technological production of strategic services and inputs at the service of promoting the health of the population, reducing social inequalities and inequities, consolidating and strengthening the SUS and assisting in the development and improvement of public health policies.

Fiocruz is the most prominent strategic public healthcare institution in South America. Founded in 1900 by Dr. Oswaldo Cruz, it is responsible for numerous public health advances in Brazil. The Brazilian Unified Healthcare System (SUS) was developed from Fiocruz projects.

Currently, Fiocruz is responsible for 80% of the world production of yellow fever vaccines. It was the first institution to use the vaccine against the disease in Brazil, through a partnership with the Rockefeller Foundation in 1937.

In 1987 it was the first institution in Latin America to isolate the HIV virus, and in 2011 it developed a test that confirms diagnosis of the virus in just 20 minutes.

Established under the Ministry of Health, Fiocruz has 26 *stricto sensu* post-graduate programs and runs more than 1,700 research and innovation projects.

The Foundation is present in 11 Brazilian states (with units and offices), and also has an office in Mozambique, Africa. Among its institutes is the Bio-Manguinhos laboratory, which is the largest production center of vaccines, kits and reagents for diagnosis of infectious and parasitic diseases in Latin America.

As part of its work abroad, Fiocruz has formalized partnerships with institutions in 20 countries and 6 international organizations. In the education area, it operates the Centre for International Relations in Healthcare (CRIS, in Portuguese), through which it receives students and educators from other countries and offers international courses via agreements with local institutions. It currently hosts master's degrees in Mozambique and Argentina.

In line with the international cooperation policy of the federal government and fulfilling its long-time tradition, Fiocruz has partnerships with universities and research centers in Africa (especially in Portuguese-speaking countries), Latin America and also in Europe and the United States. Similarly, the Foundation receives in Brazil students from various countries for training and academic and professional development.

In 2006 the Foundation received the World Award for Excellence in Public Health from the World Federation of Public Health Associations. In 2014, it was designated a Collaborating Centre for World Health and South-South Cooperation by the World Health Organization.

GLOBAL EPIDEMICS

Since the beginning of this century, WHO has seen a historically unprecedented number of disease outbreaks. During the first three months of 2015 WHO detected and investigated 75 outbreaks, of which 62 were found to be of international concern.

The incidence of dengue fever has grown significantly worldwide in recent decades. The actual number of dengue cases is difficult to estimate because not all countries report their cases properly. A recent estimate indicates 390 million dengue fever infections every year. Another study analyzing dengue prevalence estimates that 3.9 billion people in 128 countries are at risk of infection by dengue virus.

Before 1970 only nine countries had experienced severe dengue fever epidemics. The disease is now endemic to more than 100 countries in Africa, the Americas, the Eastern Mediterranean, Southeast Asia, and the Western Pacific. The Americas, Southeast Asia and Western Pacific regions are the most seriously affected.

The increase of global epidemics is attributed to the ease of mobility of people and goods, together with the globalization of the economy, which has promoted large movements of people and products around the world. Furthermore, the proliferation of most mosquitoes is commonly associated with global warming.

Another compounding factor is the even greater capacity for reporting cases and exchanging information worldwide promoted by new communication technologies, which has led to greater knowledge about the outbreak of diseases by both healthcare professionals and the population in general.