World Health Organization

ZIKA VIRUS MICROCEPHALY AND GUILLAIN-BARRÉ SYNDROME

SITUATION REPORT
19 FEBRUARY 2016

SUMMARY

- Between 1 January 2007 and 17 February 2016, a total of 48 countries and territories reported local (autochthonous) transmission of Zika virus, including those where the outbreak is now over, and including countries and territories that provided indirect evidence of local transmission. Among the 48 countries and territories, Aruba and Bonaire are the latest to report autochthonous transmission of Zika virus.
- Geographical distribution of Zika virus has steadily broadened since the virus was first detected in the Americas in 2015. Zika transmission has been reported in 28 countries/territories. The discovery of Zika virus in additional countries within the geographical range of competent mosquito vectors — especially *Aedes aegypti*— is considered likely.
- Six countries/territories (Brazil, French Polynesia, El Salvador, Venezuela, Colombia and Suriname) have reported an increase in the incidence of cases of microcephaly and/or Guillain-Barré syndrome (GBS) following a Zika virus outbreak. Microcephaly has so far been reported only from Brazil and French Polynesia. Puerto Rico and Martinique have also reported cases of GBS associated with Zika virus infection, but without evidence of an overall increase in the incidence of GBS.
- Evidence that neurological disorders, including microcephaly and GBS, are linked to Zika virus infection remains circumstantial, but a growing body of clinical and epidemiological data points towards a causal role for Zika virus.
- The global prevention and control strategy launched by WHO as a Strategic Response Framework (SRF)[1] encompasses surveillance, response activities, and research. Following consultation with partners and taking changes in caseload into account, the SRF will be updated at the end of March 2016 to reflect epidemiological evidence coming to light and the evolving division of roles and responsibilities for tackling this emergency.

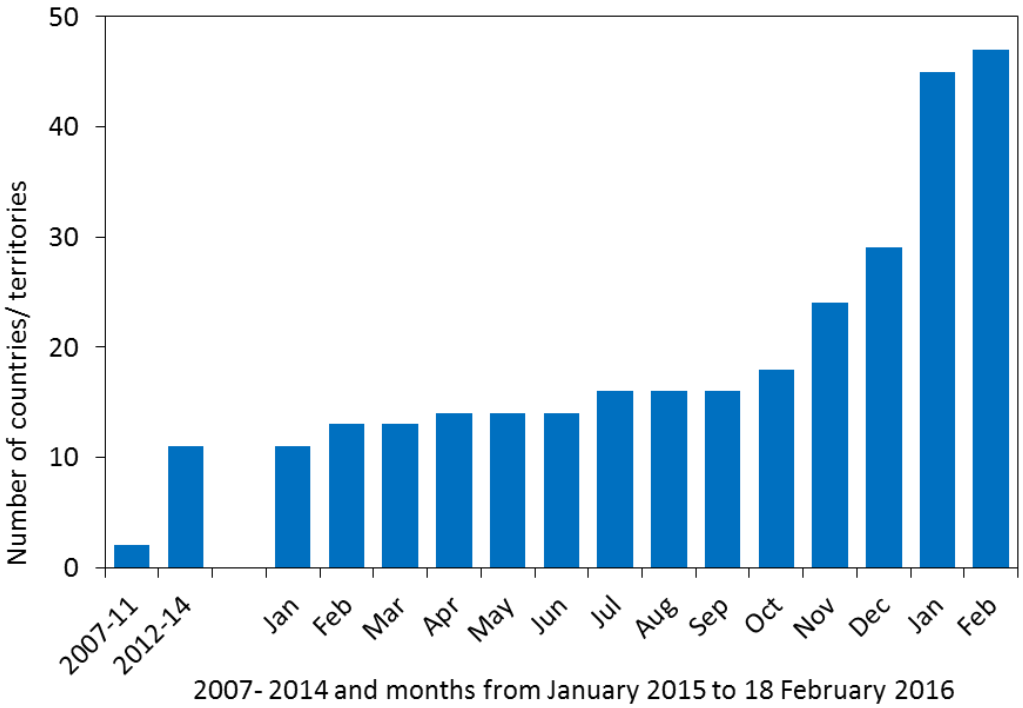
[1] Zika Strategic Response Framework & Joint Operations Plan: http://apps.who.int/iris/bitstream/10665/204420/1/ZikaResponseFramework_JanJun16_eng.pdf?ua=1

I. SURVEILLANCE

Incidence of Zika virus

- From 1 January 2007 to 17 February 2016, Zika virus transmission was documented in a total of 48 countries and territories (Fig. 1 and Fig. 2). This includes 36 countries which reported local transmission between 2015 and 2016, six countries with indirect evidence of viral circulation, five countries with reported terminated outbreaks and one country with a locally acquired case but without vector-borne transmission (Table 1). Among the 48 countries and territories, Aruba and Bonaire are the latest to report autochthonous transmission.

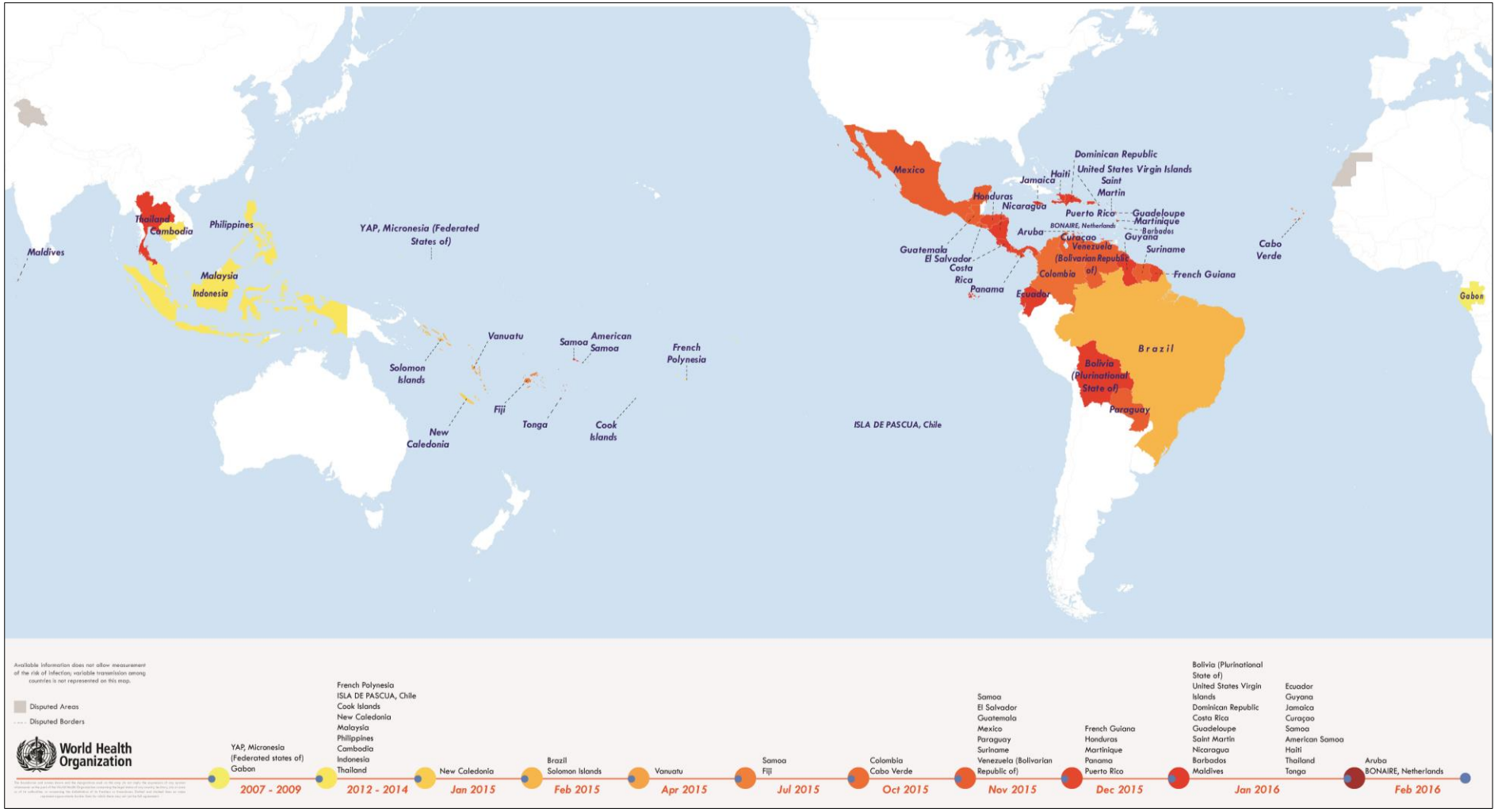
Figure 1: Cumulative number of countries/territories reporting Zika transmission, 2007-2014, and monthly from 1 January 2015 to 18 February 2016.



- In late 2014, Brazil detected a cluster of cases of febrile rash in the Northeast Region of the country. The diagnosis of Zika virus infection was confirmed (RT-PCR test for viral RNA[2]) in May 2015. Due to the size of the outbreak, Brazil ceased counting cases of Zika virus. The Brazilian Ministry of Health estimates that between 497 593 and 1 482 701[3]cases of Zika virus infection have occurred since the outbreak began.
- Recently the virus has spread rapidly in the region. By 11 February 2016, 28 countries/territories in the Americas had reported local transmission of the virus. The reported rate of its spread across South and Central America accelerated from October 2015 onwards (Fig. 1)

[2] Reverse transcription polymerase chain reaction (RT-PCR).
[3] The full report is available in Spanish at:
http://portalsaude.saude.gov.br/images/pdf/2016/janeiro/22/microcefalia-protocolo-de-vigilancia-e-resposta-v1-3-22jan2016.pdf

Figure 2: Countries/territories with local (autochthonous) Zika virus circulation[4], 2007-2016.



Available information does not permit measurement of the risk of infection in any country; the variation in transmission intensity among countries is therefore not represented on this map. Zika virus is not necessarily present throughout the countries/territories shaded in this map.

[4] http://www.who.int/emergencies/zika-virus/situation-report/19-february-2016/en/

- From October 2015 to 6 February 2016, Colombia reported 31 555 cases, including 1504 laboratory confirmed cases. The number of cases reported each week accelerated between December 2015 and February 2016 (Fig. 3).
- From October 2015 to 31 January 2016 Cabo Verde reported 7258 suspected cases of Zika virus disease.

Table 1. Countries/territories/areas with autochthonous transmission of Zika virus, 2007–2016*.

	WHO Regional Office	Country or territory or area[#]
Reported autochthonous transmission[a] (n=36)	**AFRO (N=1)**	Cabo Verde
	AMRO/PAHO (n=28)	Aruba, Barbados, Bolivia, Bonaire, Brazil, Colombia, Costa Rica, Curaçao, Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Nicaragua, Panama, Paraguay, Puerto Rico, Saint Martin, Suriname, US Virgin Islands, Venezuela
	SEARO (n=2)	Maldives, Thailand
	WPRO (n=5)	American Samoa, Samoa, Solomon Islands, Tonga, Vanuatu
Indication of viral circulation[b] (n=6)	**AFRO (n=1)**	Gabon
	SEARO (n=1)	Indonesia
	WPRO (n=4)	Cambodia, Fiji, Philippines, Malaysia,
Countries/territories/areas with outbreaks terminated[c] (n=5)	**AMRO/PAHO (n=1)**	ISLA DE PASCUA, Chile
	WPRO (n=4)	Cook Islands, French Polynesia, New Caledonia, Federated States for Micronesia (Yap)
Locally acquired without vector borne transmission[d] (n=1)	**AMRO/PAHO (n=1)**	USA (Texas)

**Available information does not permit qualification of the intensity of viral circulation and therefore the risk of infection; the situation is extremely variable according to countries, and this information should be used with caution.*
[#]For overseas territories/countries/provinces or islands, the affected area rather than the country is reported.
[a]Autochthonous transmission: Formal notification through International Health Regulations (2005), of at least one case of autochthonous transmission reported by the affected Member State or the Member State where the diagnosis has been performed.
[b]Indication of viral circulation: Indirect information of at least one Zika biologically confirmed case (by RT-PCR or sero-neutralisation) either diagnosed domestically or exported and diagnosed abroad.
[c]Countries/Territories/areas with outbreaks terminated: Countries/territories where the interruption of the viral circulation has be documented can through the surveillance data (including syndromic surveillance, laboratory confirmation of suspected cases, etc.) and/or where no suspect case has been reported since 31 December 2014.
[d]Locally acquired without vector-borne transmission: Autochthonous infection but through another mode of transmission than vector borne (including sexual, blood-borne, or organ transplant) and for where vector population is unlikely to allow sustained vector borne transmission.

Incidence of microcephaly

- From November 2015 to 13 February 2016, a total of 5280 cases of microcephaly and/or central nervous system (CNS) malformation were reported by Brazil, including 108

deaths. This contrasts with the period from 2001 to 2014, when an average of 163 microcephaly cases were recorded nationwide per year.

- Investigations have been concluded for 1345 cases of microcephaly and/or CNS malformation in Brazil. Of these cases, 837 were discarded, 508 were confirmed and 3935 remain under investigation[5]. Of the 462 cases confirmed on 6 February, 421 had radiological findings compatible with a congenital infection and 41 had laboratory confirmation of Zika virus infection[6].
- 70 of the 108 deaths that occurred after childbirth or during pregnancy (through miscarriage or stillbirth) among the 5280 cases of microcephaly and/or CNS malformation remain under investigation. Eleven others have been discarded and 27 have been confirmed as microcephaly and/or CNS malformation. A case of microcephaly associated with Zika virus infection was reported by the Hawaii State Department of Health on 8 January 2016 and another such case was reported by Slovenian public health professionals on 10 February 2016. Both mothers spent time in Brazil in early pregnancy and experienced symptoms compatible with Zika virus disease during that period. Neither mother had laboratory testing for Zika virus infection at that time. A Zika virus infection was laboratory confirmed in the baby born with microcephaly in Hawaii[7], and after the autopsy of the fetus (mandatory in all cases of termination of pregnancy) in Slovenia[8]. No autochthonous transmission of Zika virus has been reported in Hawaii or Slovenia.
- French Polynesia reported an increase in the number of CNS malformations in children born between March 2014 and May 2015. In this period 18 cases were reported, including nine microcephaly cases, compared to the national average of 0 to 2 cases per year.
- Zika virus is not proven to be a cause of the reported increase of microcephaly in Brazil. However, given the temporal and geographical associations between Zika infections and GBS, and in the absence of a compelling alternative hypothesis, a causal role for Zika virus is a strong possibility that requires further investigation.

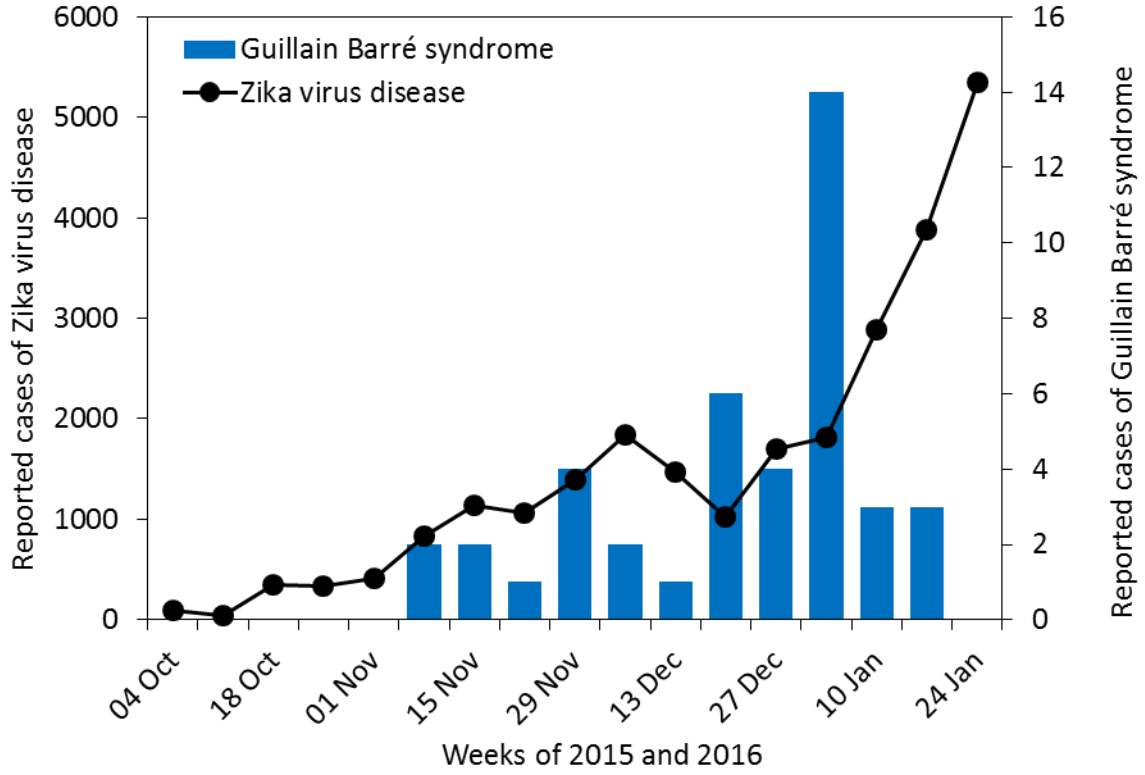
Incidence of Guillain-Barré syndrome

- In the context of Zika virus outbreaks, Brazil, Colombia, El Salvador, Suriname and Venezuela have reported an increase of Guillain-Barré syndrome (GBS). This syndrome was also detected during the 2013-2014 Zika virus outbreak in French Polynesia.
- In July 2015, Brazil reported 42 GBS cases in the state of Bahia, among them 26 (62%) with a history of symptoms consistent with Zika virus infection. In November 2015, seven

[5] http://portalsaude.saude.gov.br/images/pdf/2016/fevereiro/17/coes-microcefalia-ie13-se06-2016--17fev2016.pdf
[6] http://portalsaude.saude.gov.br/images/pdf/2016/fevereiro/12/COES-Microcefalias-Informe-Epidemiologico-12-SE-05-2016-12fev2016-13h30.pdf
[7] http://governor.hawaii.gov/newsroom/doh-news-release-hawaii-department-of-health-receives-confirmation-of-zika-infection-in-baby-born-with-microcephaly/
[8] http://www.nejm.org/doi/pdf/10.1056/NEJMoa1600651

patients presenting neurological syndromes including GBS were laboratory confirmed for Zika virus infection. In 2015, a total of 1708 cases of GBS were registered nationwide, representing a 19% average increase from the previous year (1439 cases of GBS), though not all states reported an increase in incidence. Further investigation is ongoing.

Figure 3: Reported cases of illness due to suspected and confirmed Zika infections (line), along with reported cases of Guillain-Barré syndrome in Colombia (bars).



Source: Instituto Nacional de Salud, Colombia, and PAHO.

- In February 2016, Colombia reported an increase in cases of GBS, which appears to have begun during 2015 (Fig. 3). Over the past seven years (2009-2015) Colombia has registered an average of 223 GBS cases per year. During the five weeks from mid-December 2015 to late January 2016, 86 GBS cases were reported. If Zika virus is also a cause of microcephaly then microcephaly cases in Colombia should be expected in the course of 2016.
- From 1 December 2015 to 9 January 2016, 118 GBS cases were recorded in El Salvador, including 5 deaths, while the average number of GBS cases per year prior to 2015 cases was 169. Of the 22 patients whose information was available, 12 (54%) presented with febrile rash illness consistent with Zika virus infection in the 15 days prior to the onset of symptoms. To date, none of the GBS cases reported in El Salvador have been laboratory tested for Zika virus infection or other causes.
- On 29 January 2016, Suriname reported increased incidence of GBS in 2015. While Suriname registered on average four cases of GBS per year prior to 2015, 10 GBS cases

were reported in 2015 and three in the first three weeks of 2016. Zika virus infection was confirmed in two of the 10 GBS cases reported in 2015.

- On 2 February 2016, Venezuela reported an increase in GBS since the second week of January 2016. From 1 January to 31 January 2016, 252 GBS cases with a spatiotemporal association to Zika virus. Cases were recorded in most parts of the country; 66 of these were detected in the state of Zulia, mainly in Maracaibo municipality. Preliminary analysis of GBS cases in Zulia indicating a clinical history consistent with Zika virus infection was observed in the days prior to onset of neurological symptoms in 76% of GBS cases. Zika virus infection was confirmed by RT-PCR in three patients with GBS.
- In French Polynesia, 42 GBS cases were identified during the 2013-2014 Zika outbreak, 88% of which presented an illness compatible with Zika virus infection. Retrospective sero-neutralisation tests revealed that all 42 cases suffered dengue and Zika virus infection.
- As with microcephaly, Zika virus is not proven to be a cause of increased GBS incidence in Brazil, Colombia, El Salvador, Suriname or Venezuela. However, a causal role for Zika virus is a strong possibility. Confounding factors include the contemporary circulation of dengue and chikungunya in the Americas, which are transmitted by the same species of mosquito. Further investigations are needed to identify the potential role of other factors (including infections) known to be associated, or potentially associated, with GBS.

II. RESPONSE

- The principal activities being undertaken jointly by WHO and international, regional and national partners in response to this public health emergency are laid out in Table 2.
- WHO is appealing for the sum of US$ 56 million for an inter-agency, international response to the spread of Zika virus disease and subsequent spikes in cases of microcephaly and neurological disorders. The request represents the consolidated requirements of 23 partner organizations to address this emergency over the next six months. US$ 25 million is required to fund the WHO and PAHO emergency response and US$ 31 million to fund partners' activities. Approximately 45 donors attended a meeting to discuss the Strategic Response Framework. WPRO, SEARO, EURO and PAHO participated. Donors are reviewing stated needs and requirements.
- On 18 February 2016 the World Bank Group announced that it had made US$ 150 million immediately available to support countries in Latin America and the Caribbean affected by the Zika virus outbreak. This amount follows the WHO declaration of a Public Health Emergency of International Concern (PHEIC) on 1 February 2016 for the recent cluster of microcephaly cases and other neurological disorders reported in the Americas amid the growing Zika virus outbreak. The World Bank Group has engaged with governments across the region, including sending technical experts to affected countries. If additional financing is needed, the World Bank Group stands ready to increase its support. These initial estimates assume that the most significant health risks are for pregnant women.

- WHO has developed new advice and information on Zika case definitions, prevention of sexual transmission of Zika virus, vector control and blood safety[9].

Table 2. Strategic Response Framework and Joint Operational Response Plan: response activities

Public health risk communication and community engagement activities	▪ Activate networks of social science experts to advise on community engagement. ▪ Coordinate and collaborate with partners on risk communication messaging and community engagement for Zika. ▪ Develop communication and knowledge packs and associated training on Zika and all related and evolving issues for communication experts. ▪ Engage communities to communicate risks associated with Zika virus disease and promote vector control, personal protection measures, reduce anxiety, address stigma, and dispel rumours and cultural misperceptions. ▪ Disseminate material on Zika and associated complications for key audience such as women of reproductive age, pregnant women, healthcare workers, clinicians, and travel and transport sector stakeholders. ▪ Conduct social science research to understand perceptions, attitudes, expectations and behaviours regarding fertility decisions, contraception, abortion, pregnancy care, and care of infants with microcephaly and persons with GBS. ▪ Support countries to monitor impact of risk communications.
Vector control and personal protection against mosquitoes	▪ Regularly update guidelines/recommendations on emergency *Aedes* mosquito control and surveillance. ▪ Disseminate guidelines/recommendations on emergency *Aedes* mosquito control and surveillance. ▪ Support insecticide resistance monitoring activities. ▪ Support countries in vector surveillance and control, including provision of equipment, insecticides, personal protection equipment (PPE) and training.
Care for those affected and advice for their carers	▪ Assess and support existing capacity and needs for health system strengthening, particularly around antenatal, birth and postnatal care, and neurological and mental health services, and contraception and safe abortion. ▪ Map access barriers limiting women's capacity to protect themselves against unintended pregnancy. ▪ Develop guidance for: families affected by microcephaly, GBS or other neurological conditions; women suspected or confirmed to have Zika virus infection, including women wanting to get pregnant, pregnant women, and women who are breastfeeding; and healthcare professionals on Zika virus health care, blood transfusion services, tools for triage of suspected Zika, chikungunya and dengue cases, guidance on health services management following a Zika virus outbreak. ▪ Provide technical support to countries on health service delivery refinements and national level planning to support anticipated increases in service needs, as required. ▪ Procure and provide equipment and supplies for prioritized countries/territories to prepare their healthcare facilities in provision of specialized care for complications of Zika virus.

[9] **Sexual transmission:** http://who.int/csr/resources/publications/zika/sexual-transmission-prevention/en/
Vector control: http://www.who.int/emergencies/zika-virus/articles/mosquito-control/en/
Blood safety: http://who.int/csr/resources/publications/zika/safe-blood/en/index.html

III. RESEARCH

- Public health research is critical for establishing the causal link between Zika virus infection in pregnant women and microcephaly in their babies and for understanding the pathogenesis of Zika virus infection. Technical assistance is being coordinated with various partner agencies globally and in particular in affected countries to identify and answer critical questions.
- A meeting on defining the public health research agenda is being organized by PAHO in Washington, D.C. from 1 to 2 March 2016. A global expert consultative group will convene on 7 March 2016 to assess evidence and plan for additional research.

Table 3. Strategic Response Framework and Joint Operational Response Plan: research objectives and activities

Public health research	Investigate reported increase in incidence of microcephaly and neurological syndromes and their possible association with Zika virus infection.	▪ Conduct research studies to assess link between Zika and microcephaly. ▪ Conduct research to assess potential sexual transmission and mother-to-child transmission. ▪ Research women's and health workers' perceptions of pregnancy risk and consequent decisions on contraceptive use, safe abortion and post abortion care in context of Zika.
Research and development	Fast-track research and development of new products including diagnostics, vaccines and therapeutics.	▪ Coordinate supportive research activities including fast-tracking clinical trials. ▪ Develop research protocols for Zika-related studies. ▪ Research on novel vector control approaches and insecticide resistance. ▪ Support and conduct research related to Zika diagnostics, therapeutics and vaccines. ▪ Coordinate supportive public health research activities.

Annex 1: Additional resources

Zika Virus

- Zika virus disease is caused by a virus transmitted by *Aedes* mosquitoes. Other transmission modes are still under investigation.
- People with Zika virus disease usually have a mild fever, skin rash (exanthema), and conjunctivitis. These symptoms normally last for 2-7 days.
- At present there is no specific treatment or vaccine currently available. The best form of prevention is protection against mosquito bites.
- Zika virus is known to circulate in Africa, the Americas, Asia, and the Pacific region. Zika virus had only been known to cause sporadic infections in humans until 2007, when an outbreak in Micronesia infected 31 people.

Microcephaly

- Microcephaly is an uncommon condition where a baby's head circumference is less than expected based on the average for their age and sex. The condition is usually a result of the failure of the brain to develop properly, and can be caused by genetic or environmental factors such as exposure to toxicins, radiation, or infection during development in the womb. Microcephaly can be present as an isolated condition or may be associated with other symptoms such as convulsions, developmental delays, or feeding difficulties.

Guillain-Barré syndrome

- Guillain-Barré syndrome in its typical form is an acute illness of the nerves that produces a lower, bilateral, and symmetrical sensorimotor development deficit. In many cases there is a history of infection prior to the development of the Guillain-Barré syndrome. The annual incidence of GBS is estimated to be between 0.4 and 4.0 cases per 100,000 inhabitants per year. In North America and Europe GBS is more common in adults and increases steadily with age. Several studies indicate that men tend to be more affected than women.

WHO Factsheets

- Zika virus: http://www.who.int/mediacentre/factsheets/zika which has been viewed more than one million times in English, Spanish and Russian alone. It will be regularly updated.
- Microcephaly: http://www.who.int/emergencies/zika-virus/microcephaly/en/
- Guillain-Barré syndrome: http://www.who.int/mediacentre/factsheets/guillain-barre-syndrome/en/