Zika Virus
April 14, 2016

Biosafety Advisory

This biosafety advisory is being provided by the Public Health Agency of Canada (PHAC) to assist clinical diagnostic and research facilities in implementing appropriate biosafety procedures when handling samples containing Zika virus (ZIKV). ZIKV caused an outbreak that began in Brazil in spring 2015, and has rapidly spread through Latin America and the Caribbean. This advisory is based on currently available scientific evidence as of March 2016, and is subject to review and change as new information becomes available. ZIKV is a Risk Group 2 (RG2) human pathogen. Although able to infect some animals, there is no evidence to suggest that ZIKV causes disease in animals and the PHAC, therefore, classified it as a Risk Group 1 (RG1) biological agent for animals[1]. ZIKV must be handled in a containment level 2 (CL2) zone for all activities except those involving indigenous arthropod vectors, which must be performed in a CL3 facility.

1.0 Background

ZIKV disease is a flaviviral disease caused by ZIKV. *Aedes* mosquitoes, *A. aegypti* and *A. albopicus*, serve as the primary vectors for transmission, although other competent mosquito vectors may exist. ZIKV is related to other *Flaviviridae*, including West Nile, yellow fever, and dengue viruses. In humans, most infections by ZIKV are asymptomatic. Evidence suggests a possible association of the virus with the development of Guillain-Barré syndrome (GBS) in some patients.[2], [3] In addition, a significant increase in the number of babies born with microcephaly coincided with ZIKV circulation in Brazil.[4] Although still under investigation, there is increasing clinical and epidemiological evidence of a causal relationship between ZIKV infection and the development of fetal malformations and neurological disorders.[5]

ZIKV is primarily transmitted indirectly between humans through a bite of infected mosquitoes namely mosquitoes of the species *Aedes*. The risk of direct zoonotic transmission is low. Direct transmission between humans has been observed, including blood-associated, sexual, and vertical transmission, and blood, urine and semen are considered possible sources of infection.[6], [7], [8], [9]

On 1 February, 2016, the World Health Organization (WHO) declared a Public Health Emergency of International Concern, due to the clusters of cases of microcephaly and other neurological disorders reported in some areas affected by ZIKV. For the latest updates on countries affected by ZIKV, please visit the WHO's website. For the latest map of confirmed cases in the Americas, please visit the Pan American Health Organization's website. Please refer to the Government of Canada website for Zika-related public health and travel health notices.

2.0 Biosafety Requirements

ZIKV is classified as an RG2 human pathogen based on the moderate individual risk and low community risk. Primary lab hazards include contact with infected specimen (e.g. blood, urine, semen) and work with the arthropod vector. Pregnant women and women planning to become pregnant should take extra precautions to mitigate risks to the fetus.

Work with ZIKV must be done in a CL2 facility for all *in vitro* and *in vivo* activities, with the exception of work with ZIKV involving arthropod vectors that are indigenous to Canada, which must be performed at CL3.

The PHAC will continue to monitor the situation and will update this advisory based on new information, if appropriate. Laboratories should refer to the *Canadian Biosafety Standard* (CBS), 2nd Edition, 2015 for a complete listing of biosafety requirements.[10]

The following table summarizes the physical containment and operational practice requirements for facilities working with ZIKV.

Sample Type and Activity	**Minimum Containment Level Required**	
	CL2	**CL3**
Non-Propagative Clinical/Diagnostic Activities Examples of these activities include, but are not limited to: ▪ preparing human or animal diagnostic specimens or arthropod specimens with the goal of concentrating or isolating virus (e.g., concentration of virus by filtration or centrifugation of sample).	■	
Propagative *in vitro* Activities Examples of these activities include, but are not limited to: ▪ culture of specimens likely to contain, or known to contain, the virus; ▪ preparatory work for *in vivo* activities; and, ▪ processing positive cultures for packaging and distribution to laboratories.	■	
***In vivo* Work** Examples of these activities include, but are not limited to: ▪ preparing inoculum; ▪ inoculating animals; and, ▪ collecting specimens from experimentally infected animals (e.g., bronchial lavage).	■*	
***In vivo* Work with Indigenous Arthropod Vectors** Examples of these activities include, but are not limited to: ▪ Inoculating mosquitos vectors; and, ▪ Transmission experiments with animals.		■*

** Work in small animal containment zones (SA zones) must meet the requirements in the CL2 column of the CBS and work in large animal containment zones (LA zones) must meet the requirements in the CL2-Ag column of the CBS.*

3.0 Additional Biosafety Requirements

Facilities conducting experiments on mosquitoes that are endemic to Canada to study the transmission of ZIKV are required to meet the physical containment and operational practice requirements for a CL3 zone, as specified in Chapters 3, 4, and 5 of the CBS.[10]

4.0 Biosafety Considerations

Many of the requirements in the CBS are risk- and performance-based and, as such, are dependent on the local risk assessment (LRA) performed. Based on the risks associated with work involving ZIKV, the following items are being highlighted to assist with the development of LRAs and standard operating procedures.

- Due to the risk to the fetus, pregnant women, or women trying to become pregnant, as well as the sexual partners of these women, should take extra precautions to protect against possible exposures when working in a laboratory where ZIKV is propagated or handled, or avoid working in this laboratory setting, if possible.

5.0 Transportation

Packaging, shipping, and transport of specimens of ZIKV must comply with the requirements of the *Transportation of Dangerous Goods Regulations (2015)* and Transport Canada for transportation by road or railway vehicle.[11], [12] Transportation by air must comply with the requirements of the Technical Instructions for the Safe Transport of Dangerous Goods by Air, published by the International Civil Aviation Organization (ICAO).[13]

- For both road and air shipments, all specimens (cultures and patient/primary samples) must be shipped as Category B, UN3373.

For regulatory questions regarding the TDG Regulations or the ICAO Technical Instructions, please contact Transport Canada at TDG-TMD@tc.gc.ca or visit the Transport Canada Transportation of Dangerous Goods website

In the event of an emergency involving dangerous goods, call CANUTEC at 1-888-CANUTEC (226-8832), 613-996-6666 or *666 on a cellular phone.

6.0 Contact Information

Please note that this advisory is based on currently available scientific evidence and is subject to review and change as new information becomes available. Further biosafety information may be obtained from the:

- Public Health Agency of Canada website, by phone at (613) 957-1779, fax (613) 941-0596, or by email: biosafety_biosécurité@phac-aspc.gc.ca

7.0 Resources

1. Public Health Agency of Canada. Public Health Notice.
2. World Health Organisation (WHO) update on mosquito-borne virus.
3. Pan American Health Organization (PAHO). Public health Emergency of International Concern. www.paho.org

4. Transport Canada, Transportation of Dangerous Good Directorate.

8.0 References

1 Order in Council SI/2013-41 transferred authorities under Section 51(a) of the Health of Animals Regulations to the PHAC on April 1, 2013.

2 Musso, D., Nilles, E.J., and Cao-Lormeau, V.-M. (2014). Rapid spread of emerging Zika virus in the Pacific area. Clinical Microbiology and Infection. 20(10):O595-O596.

3 Cao-Lormeau, V.-M., Blake, A.,Mons, S., Lastère, S., Roche, C., Vanhomwegen, J. et al. (2016). Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet. Retrieved on 03/09, 2016 from www.thelancet.com

4 Pan American Health Oganization. (2016). Epidemiological Alert: Neurological syndrome, congenital malformations and Zika virus infection. Implications for public health in the Americas. Retrieved 03/17, 2016 from www.paho.org

5 Mlakar, J., Korva, M., Tul, N., Popovic, M., Poljšak-Prijatelj, M. et al. (2016). Zika Virus Associated with Microcephaly. New England Journal of Medicine. 374:951-958

6 Fonseca, K., Meatherall, B., Zarra, D., Drebot, M.; MacDonald, et al. (2014). Case Report: First Case of Zika Virus Infection in a Returning Canadian Traveler. Am J. Trop Med. Hyg. 91 (5):1035-1038.

7 Gourinat, A.-C., O'Connor, O., Calvez, E., Goarant, C., Dupont-Rouzeyrol, M. (2015). Detection of Zika Virus in Urine. Emerging Infectious Diseases. 21(1):84-86.

8 Mansuy JM, Dutertre M, Mengelle C, Fourcade C, Marchou B, Delobel P, Izopet J, Martin-Blondel G. (2016). Lancet Infectious Diseases. Retrieved 03/17, 2016 from http://dx.doi.org/10.1016/ S1473-3099(16)00138-9

9 Hills, S., Russell, K., Hennessey, M., Williams, C., Oster, A., Fischer, M., and Mead, P. (2016). Transmission of Zika Virus Through Sexual Contact with Travelers to Areas of Ongoing Transmission - Continental United States, 2016. MMWR. 65(8):215-216

10 Government of Canada. (2015). Canadian Biosafety Standard (2nd ed.). Ottawa, ON, Canada: Government of Canada.

11 *Transportation of Dangerous Goods Regulations (SOR/2001-286). (2015).*

12 Transport Canada

13 International Civil Aviation Organization (ICAO). (2015). Technical Instructions for the Safe Transport of Dangerous Goods by Air. www.icao.int

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