SC1-PM-XX–2016: Addressing the urgent research gaps against the Zika virus and other emerging threats in Latin America.

Specific Challenge:

Zika virus (ZIKV) disease is a mosquito-borne viral disease, similar to other diseases caused by Flaviviruses (such as dengue, yellow fever, West Nile) but until recently was believed to be more benign. However, the recent rapid spread of the virus in previously unaffected regions like South Pacific islands and Latin America has provided epidemiological evidence for the first time that it may be associated with neurological complications in adults and with a twentyfold increase in severe congenital brain malformations of newborns.

On 1 December 2015, the Pan American Health Organization/World Health Organization (PAHO/WHO) issued an Epidemiological Alert on: 'Neurological syndrome, congenital malformations, and Zika virus infection: Implications for Public Health in the Americas'. On 10 December 2015 the European Centre for Disease Prevention and Control (ECDC) noted in a ZIKV Rapid Risk Assessment that with the spread of the ZIKV epidemic in the Americas, the likelihood of travel-related cases in the EU is increasing. Imported and autochthonous cases in the EU Overseas Countries and Territories and the EU Outermost Regions, with onward transmission in EU Member States during the summer season in areas where Aedes albopictus or Aedes aegypti (the potential vectors) are established, cannot be excluded. In January 2016, the CDC and ECDC cautioned pregnant women against travel in Zika-affected countries.

Research studies are urgently needed to address the reported association of ZIKV infection during pregnancy with congenital brain malformations, as well as with other neurological complications in adults. If such an association is confirmed, additional studies (e.g. on potential preventive and treatment strategies) should rapidly follow.

3 http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1.htm
The ongoing ZIKV outbreak has exposed the challenges associated with the implementation of urgently needed research in the Latin America region, and has underlined the need for a coordinated research network across the whole region that can rapidly respond to emerging threats. However, the ZIKV outbreak also presents an opportunity to foster the development of a regional preparedness network. Such a network would not only facilitate research against ZIKV, but would also be available to rapidly respond to any future emerging threats in Latin America.

Thus the specific challenge is to set up a research network across the Latin America region to facilitate, coordinate and implement urgent research against the current ZIKV outbreak, and eventually lay the foundation for a preparedness research network against any future emerging severe infectious threats.

Scope:

The objective is to establish a multinational and multidisciplinary consortium across Latin America and other affected or at risk regions, able to implement the urgently needed research during the ongoing ZIKV outbreak. The proposal should address all of the following issues:

i. The evaluation of the potentially causative relationship between ZIKV and the severe reported complications, as well as the exploration of the mechanisms involved or of alternative aetiologies if needed. All relevant research is possible, ranging from basic research, research in animal models, virology and immunology studies, to a coordinated set of clinical studies (including for example prospective, cross-sectional or retrospective epidemiological or cohort studies, supported by harmonised case definitions and the development of improved ZIKV diagnosis and differential diagnosis assays, etc.) as necessary.

ii. If such an association is confirmed, the consortium should be ready to rapidly launch additional studies (e.g. observational studies aimed at establishing the natural history, pathogen and host determinants of severity of the disease, phase II or III interventional trials in primary and/or secondary care aimed at providing evidence for potential prevention (including vaccines) and/or treatment strategies). Depending on the evolution of the outbreak, the timeline of the proposed actions, and ZIKV research efforts implemented by other stakeholders, the proposed action plan should maintain the flexibility to address remaining research gaps against ZIKV. This should include the flexibility to include additional partners depending on the specific expertise required and/or the need to extend geographic scope.

iii. The consortium should further capitalise on the platforms established and the experience gained through this urgent ZIKV research response, in order to evolve into a network capable of rapidly launching a research response to future severe infectious outbreaks caused by emerging pathogens with pandemic potential or potential to cause significant damage to health and socio-economics.
in the region\(^5\). Provisions should be made so that this initial research platform may be further developed through a comprehensive 'inter-epidemic' action plan addressing and fine-tuning the response to any obstacles identified during the ZIKV research response (e.g. resolving regulatory and other bottlenecks, development of adaptable study protocols, strengthening ICT infrastructure for communication and information exchange, developing a training programme to enhance the local partners' capacity for laboratory and clinical research, developing a communication strategy for patient and public engagement, etc).

A comprehensive data management framework allowing the standardised collection, storage, analysis and sharing of data should be implemented, initially focusing on Zika data but eventually evolving as a critical part of the preparedness research network.

Additionally, a sustainability strategy that would enable the continuation of the network beyond the timeline of the EU grant should be explored and developed during the project's duration.

The consortium is expected to collaborate with relevant initiatives already existing or under development at national, regional, and international level, in order to maximise synergy and complementarity and avoid duplication of the research efforts. Specific propositions on how this can be achieved should be included in the proposal.

If more than one proposal is successful, proposals should collaborate and this should be indicated in the proposal.

The Commission considers that proposals requesting a contribution from the EU of between EUR 5 and 10 million would allow this specific challenge to be addressed appropriately. Nonetheless, this does not preclude submission and selection of proposals requesting other amounts.

Taking into consideration that, according to PAHO/WHO, Brazil is the country most severely affected by ZIKV, legal entities established in Brazil are eligible for funding.

**Expected impact:** The proposed preparedness research network would have a major impact in the public health of Latin America, by:

- Implementing the urgently needed research on ZIKV, thus providing evidence to public health authorities on optimal prevention and clinical management strategies, particularly for pregnant women.
- Building up the overall capacity for preparedness research against severe infectious outbreaks caused by emerging pathogens with pandemic potential or potential to cause significant damage to health and socio-economics in the

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\(^5\) These should include emerging severe acute infections (e.g. haemorrhagic fevers, or acute respiratory, neurological or gastrointestinal infections), infections from fast-spreading multi-drug resistant pathogens, as well as emerging infections with severe complications in high-risk groups (e.g. children, elderly, pregnant women and their infants).
region. This research would rapidly provide evidence for a coherent, adequate and rapid public health response to emerging threats.

- Coordinating with relevant initiatives at a national, regional and international level, particularly within the context of the GloPID-R (Global Research Collaboration for Infectious Diseases Preparedness)\(^6\).

- Acting to leverage and facilitate additional research from other funders, primarily against ZIKV and emerging pathogens but also against poverty related and neglected infectious diseases of importance to the Latin America region.

Type of Action: Research and Innovation action

\(^6\) [http://www.glopid-r.org/](http://www.glopid-r.org/)