Zika virus (ZIKV) outbreak

Overview of relevant research, projects and expertise

03rd February 2015

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1. OVERVIEW OF ON GOING PROJECTS AND RESEARCH ACTIVITIES

1.1. ZIKA – RESEARCH CAPACITY MAPPING

- **Current activity**

  Through our teleconferences with our regional focal point at Fiocruz there are a number of issues arising with regard to diagnostics, clinical characterisation, and potential treatment interventions. The value of clinical characterisation has been discussed, as have epidemiological studies that could, in the short term, inform clinical management before considering any intervention, should it become available.

  The key research questions that are emerging are:

  - Relationship between Zika virus microcephaly and other neurological abnormalities
  - Clinical characterisation (for the differential diagnosis of Dengue and Chikungunya)
  - Rapid diagnostics that are specific to Zika
  - Potential intervention – convalescent plasma or other potential treatments

  Please refer to the recommendations submitted from the GloPID-R Outbreak Response Committee.

- **Research Groups identified**

  In Brazil Fernando Bozza at Fiocruz is seeking to set up a population-based cohort to investigate the impact of arboviral infections (DENV, ZIKV, CHIKV) in large urban tropical areas. This would include highly sensitive surveillance for emerging pathogens, longitudinal prospective studies, studies of natural history of diseases, disease transmission models, economic burden, and innovative approaches to diagnostic and future interventions. Dr Bozza also plans to use the research network BRICnet (Brazilian research in critical care network) for surveillance of severe neurological conditions.

  Also in Brazil in a collaboration between Fiocruz, USA CDC and LSHTM, there is another study that aims to investigate cases of microcephaly in the country. The objective of this study is to identify which factors, other than the Zika virus, are related to the increase in cases of microcephaly in the country. The study uses the method of case control, comparing a group of 200 children, living or dead born with microcephaly and another group of 400 children without this congenital malformation. The coordinator of this study is **Dr Celina Turchi Marteli**.

  Germany – Brazil collaboration: **Federal University of Bahia and Institute of Virology University of Bonn Medical Centre, German Centre for Infection Research (DZIF) – Prof Jan Felix Drexter and Prof Christian Drosten –** just formalized an official 5 year collaboration agreement between these institutions to facilitate transfer of equipment and funds. Working with the local ethics committees to get some simple protocols approved before March 2016. They could screen and enrol pregnant women and patients with rash and fever for basic molecular diagnostics of Dengue, Zika and Chikungunya – could establish serosurveys based on highly specific neutralization tests.

  WHO: HQ has set up a SharePoint to liaise with WHO and clinicians dealing with Zika. WHO HQ Emerging diseases Clinical Management Coordinator – Prof. Nikki Shindo is closely working with ISARIC on the **possibility for ISARIC to coordinate the clinical calls**.

  TGHN, with FIOCRUZ and ISARIC, are building a Zika virus website to host information for professionals.

  IDAMS consortium - Dr Thomas Jaenisch, working between Germany with Fortaleza, Recife, Rio de Janeiro, Valencia (Venezuela) and San Salvador (El Salvador). They have a prospective clinical observational study that can capture the natural history of Zika infections. They have a CRF developed between University of Oxford Clinical Research Unit Vietnam and Heidelberg University Hospital. The CRF is aimed at the documentation of the acute phase of the disease and currently does not enrol children under 5 years. With this CRF they can achieve a detailed clinical characterization of the undifferentiated clinical illness episode. Collects prospective information for a max of 6 days (plus convalescent visit). They are also in the process of adding an assessment of persistent symptoms in some of the sites – 3-6 months after the acute phase of the disease. They do not include neurodevelopmental scores at this point. In Brazil, IDAMS work with Fiocruz (Ernesto Marques, Brazil)

Professor Koopmans from Erasmus in the Netherlands, and a member of the European PREPARE consortium has offered to share a flavivirus multiplex platform with Fiocruz, which might help with their serological difficulties.

Prof Eric van Gorp from the Dept. of Viroscience Erasmus MC and his group has offered their experience on neurological complications in virus infection and is working with colleagues in Suriname.

There is project led by **Prof Arturo Reyes-Sandoval between Oxford and Mexico**. Their project aims to set a collaboration between NDM/Oxford and Mexican institutions (public health labs and hospitals) establishing suitable infrastructure for research projects in emerging infectious diseases such as Dengue, Chikungunya and Zika virus. Their lab proposal includes a T cell-based vaccine against dengue that should protect against all dengue serotypes, a Chikungunya vaccine and they are in the **process of developing a new Zika vaccine** using the leading vaccine platforms from the Jenner Institute.

REACTing group - Prof Yazdan and Eric D'Ortenzio have colleagues working in French Guyana, French Antilles and Martinique, in Chikungunya and Dengue.

GABRIEL network members are not currently working on Zika. However their member from Paraguay indicated that the University will be interested to have a diagnostic test.
In India, a GABRIEL partner is interested in starting a clinical survey, although which lab could perform the diagnosis in India is yet to be determined.

PENTA European wide Paediatric network have provided input into the draft ISARIC PREPARE Zika CRFs and sampling algorithm.

1.2. EU FUNDED ON GOING PROJECTS

- **IDAMS**
  Coordinator: Thomas Jaenisch
  FP7 project 'International Research Consortium on Dengue Risk Assessment, Management and Surveillance' (end date 31/8/2016) that aims at improving diagnosis and clinical management of dengue and to differentiate between dengue and other common febrile illness, and to be able to predict the likelihood of evolving to a more severe disease course, as well as assessing the risk of dengue spread through mapping and modelling techniques to define the current extent of dengue disease globally and to evaluate possible scenarios of spread or risk to previously uninfected regions in the future, and developing effective and affordable early warning and outbreak response systems.

- **DENGUE TOOLS**

  Coordinator: Annelies Wilder-Smith

  FP7 project 'Innovative tools and strategies for surveillance and control of dengue" (end date 29/2/2016) that endeavours to achieve better diagnosis, surveillance, prevention, prediction and/or prevention of the spread of dengue fever to previously uninfected regions in the context of climate change, through research on diagnostic and monitoring tools and strategies for dengue surveillance and early warning systems, novel strategies for the prevention of dengue in children and measuring the risk of global spread of dengue and introduction into Europe.

- **DENFREE**

  Coordinator: Anajav Sakuntabhai

  FP7 project 'Dengue research Framework for Resisting Epidemics in Europe' (end date 31/12/2016) that aims to find key factors determining dengue transmission and dynamics in order to develop new tools and strategies for controlling dengue transmission. To estimate the risk of spreading the virus to uninfected areas, especially in Southern Europe where susceptible vectors already exist. The tools generated will be predictive models that enable specific interventions, whether concerning the environment, mosquito or human, to be made and that can undermine an epidemic. To develop an easy-to-use point of care diagnostic tool that is sensitive to detect virus in both human and mosquito samples to improve virus surveillance.

- **PREDEMICS**

  Coordinator: Sylvie van der Werf

  FP7 project 'Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses with Pandemic Potential using Multidisciplinary Approaches' (end date 31/10/2019) that aims at providing Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses with Pandemic Potential using Multidisciplinary Approaches, to unravel the complex interactions between the factors involved in the four stages of emergence, i.e. exposure and introduction into a new host species, infection causing local chains of transmission, spread in human populations and post-transfer adaptation leading to widespread transmission and pandemics, of selected zoonotic RNA viruses with epidemic potential in Europe: influenza virus (IAV), hepatitis E virus (HEV), Japanese encephalitis virus and related flaviviruses (JEVr), and lyssaviruses (LYS).

- **PREPARE**

  Coordinator: Herman Goossens

  FP7 project 'Platform foR European Preparedness Against (Re-)emerging Epidemics' (end date 31-1-2019) that aims to establish a European clinical research framework covering over primary care and hospital care in 27 EU member States. The project implements 'inter-epidemic' large-scale clinical studies and patient-oriented pathogenesis studies and develop novel diagnostics. In addition the project develops and tests solutions to bottlenecks that prevent rapid clinical research responses in the face of new infectious disease threats. The project has the goal

of mounting a rapid, coordinated deployment of Europe's clinical investigators within 48 hours of a severe infectious disease outbreak in Europe.

- **ANTIGONE**
  Coordinator: Thijs Kuiken
  FP7 project "Anticipating the global Onset of Novel Epidemics" (end date 31/10/2016) that aims at identifying the key factors that render zoonotic pathogens prone to cross the species barrier and gain efficient transmissibility among humans. The project performs primary research studies to fill important gaps in the understanding of how zoonotic pathogens can gain pandemic potential. These studies focus on selected viruses and bacteria, including SARS, coronavirus, Crimean-Congo haemorrhagic fever, virus, Nipah virus, Ebola virus, E. coli, M. bovis, B. burgdorferi, C. burnetii and S. suis. The project will also look into key issues in infectivity, pathogenicity, and transmissibility of zoonotic pathogens and determine general criteria to assess the risk of these pathogens to gain human pandemic potential.

- **COMPARE**
  Coordinator: Frank Møller Aarestrup
  Horizon 2020 project "COllaborative Management Platform for detection and Analyses of (Re-)emerging and foodborne outbreaks in Europe" (end date 30/11/2019) that aims to harness the rapid advances in molecular technology to improve identification and mitigation of emerging infectious diseases and foodborne outbreaks. To this purpose the project will establish a "One serves all" analytical framework and data exchange platform that will allow real time analysis and interpretation of sequence based pathogen data in combination with associated data (e.g. clinical, epidemiological data) in an integrated inter-sectorial, interdisciplinary, international, "one health" approach.

1.3. AMED FUNDED RESEARCH ON ZIKA VIRUS AND RELATED SUBJECTS

- The AMED research projects on Zika-Virus related subjects are funded under the 'Research Program on Emerging and Re-emerging Infectious Diseases'.
- The AMED 2015 budget for the Zika Virus related research was about ￥4 million（≒$ 30 thousand).

The followings are the AMED funded research projects that currently address the ZIKA Virus and related subjects. Both projects are implemented **under the leadership and guidance of Dr. Tomohiko Takasaki**, MD, PhD, Department of Virology 1, National Institute of Infectious Diseases, Tokyo, Japan.

- **Application of Flavivirus Single-Round Infectious Particles(SRIPs) Yields to ZIKA Virus**
  (Dr. Eiji Konishi, Professor, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan)

Japan faced its first dengue fever outbreak in 70 years in 2014. There are similarities between Zika fever and dengue fever, and the diseases must be distinguished from each other. For the past two years, three cases of Zika fever have been reported in Japan, and it is therefore imperative to establish laboratory diagnostic method.

A rapid system to produce flavivirus single-round infectious particles (SRIPs) was recently developed using a Japanese encephalitis virus (JEV) replicon plasmid. This research project aims to prepare the ZIKV SRIPs using the JEV replicon plasmid system. The researchers have already prepared ZIKV SRIPs and demonstrated the utility of ZIKV SRIPs for a neutralization assay antigen using the serum collected from imported cases of the disease. This will make easier the measurement of infection-neutralizing antibodies. Detailed information.

- **Evaluation of the Susceptibility of *Aedes Albopictus* Mosquitoes to Chikungunya Virus and Zika Virus.**

  (Dr. Yuki Eshita, Visiting Senior Scientist, Department of Infectious Disease Control, Faculty of Medicine, Oita University, Oita, Japan)

  Zika virus (ZIKV) is a member of arthropod-borne viruses (arbovirus) and is similar to dengue (DENV) as well as chikungunya virus (CHIKV). There was an outbreak of dengue fever in Japan in 2014 summer, and Zika-imported case was also reported in Japan in 2014. ZIKV is regarded as related species to dengue virus (DENV). Worldwide *Aedes albopictus* is incriminated as ZIKV, DENV as well as CHIKV vector. The research on the vector competence of Aedes albopictus mosquitoes distributed commonly in Japan is important to discriminate among DENV, CHIKV and ZIKV.

  The research project aims to determine the susceptibility and transmission ability of Japanese *Aedes albopictus* against those viruses using intrathoracic inoculation in their thorax bodies and oral infection. This project also aims to compare the susceptibility among those viruses through the oral infection of Japanese *Aedes albopictus*. Detailed information.

1.4. RESEARCH ON ZIKA VIRUS IN CANADA

Canadian Institutes of Health Research (CIHR) does not fund any research on the Zika virus per se. However, we do fund a project on Flavivirus host cell interactions.
Other funded related projects includes:

- Study of the antiviral function of IFITM proteins
- Discovery & Development of Novel Small Molecule Inhibitors of Viroporin Proteins for the Treatment of Acute & Chronic Viral Infections.
- The Cost-Effectiveness of West Nile Virus Mitigation Strategies. A Computer Simulation Model.
- Modulation of Hemostasis by Enveloped Viruses.

To our knowledge, there are no active networks for the study of Zika virus or related flavivirus in Canada.

1.5. US DEPT HHS ACTIVITIES ON ZIKA VIRUS AND FLAVIVIRUS

- The US Department of Health and Human Services is engaged in the following activities related to Zika Virus and similar Flaviviruses:

  - In early December, NIAID and Fiocruz jointly sponsored a 3-day arbovirus seminar in Brazil, and Zika was a primary focus. This scientific workshop intended to foster exchange of knowledge and scientific collaboration with regard to the disease epidemiology, ecology, pathogenesis, surveillance, and control strategies that are needed for emerging and re-emerging Chikungunya, dengue, Zika, and other arthropod-borne viruses in Brazil.
  - A number of relevant meetings will convene in the National Capital Region over the next two months, including a workshop sponsored by the National Academy of Medicine to define Zika research priorities (February 16), a meeting sponsored by PAHO to define a regional research agenda (March 1-2), the meeting of the GloPID-R General Assembly (March 14-15), and an HHS expert consultation to accelerate the development of medical countermeasures (March 28-29).

- U.S. Centers for Disease Control and Prevention
  - Uganda Virus Research Institute (UVRI)

    CDC collaborates with the Uganda Virus Research Institute to improve and maintain an effective, coordinated program of diagnostics and surveillance of vector-borne viral infections, and to collect data and information on arboviruses, vectors and reservoir systems, ensuring prompt recognition, and confirmation of arboviruses disease outbreaks. In particular, CDC has supported the building of laboratory capacity to rapidly and accurately identify arboviruses. It has provided extensive training, salary support, equipment and supplies to sequence, isolate, culture and conduct serological tests. The laboratory recently received a one-star rating from WHO SLIPTA. CDC has also equipped a mosquito identification lab and trained its entomologists.

    CDC funds a pilot acute febrile illnesses surveillance project to identify the major causes of undifferentiated fever at six sentinel sites throughout Uganda. It has helped establish a transport system for moving specimens from the sentinel hospitals to laboratories it is also supporting in Kampala and Entebbe. Eventually lab capacity will also be enhanced at the sentinel sites.

  - Pan American Health Organization (PAHO)

    CDC collaborates with PAHO on a project to enhance surveillance for the prevention and control of arbovirus and other emerging/re-emerging viruses in the Americas. CDC continues to provide expert consultation to PAHO and at PAHO request to member states in the evaluation, prevention and control of Zikavirus transmission. The purpose of this collaboration is to strengthen country capacity for an integrated arbovirus and other emerging/re-emerging virus surveillance, and outbreak investigation and response.

Additionally, this project seeks to strengthen the National Public Health laboratory capacity through training, proficiency evaluation and adequate supply of high-quality reagents, supplies and equipment to diagnose arboviral and other emerging/re-emerging viral infections.

- International Centre for Diarrheal Disease Research, Bangladesh (ICDDRB)

CDC collaborates with ICDDRB to improving surveillance for vaccine preventable and emerging public health threats in Bangladesh. Specifically, this project describes seasonal and age distribution of human cases of Japanese encephalitis.

- World Health Organization

CDC has actively participated in WHO expert advisory groups on the prevention and treatment of dengue, yellow fever, Japanese encephalitis and other arboviruses and in the evaluation of pesticides.

CDC collaborates with WHO to conduct field trials of a standardized kit for diagnosis of acute yellow fever virus (YFV) infection in resource-limited settings. The CDC YFV MAC-ELISA has been reconfigured to a half-day test (YF MAC-HD), standardized into a user-friendly kit format containing all the components in ready-to-use dilutions, and stabilized against adverse storage conditions. CDC, as a WHO Collaborating Reference Center for Dengue, has also actively participated in advisory groups setting standards for dengue diagnostic kits.

- Indonesia

CDC built and supports the only facility with the capacity to isolate, identify and sequence emerging arboviruses in Indonesia. In this capacity, CDC collaborates with Eijkman Institute of Molecular Biology, which is under the Ministry of Science, Technology and Higher Education, the Ministry of Health, and medical schools. This laboratory can identify the 22 families of pathogenic viruses, can perform serological testing, culture, sequencing and sophisticated analyses. CDC supports staff salaries, and has equipped and supplied the operation. CDC is also supporting a pilot acute febrile illness surveillance investigation at 5 sites on 5 islands.

- U.S. National Institutes of Health

NIAID funds a robust portfolio of flavivirus research (>$90M per annum), including West Nile and dengue, as well as research focused on arboviruses, such as chikungunya. To further stimulate research on Zika virus, NIAID recently issued a notice to highlight NIH's interest in supporting research and product development to combat Zika virus.

NIAID is expanding its flavivirus research portfolio in the following areas.

- Basic Research:

NIAID is working to develop an improved understanding of flavivirus infection, replication, pathogenesis, and transmission. NIAID is developing and providing resources for researchers,

such as distributing virus samples and other reagents for study. This effort includes the development of animal models of Zika virus infection to understand disease pathogenesis, especially during pregnancy. NIAID also supports a wide array of genomic, proteomic, bioinformatics, and systems biology efforts to increase understanding of flaviviruses.

o Vaccines:

NIAID is encouraging a variety of approaches to Zika virus vaccine development. Two strategies NIAID investigators are pursuing include a DNA-based vaccine, using a strategy similar to that employed for another flavivirus, West Nile Virus, and a live-attenuated vaccine, building on similar and highly immunogenic approaches used for the closely related dengue virus. Another approach NIAID is supporting is the development of a recombinant VSV-virus expressing Zika virus E glycoprotein. In addition, NIAID supports a range of gap-filling preclinical services for vaccine development that could be applied to evaluate and manufacture Zika virus vaccine candidates.

o Therapeutics:

Development of drugs against Zika virus, including broad-spectrum therapeutics with antiviral activity against a range of flaviviruses, is a priority for NIAID. Currently, NIAID is supporting the development of assays to test therapeutics for activity against Zika virus. Future studies will support evaluation of antiviral candidates in animal models.

o Diagnostics:

NIAID is supporting several projects focused on the development of diagnostic platforms for detection and identification of multiple viral pathogens, including Zika virus. One example includes evaluation and validation of RT-PCR assays for a diagnostic that allows rapid detection of all dengue strains, Chikungunya and Zika virus. NIAID is also working to expand translational research activities focused on discovery and preclinical development of new diagnostic technologies. In addition, NIAID is focused on working to improve serologic tests for Zika virus, particularly to minimize cross-reactivity with other flaviviruses.

o Vector Biology:

NIAID supports research focused on disease-carrying vectors, including the mosquitoes that carry flaviviruses. Currently, NIAID is supporting research to reduce the population of the Zika virus vectors, including Aedes *aegypti* and Aedes albopictus, as well as evaluation of the efficacy of the bacteria *Wolbachia* as a vector control strategy. In addition, NIAID supports research focused on the biology of mosquito vectors, vector competence studies for replication and transmission of flaviviruses, host-virus interaction and studies on novel vector control methods.

o Natural History/ Epidemiology:

NIAID supports research to determine the natural history of dengue virus infection and related risk factors for disease severity in several endemic countries, including Nicaragua, Peru, Philippines, Thailand, and India.

- Biomedical Advanced Research and Development Authority
  To date, BARDA has not funded any medical countermeasure programs directly related to Zika but it has developed a medical countermeasures landscape analysis focusing of the vaccines, therapeutics, diagnostics, and pathogen reduction systems for donated blood that are under development.
  BARDA has an open Broad Agency Announcement (BAA-16-100-SOL-00003) that supports the development of platform technologies that enhance capabilities for the development and manufacturing of MCMs. Pending the availability of funds, this mechanism will be used to support promising Zika vac

1.6. ISARIC ACTIVITIES RELATED TO ZIKA

- Current activity – 18th December 2015
  At the ISARIC Stakeholders' meeting in London Dec 1st our South American regional focal point Fernando Bozza of FioCruz presented on Zika virus in Brazil. A small group of us got together to discuss how we could support Fernando and his team. We agreed to set up a teleconference call and adapt what CRFs and protocols we could that might be of use in the study of microcephaly.

  Since then ISARIC has convened a small working group to make the adaptations. We have developed three Case Report Forms with PREPARE Europe colleagues & experts in the area of e.g. neurodevelopment. By doing so we hope that we can gain marchmarch agreement on what the minimum core data set should be for microcephalic children or pregnant women. We plan to present the forms in a modular fashion and tiered which should allow for adaptability dependent on resources available; as data collection can be labour intensive. One key gap is that of an openly available data management and data sharing platform to assist with rapid collection and analysis of the data.

  We also have a draft sampling algorithm and are in the process of adapting the WHO ISARIC Clinical Characterisation Protocol, which may be of use as an overreaching emerging pathogen observational study with biological sampling. By getting such a protocol adapted locally and through ethical and R&D approvals it should allow for a future response to other pathogens.

  Through a rapid mapping exercise ISARIC is aware of a number of excellent initiatives and pre-existing networks which could be adapted to support Zika related epidemiological or clinical research studies. We are trying to avoid duplication of work and to encourage data sharing across the studies and to facilitate awareness across multiple sites regarding knowledge and activities.

  Professor Fred Hayden has been in touch with a number of industrial colleagues to establish who is performing in vitro studies on Zika virus.

Professor Shindo of WHO Geneva has asked ISARIC to host a clinical network call with her for the affected countries. We hope that this will take place the week of December 21st with support from PAHO.

In our support of our regional focal point Fernando Bozza we have applied to the Wellcome Trust Collaborative Award Scheme for funds to establish a regional hub addressing local issues.

As part of the GloPID-R Secretariat and Outbreak Response Committee we have contributed to discussions and recommendations.

2. OPEN ON-GOING CALLS

- National Institute for Allergies and Infectious Diseases (**NIAID**) issued a Notice to highlight its interest in research on, and product development for, Zika virus (ZIKV). Detailed information.

- H2020 **INFRASTRUCTURES Work Programme Topic INFRAIA-01-2016-2017**: Integrating Activities for Advanced Communities on 'Research Infrastructures for the control of vector-borne diseases' to integrate specialised facilities in Europe for the study of insect-transmitted disease with the objective to validate and roll out new control measures targeting insect vectors that pose the greatest threats to human health and animal industries. These facilities, supporting research and product development, include P3 secure insectaries for research on vectors and pathogens, large scale production of mosquitoes, facilities for the testing and evaluation of insecticides, and facilities for high-throughput genetic analysis of insect vectors and pathogens. The facilities of this activity and associated networking and research activities will play a critical role in consolidating European leadership in the field of insect vector biology and disease control. Synergies with relevant ESFRI Infrastructures such as ELIXIR should be duly exploited. Proposals can request a contribution from the EU of up to EUR 10 million. Legal entities established in Australia, Brazil, Canada, China, India, Japan, Russia, Mexico and USA, which provide, under the grant, access to their research infrastructures to researchers from Members States and Associated countries, are eligible for funding from the Union. **Deadline: 30th March 2016.** Detailed information (p.18).

- FP7 **ERA NET LAC - Topic 8 HEALTH**: Research in prevention of infectious diseases and promotion of well-being. Specific challenge: Despite the spectacular progress of modern medicine, infectious diseases remain a global threat for public health, especially in poor countries. Moreover, due to the lack of enough interest from the industry and limited market potentials other diseases have been neglected. Since poverty-related and neglected diseases are of high relevance to the present call due to their high burden in the LAC region, the present call will aim at fostering high quality research in the field. Scope: Project proposals shall address inter/multidisciplinary research in type II (e.g. malaria, TB, HIV/AIDS) and type III (neglected) infectious diseases of zoonotic and non-zoonotic origin corresponding to the classification used by the Consultative Expert Working Group (CEWG)1. Each project proposal must seek the translation from basic scientific findings to intervention and/or implementation. Research should

focus on one or more of: early detection, including both screening and diagnosis tools; facilitating new therapeutic strategies led to decrease antimicrobial resistance or other complications related to infectious diseases; molecular epidemiological studies leading to clinical trials or prediction and prevention tools/strategies; observational studies; Vaccine studies and clinical trials are excluded. Expected impact: Project proposals must clearly demonstrate the potential health and/or economic impact as well as the added-value of transnational and regional collaboration by e.g. gathering a critical mass of patients/biological material, sharing of resources (models, databases, diagnosis etc.), comparison and harmonization of data and clinical practice, sharing of specific know-how and facilities and/or innovative technologies, etc. Projects should deliver: New insights of scientific evidences for better diseases prevention, diagnosis and care of the persons and population affected; Knowledge related to regional differences in prevalence, molecular epidemiology and antimicrobial resistance in order to develop better control programs; Early warning systems and methods for rapid control of community effectiveness; Solid evidences of effectiveness as best-value-for-money interventions **Deadline 10th March 2016**. Detailed information.

- H2020 **Societal Challenges Work Programme - Topic SC1-PM-06-2016**: Open call for "Vaccine development for malaria and/or neglected infectious diseases", where ZIKV is clearly eligible (published since October, **deadline 13th April 2016**. Detailed information.

- Moreover the European Commission is currently preparing a call addressing several gaps in urgently needed ZIKV research. A detailed pre-publication is available. Detailed information.

- Medical Research Council (**MRC**) published a Zika Rapid Response Initiative funded by the Global Challenges Research Fund. **Closing date: 22th February 2016.** Detailed information.

3. EXPERTISE

3.1. GERMAN EXPERTS

- Christian Drosten (University of Bonn)
  Head of the Institute of Virology and member of the German Center for Infection Research (DZIF).
  Member of ongoing EU Projects Antigone, Prepare, Compare.
  Flavivirus and arbovirus diagnostics, basic research on ecology and emergence of arboviruses (Team members: Drs Sandra Junglen and Isabella Eckerle).

- Prof Jan Felix Drexler (Inst of Virology, University of Bonn).
  Member of German Center for Infection Research (DZIF).
  Basic and applied research on mammalian virus evolution and detection. Several nationally funded projects in Brasil.

- Dr Thomas Jaenisch, University of Heidelberg Medical Centre (coordinator of IDAMS, expertise and link see below).

- Prof Ralf Bartenschlager, University of Heidelberg
  Basic research on Dengue and other flaviviruses (international opinion leader in the field).

- Dr Sebastian Ulbert
  Fraunhofer Institut für Zelltherapie und Immunologie, Leipzig.
  Applied Research on Flavivirus Diagnostics and vaccines.
  Coordinator of EU-Projecs WINGS (West Nile Integrated Shield Project).

- Prof Jonas Schmidt-Chanasit
  Bernhard Nocht Institute for Tropical Medicine, Hamburg.
  Applied research on Dengue and other Flavivirus Diagnostics.
  Member of the German Center for Infection Research (DZIF).

3.2. EUROPEAN COMMISSION EXPERTS ON VECTOR BORNE VIRUS DISEASES

- Thomas Jaenisch coordinator of IDAMS FP7 project 'International Research Consortium on Dengue Risk Assessment, Management, and Surveillance' (end date is 31/8/2016). It aims at improving diagnosis and clinical management of dengue and to differentiate between dengue and other common febrile illness, and to be able to predict the likelihood of evolving to a more severe disease course, as well as assessing the risk of dengue spread through mapping and modelling

techniques to define the current extent of dengue disease globally and to evaluate possible scenarios of spread or risk to previously uninfected regions in the future, and developing effective and affordable early warning and outbreak response systems.

- Annelies Wilder-Smith coordinator of DENGUE TOOLS FP7 project 'Innovative tools and strategies for surveillance and control of dengue" (end date 29/2/2016) that endeavours to achieve better diagnosis, surveillance, prevention, prediction and/or prevention of the spread of dengue fever to previously uninfected regions in the context of climate change, through research on diagnostic and monitoring tools and strategies for dengue surveillance and early warning systems, novel strategies for the prevention of dengue in children and measuring the risk of global spread of dengue and introduction into Europe.

- Anajav Sakuntabhai coordinator of DENFREE FP7 project 'Dengue research Framework for Resisting Epidemics in Europe' (end date 31/12/2016) whose objective is to find key factors determining dengue transmission and dynamics in order to develop new tools and strategies for controlling dengue transmission. To estimate the risk of spreading the virus to uninfected areas, especially in Southern Europe where susceptible vectors already exist. The tools generated will be predictive models that enable specific interventions, whether concerning the environment, mosquito or human, to be made and that can undermine an epidemic. To develop an easy-to-use point of care diagnostic tool that is sensitive to detect virus in both human and mosquito samples to improve virus surveillance.

- Sylvie van der Werf coordinator of PREDEMICS FP7 project 'Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses with Pandemic Potential using Multidisciplinary Approaches' (end date 31/10/2019) that aims at providing Preparedness, Prediction and Prevention of Emerging Zoonotic Viruses with Pandemic Potential using Multidisciplinary Approaches, to unravel the complex interactions between the factors involved in the four stages of emergence, i.e. exposure and introduction into a new host species, infection causing local chains of transmission, spread in human populations and post-transfer adaptation leading to widespread transmission and pandemics, of selected zoonotic RNA viruses with epidemic potential in Europe: influenza virus (IAV), hepatitis E virus (HEV), Japanese encephalitis virus and related flaviviruses (JEVr), and lyssaviruses (LYS).

3.3. SELECTION OF AUSTRALIAN EXPERTS RELEVANT TO ZIKV & DENGUE

Most of these experts do have an active research program or leads a diagnostic or monitoring laboratory. Many also hold or have held grants from the National Health and Medical Research Council (Australia). Prof Tania Sorrell had also been consulted when curating this list to include only the experts that are directly relevant to this purpose.

- Public Health and infectious diseases, Asia Pacific experience, WHO experience. Prof Sorrell represents

  Prof Tania Sorrell (University of Sydney)

  Email: tania.sorrell@sydney.edu.au

- Public Health Laboratories
  Cases of Zika virus infection have been imported into Australia from the Cook Islands and key members of our public health laboratory network undertake diagnostic and public health reporting and responses. They could also do genome sequencing.

  Prof David Smith (Western Australia)

  Email: david.smith@health.wa.gov.au

  Prof Dominic Dwyer (University of Sydney)

  Email: dominic.dwyer@sydney.edu.au

  Dr Mike Catton (University of Melbourne, Peter Doherty Institute for Infection and Immunity)

  Email: mike.catton@mh.org.au

- Virology researchers in pathogenesis of flavivirus infections, dengue, RNA viruses

  Prof Paul Young (University of Queensland)

  Email: p.young@uq.edu.au

  Prof Alexander Khromykh (University of Queensland)

  Email: alexander.khromykh@uq.edu.au

- Basic flavirology research, diagnostics, vaccines, works in South East Asia

  Prof John Aaskov (Queensland University of Technology)

  Email: j.aaskov@qut.edu.au

- Evolutionary virology, including flaviviruses, tracking spread based on next-Gen sequencing

  Prof Edward Holmes (University of Sydney, Marie Bashir Institute for Infectious Diseases and Biosecurity)

  Email: edward.holmes@sydney.edu.au

- Dengue, immunology, diagnostics, and has worked in South East Asia

  Prof Cameron Simmons (University of Melbourne, Peter Doherty Institute for Infection and Immunity,)

  Email: csimmons@unimelb.edu.au

- Immune responses to dengue

  Prof Suresh Mahalingham (Griffith University, Queensland)

  Email: s.mahalingham@griffith.edu.au

- Basic research, dengue, genetics of transmission

  A/Prof Elizabeth McGraw (Monash University)

  Email: Beth.Mcgraw@monash.edu

- Dengue, Chikugunya, biocontrol methods

  Dr Francesca Frentiu (Queensland University of Technology)

  Email: francesca.frentiu@qut.edu.au

- Dengue in Asia Pacific region, vector-borne disease control

  Prof Scott O'Neill (Monash University)

  Email: Scott.Oneill@monash.edu

- Dengue control

  Prof Scott Richie (James Cook University, Queensland)

  Email: scott.ritchie@jcu.edu.au

3.4. FRANCE AND OVERSEAS EXPERTS RELEVANT TO ZIKV & DENGUE

Some of the projects currently ongoing in French Caribbean's in particular around Zika but mostly Chik and Dengue and experts (from INSERM and Institut Pasteur) conducting them.

- **INSERM experts**

  Virology

  Xavier de Lamballerie

  UMR "Emergence des Pathologies Virales"; Aix-Marseille University - , Institute of Research for Development IRD - IINSERM - EHESP – EFS & French National Reference Centre for Arboviruses – IRBA

  - Infectious clones
  - Zika strains (collection, characterisation, distribution, evolution) and Isolation
  - RT-PCR + controls + evaluation**; new serology techniques
  - Genomics

- Experimental entomology

Email: xavier.de-lamballerie@univ-amu.fr

Isabelle Leparc-Goffart (virologist)

French National Reference Centre for Arboviruses, Marseille, France

Unité de Virologie, Institut de Recherche Biomédicale des Armées, Institut de Médecine tropicale du Service de Santé des Armées, Marseille.

Email: goffart1@aliceadsl.fr (isabelle.leparcgoffart@gmail.com)

Clinicians

Pr André Cabié

Service de maladies infectieuses, Centre Hospitalier Universitaire, Centre d'Investigation Clinique 1424, Fort-de-France, Martinique

Coordinator of project 'Caribbean Arbovirosis Cohort'

Objective: To identify demographic, clinical, biological, virologic, immunologic and n genetic factors associated with or predictive of severe complications of arbovirosis (organ failure) in a cohort of children and adults with confirmed arbovirosis, in French West Indies or French Guiana.

Email: andre.cabie@chu-fortdefrance.fr

Pr Bruno Hoen

Service de maladies infectieuses, Centre Hospitalier Universitaire, Pointe-à Pitre, France

- Prevention of Mother-to-Child Transmission of Chikungunya Infection: Clinical Evaluation of Anti-CHIKV Hyperimmune IVIg

Email: bruno.hoen@chu-guadeloupe.fr

Felix Djossou

Service de maladies infectieuses, Centre Hospitalier Universitaire, Cayenne, Guyane

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Epidemiologist

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Regional Office of French Public Health Institute Antilles–Guyane, Martinique, France

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- **Institut Pasteur Paris**

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- **Institut Pasteur New Caledonia**

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