

REACTing: the French response to infectious disease crises



In the past decade, scientific and health systems have been challenged by an increase in the emergence of infectious diseases such as Middle East respiratory syndrome coronavirus, chikungunya, Ebola virus disease, and Zika virus.¹⁻⁴ An effective and global public health response to these crises depends on our ability to anticipate these events and our level of preparedness. However, the development of research programmes in response to a rapidly emerging infectious disease in an emergency context is a challenge. Any delay in the response can result in serious consequences for the evolution of the crisis.⁵

In France, after the 2009 pandemic of influenza A H1N1, many obstacles were identified when organising the research response.⁶ These issues included delays in political commitment and the mobilisation of the researchers; little coordination of the different stakeholders; problems with raising funds; administrative, regulatory, and ethical difficulties; and insufficient national and international collaboration.

Lessons learnt from this pandemic led different French research organisations involved in biomedical research to propose REACTing (REsearch and ACTION targeting emerging infectious diseases), a new concept for scientific coordination and fundraising to improve research preparedness during peacetime and to optimise research capacity for a prompt response during a crisis.

REACTing is a national collaborative network of existing organisations and research groups involved in human and animal health and life sciences covering various fields: surveillance, mathematical modelling, diagnosis and pathogen characterisation, clinical research, social science, and ethics. One key objective of REACTing is to re-inforce interactions with low-income and middle-income countries, where French research platforms already exist (eg, Institut Pasteur, Institut de recherche pour le développement, and L'Agence nationale de recherches sur le sida-Institut national de la santé et de la recherche médicale). REACTing is also a single point-of-contact for international organisations to avoid duplication and absence of visibility of actions developed in France. In this context, REACTing establishes close cooperation with international organisations and consortia, in particular, the Global Research Collaboration for Infectious

Diseases Preparedness (known as GloPID-R in French) consortium, which coordinates health research funders to enhance the research response to emerging outbreaks of infectious disease, and also with the European Union, WHO, or the US National Institutes of Health (NIH).

Over the past 2 years, REACTing has been involved in the coordination of two epidemics: Ebola and Zika. In July, 2014, while west African countries were struggling with the Ebola epidemic,³ REACTing mobilised not only the community of researchers from several institutions and with a range of expertise, but also regulatory and administrative stakeholders from different ministries, to assess the epidemic, address key research issues, and define research priorities relevant to the public health authorities. In less than 2 months, several projects (eg, diagnosis, treatment, vaccines, and social sciences) were proposed and rapidly launched, in Guinea in particular. Of note, this scientific programme was proposed to the political authorities and was included on the agenda of the French interministerial response to the epidemic with security, diplomatic, and health measures within the task force set up by the French Government.

Regulatory authorities were involved in the process to facilitate rapid implementation of projects and funding was obtained from different sources at the national and European level, thanks to the rapid response of the European Commission. At the logistical and scientific levels, existing French research agency platforms (known in French as ANRS) in sub-Saharan Africa, working on HIV, were asked to hastily reorient their priorities to be involved in Ebola research with colleagues in Guinea. Clinical trials to evaluate treatment (ie, favipiravir, Zmapp, and convalescent plasma)⁷⁻⁹ and vaccines in collaboration with the private sector in the setting of international partnership and clinical cohorts to evaluate the effects of the disease in survivors were rapidly initiated.¹⁰

REACTing also established close contacts with other existing international research organisations, such as the Institute of Tropical Medicine of Antwerp,⁸ the NIH,⁹ and the London School of Hygiene & Tropical Medicine, for vaccine clinical trials. In this epidemic, REACTing also quickly recognised the importance of involving international non-governmental organisations (NGOs) that were organising care with the governments of west

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African countries in research projects. Médecins Sans Frontières, Croix Rouge Française, and, in particular, ALIMA (Alliance for International Medical Action), were extensively involved in the research conduct. For the future, we are planning to reorient French research platforms working on HIV in developing countries towards emerging infectious disease and to create long-term collaborations between these platforms and NGOs.

In 2015, cases of Zika virus infection were reported in Brazil. Given the threat for the neighbouring French territories, REACTing organised a meeting to define research needs in September, 2015. At that time, we decided to extend an existing descriptive and prognosis cohort of arbovirus infections in Martinique, Guadeloupe, and French Guiana, launched a few years ago,¹¹ to Zika virus cases. In December, 2015, soon after the Brazilian authorities became aware of a possible association between neonatal microcephaly and Zika virus infection during pregnancy, REACTing organised a second meeting to address and reconsider key research issues, among which evidence of a potential causal association between microcephaly and Zika virus infection was clearly a priority. For this issue, we took advantage of retrospective studies using data collected during the Zika epidemic in French Polynesia to assess the association between neonatal microcephaly and Guillain-Barré syndrome with Zika virus infection.¹² Additionally, we launched prospective large cohorts in the French territories in the Americas to evaluate the effect of Zika virus infection during pregnancy and in neonates. An international collaboration between

French and European researchers and Fundação Oswaldo Cruz (FIOCRUZ) in Brazil has also been established at the institutional level to address questions in the specialties of entomology and neuroscience.

REACTing has forged a new dynamic to face emergency situations and contribute to national and international public health decisions. However, we also faced difficulties in initiating and coordinating research in a sustained way. First, when confronted by a new epidemic, it is challenging to determine priorities for research. For example, during the Ebola epidemic, the decision to initiate research should have probably been made a few months earlier. We are currently working to establish a scale to assist us in deciding whether the need is urgent for research projects to be initiated. Although REACTing's original focus was on research preparation during peacetime, the past couple of years have not seen a break in global health crises, meaning that research was prepared during these crucial periods in a suboptimum context. Second, the research agenda continues even after the immediate public health crises, as illustrated by the examples of Ebola vaccine research or the cohorts of Ebola survivors. Third, several emerging infectious diseases might occur at the same time and challenge our capacity to mobilise resources to respond to several outbreaks in different countries. For example, with respect to the Zika virus epidemic, we should have perhaps initiated research coordination in 2014, when the epidemic occurred in French Polynesia. However, at that time, the Zika virus epidemic in French Polynesia and the beginning of the Ebola epidemic in west Africa overlapped. REACTing prioritised the Ebola epidemic when designing research activities. Finally, it is not easy to conduct research projects under an emergency flag for long periods and to keep the political and scientific commitment beyond the end of an epidemic threat. REACTing is highly dependent on our capacity to attract and convince researchers to reorient their priorities and to be involved in research targeting the emerging infectious diseases. This objective might be possible for the short term but as shown in the case of Ebola, it is more difficult in the long term. These are areas on which we should work in the future and for which we need additional resources.

Compared with the many economic and security threats that we face, the global community are underinvested and underprepared with regard to the



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threats posed by infectious diseases. Global decision makers are not sufficiently invested in addressing these global health crises, which can transform rapidly into severe societal, political, and economic crises. Pandemics are a neglected part of global security and are not contained by any borders.¹³ We need to continue the battle against emerging infectious diseases at a national and international level. It is crucial to create and reinforce international mechanisms for leading, coordinating, and providing resources for a global response to infectious disease crises. The French response, coordinated through the REACTing collaboration, is ready to play its full part in the global response.

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