



Inserm
Institut national
de la santé et de la recherche médicale





caviesan
alliance nationale
pour les sciences de la vie et de la santé

Maladies Infectieuses Emergentes, Crises Sanitaires, Quels enjeux pour la Recherche ? Comment s'y préparer ?

Pr JF Delfraissy
*Ancien Directeur de l'ANRS et de l'ITMO I3M
Président du Comité Consultatif National d'Ethique*

Séminaire de Cambo
29 septembre 2017



REACTing



Hôpitaux universitaires Paris-Sud
Assistance Publique - Hôpitaux de Paris



ANRS
Agence autonome de l'Inserm



LIBERTÉ • ÉGALITÉ • FRATERNITÉ
RÉPUBLIQUE FRANÇAISE

**EBOLA
TASK FORCE
INTERMINISTÉRIELLE**

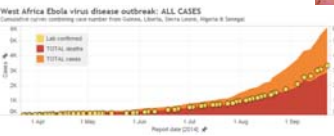
Outbreaks: a constant repetition

SARS 2003
Chikungunya 2005
H1N1 pandemic 2009
MERS-CoV 2013
Ebola 2014
Zika 2015

West Nile in the New World
Clostridium difficile 027
Dengue fever
Escherichia coli
Influenza viruses

Unknown pathogen
ZIKA !!!



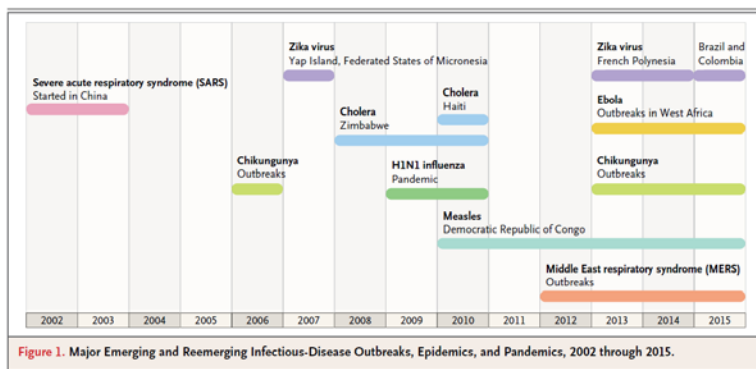



THE NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

The Neglected Dimension of Global Security — A Framework for Countering Infectious-Disease Crises

Peter Sands, M.P.A., Carmen Mundaca-Shah, M.D., Dr.P.H., and Victor J. Dzau, M.D.



Réponses aux crises sanitaires

Bilan du programme H1N1 2010

30 projets de recherche

- Cohortes: infectés, entourage
- Etudes cas-témoins
- Surveillance sérologique, Diag.
- Essais vaccinaux
- Casés: ARDS
- Sciences humaines et sociales
- Recherche fondamentale
- Pays du Sud

Financement: 13 m €

Financements publics: Inserm, Ministères Recherche & Santé, ANRS

Financements privés: Roche, GSK, Fondation Mérieux

Bilan scientifique

Publications: 89 articles dans revues internationales Colloques internationaux: > 100 communications



REACTing: a multidisciplinary network (2013-....)

Research and ACTION targeting emerging infectious disease

- **Endorsed by Ministries of Health and Research**
- **Objectives**
 - **Improve research preparedness:** governance, research tools and priorities, links between disciplines, regulatory issues, criteria of research emergency. **Funding**
 - **Timely initiation of research projects and funding**
 - **From basic science to social and human sciences**
- **Sponsored by Inserm for Aviesan**

REACTing : The French Response to infectious disease crises

Lancet, April 2016 JF Delfraissy, Y Yazdanpanah, Y Lévy



REACTing

- **Not focused on one particular disease**
 - Emerging human, zoonotic infections, non infectious diseases
- **Not focused on a particular area of research**
 - Surveillance, modelling, economics, communication etc.
- **Not focused on northern or southern countries**
 - Platforms, surveillance etc. in Southern countries

REACTing : The French Response to infectious disease crises
Lancet, April 2016 (in press) JF Delfraissy, Y Yazdanpanah, Y Lévy



REACTING in « peacetime » : Research preparedness



- Set up a **governance**: reactivity, flexibility
- Preparation of **research tools**
- Identification of research priorities: **likely scenarios of emergence**
- Establishment of **links** between different research entities
- Anticipation of **legal and ethical** issues
- Identification of potential sources of **funds** for research during the crisis

REACTING : in « peacetime »



- **Preparation of research tools**

- **Mathematical modelling:**
 - Developing databases documenting the structure of modern human populations, movement, contact networks and patterns.
- **Clinical trials/clinical research:** Identification of existing cohorts, databases and biobanks in support of clinical research (ex. Student cohort)
 - Setting up generic (mock-up) protocols;
 - Initiating contacts with regulatory administration to anticipate legal issues
 - Anticipating issues related to intellectual property
- **Social science:** attitudes toward preventive strategies such as vaccination in the context of an epidemic
- **Methodological Centers**

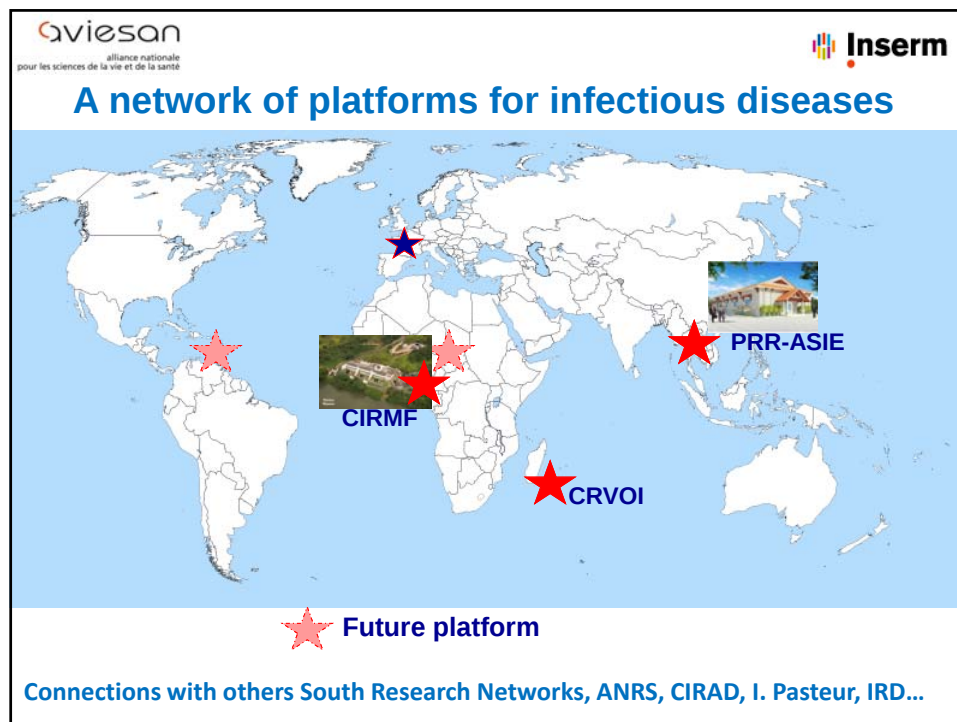
9

REACTING : During the crisis...



- **Define** strategic research priorities
- **Improve coordination** between participants
- Provide methodological assistance
- Promote **international** collaborations
- Respond to requests of relevant authorities
- Provide comprehensive **information to the public**
- Identify additional funding sources

10



REACTing in action...

– Chikungunya Outbreak in the French Caribbean - 2013

(Methodology Center, Bichat Hospital Site)

- **CHIKIVIG-01** "Prevention of Chikungunya infections in neonates : Clinical evaluation of anti-CHIKV hyperimmune intravenous immunoglobulins"

Pr Bruno Hoen

- Preparation and submission of the protocol to the regulatory authorities - Methodological support - Support to open new investigation centers abroad - Statistical analysis of the results

- **DAG-2** "West Indies-French Guiana Dengue and Chikungunya Study"

Pr André Cabié

- Preparing the amendment of protocol - Support the medical staff

- **CHIKHITA** "Natural History of Chikungunya infection"

Dr Sylvie Abel

- Preparation and submission of the protocol to the regulatory author - Funding the project kickoff - Statistical analysis of the results



THE EBOLA CRISIS



Mortality 70% !

AUGUST – SEPTEMBER 2014

04/2014

THE NEW ENGLAND JOURNAL of MEDICINE

Institut Pasteur
Inserm
Institut national
de la santé et de la recherche médicale

BRIEF REPORT

Emergence of Zaire Ebola Virus Disease in Guinea — Preliminary Report

Sylvain Baize, Ph.D., Delphine Pannetier, Ph.D., Lisa Oestereich, M.Sc.,
Toni Rieger, Ph.D., Lamine Koivogui, Ph.D., N'Faly Magassouba, Ph.D.,
Barre Soropogui, M.Sc., Mamadou Saliou Sow, M.D., Sakoba Keita, M.D.,
Hilde De Clerck, M.D., Amanda Tiffany, M.P.H., Gemma Dominguez, B.Sc.,
Mathieu Loua, M.D., Alexis Traoré, M.D., Moussa Kolié, M.D.,
Emmanuel Roland Malano, M.D., Emmanuel Heleze, M.D., Anne Bocquin, M.Sc.,
Stephane Mely, M.Sc., Hervé Raoult, Ph.D., Valérie Caro, Ph.D.,
Daniel Cadar, D.V.M., Ph.D., Martin Gabriel, M.D., Meike Pahlmann, Ph.D.,
Dennis Tappe, M.D., Jonas Schmidt-Chanasit, M.D., Benito Impouma, M.D.,
Abdoul Karim Diallo, M.D., Pierre Formenty, D.V.M., M.P.H.,
Michel Van Herp, M.D., M.P.H., and Stephan Günther, M.D.

BSL 4 Laboratory Jean Mérieux-Inserm, Lyon



Ebola, a call for action



Ebola: time to act

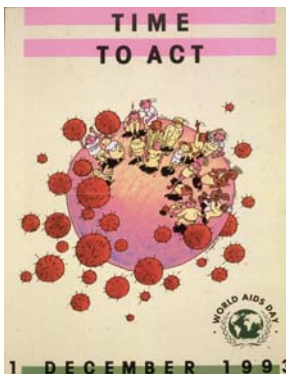
Governments and research organizations must mobilize to end the West African outbreak.

11 SEPTEMBER 2014 | VOL 513 | NATURE | 143

Ebola: learn from the past

Drawing on his experiences in previous outbreaks, David L. Heymann calls for rapid diagnosis, patient isolation, community engagement and clinical trials.

16 OCTOBER 2014 | VOL 514 | NATURE | 299







Premier ministre

French Task Force on Ebola

Main tasks in october 2014 :

- Avoid possible contamination in France
- Support affected countries to curb the epidemic dynamics
- Prevent the spread of the disease to neighboring countries
- Coordination and funding of translational research on Ebola

Coordinated response in Guinea :

- Support political coordination in Guinea
- HWs mobilisation, training, and protection
- Diagnosis and Treatment
- Sensitization, education and prevention
- Disease control measures



French Response to Ebola Crisis

A coordinated response – five pillars :

- ✓ **Support political coordination in Guinea**
 - ✓ 1 Expert with the National Coordinator, Surge capacity in Conakry (5 pers. including 2 medical officers), UNMEER
- ✓ **HWs mobilization, training, and protection**
 - Mobilization of 268 French staff (incl. 127 medical staff), training of 164 Guinean medical staff and 80 International, dedicated treatment unit (10 hospitalized 3 positives cases), intra/international evacuation capability
- ✓ **Research, Diagnosis and Treatment**
 - Laboratories with Pasteur Institute and Kplan and ETUs
 - Anti Ebola Treatment and Vaccine : Inserm
- ✓ **Sensitization, education and prevention**
 - Integrated approach at the local level
- ✓ **Disease control measures:** Conakry, Bamako, Paris, Malabo

Diagnosis - Care



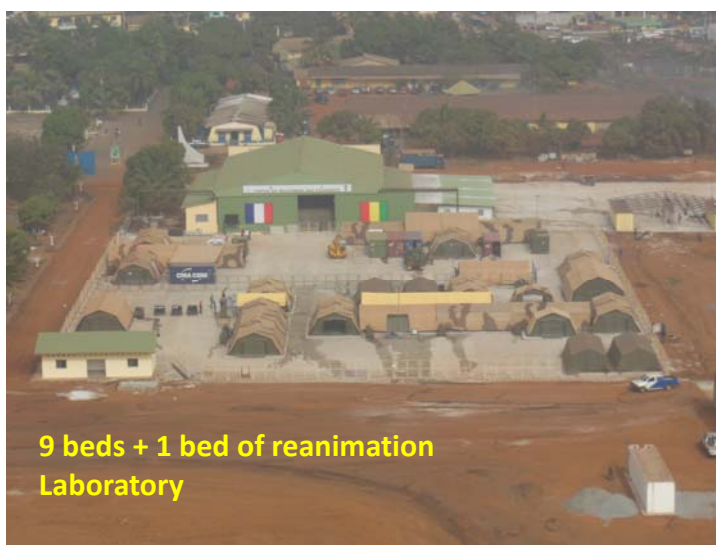
➤ Laboratories

- Donka de Conakry
- Mobile EU lab Guéckédou (additional mobile EU lab in development)
- Macenta ETU
- Beyla ETU – under construction
- Kerouane ETU - under construction
- Institut Pasteur – under construction (2016)

➤ ETU

- Macenta (50 beds, opens 14 November); *FRC – French Red Cross*
- Beyla (30-50 beds, opens mid-December) ; *WAHA – Women and Health Alliance International*
- Kérouané (30-50 beds, opens early January); *FRC – French Red Cross*
- Renovating the Forecariah transit center (20 beds, completion mid-December); *FRC – French Red Cross*
- N'zérékoré (40 beds, opens end of November) ; *ALIMA – The Alliance for International Medical Action*

Healthcare worker treatment centre in Conakry Opened in January 2015



**9 beds + 1 bed of reanimation
Laboratory**

Visite du CTS en Guinée le 7 février 2015



French Ebola TASK FORCE : Key Figures

- €200 million mobilized by France for the Ebola crisis response
- €110 million mobilized by France for action in West Africa
- €72 million mobilized for medical research, including €42.5 million in response to European Union calls for projects
- €13 million mobilized for the preparation of the French health system and treatment of suspected and diagnosed cases
- 4 Ebola Treatment Centres (ETCs) in Guinea's forest region, with a total capacity of 150 beds
- 1 healthcare worker treatment centre in Conakry
- 4 laboratories deployed in Guinea
- 600 healthcare workers mobilized for the Ebola response
230 mobilized in West Africa 370 mobilized on French territory
- More than 17,000 emergency services personnel trained in handling suspected cases
- Almost 5000 mobile emergency and resuscitation services (SMUR) personnel trained in handling suspected or possible cases
- 12 approved reference healthcare centres (ESRH)
- More than 20 research projects underway or being launched
- 6 major NGOs involved in French programmes (Médecins sans Frontières – French Red Cross – Médecins du Monde – Waha – Alima – Bioforce)



Lessons from current Ebola crisis



- Multidisciplinary approach
- Always keep watching for known highly pathogenic viruses.
- Preparedness:
 - ❖ Diagnosis
 - ❖ Vaccine
 - ❖ Therapeutics
 } For all known highly pathogenic viruses.
- Exploring the link between academic science and Industrials.
- Keep moving forward - Learn more on molecular basis of high pathogenicity.
- Search for new, related viruses (African henipa- and filoviruses)
- How to conduct operational research between Academic Institutions (Inserm...) and NGOs



Sous le haut patronage de

Laurent Fabius,
ministre des Affaires étrangères et
du Développement international

Najat Vallaud-Belkacem,
ministre de l'Éducation nationale,
de l'Enseignement supérieur
et de la Recherche

Michel Sapin,
ministre des Finances
et des Comptes publics

Jean-Yves Le Drian,
ministre de la Défense

Marisol Touraine,
ministre des Affaires
sociales de la Santé et
des Droits des femmes

Bernard Cazeneuve,
ministre de l'Intérieur

Annick Girardin,
secrétaire d'État chargée du Développement et de la Francophonie

RETOUR D'EXPÉRIENCE SUR LA GESTION DE LA CRISE EBOLA

LE JEUDI 29 OCTOBRE 2015 DE 9 H À 18 H

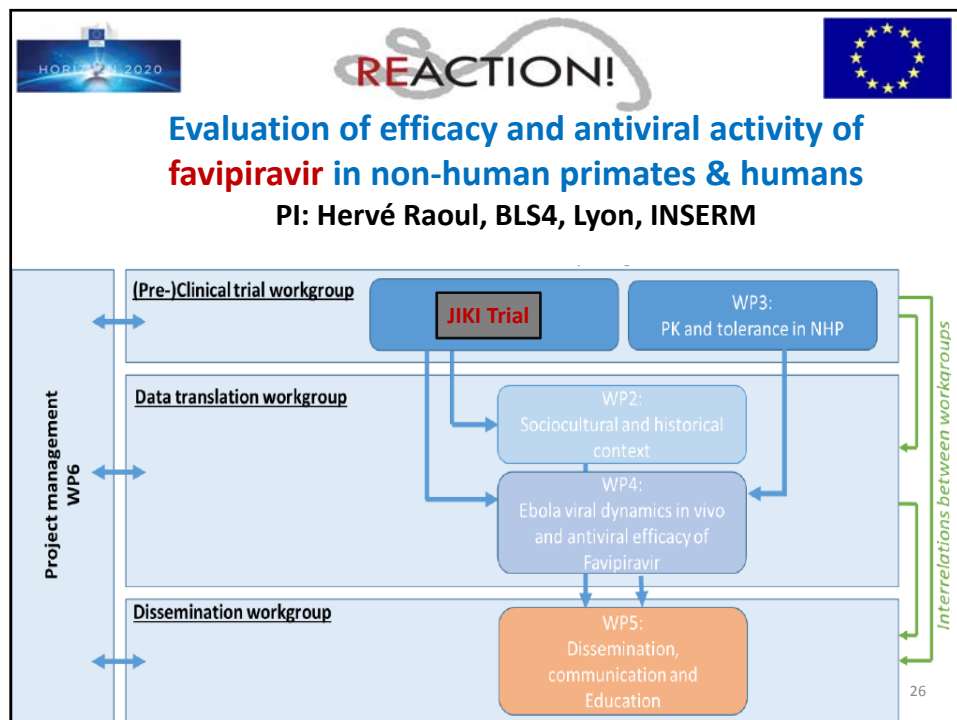
AU CENTRE DE CONFÉRENCES MINISTÉRIEL
Entrée au 27, rue de la Convention - 75015 Paris, à partir de 8 h 30

Prioritized Therapeutic Products

- **Drugs under clinical evaluation :**
 - Favipiravir: Guinea – Trial completed – considered as standard of care in Guinea
 - Brincidofovir: Liberia – Trial halted, product deprioritized
 - Zmapp: « cocktail » of 3 monoclonal antibodies (Liberia, Sierra Leone)
 - TKM-100802 (si-RNA); Sierra Leone – Trial completed, product deprioritized
 - Interferon: trial initiated in Donka (Guinea): not recruiting
- **Drugs for which clinical evaluation is envisaged:**
 - BCX-4430: adenosine analogue that disrupts viral RNA-dependent RNA polymerase function by chain termination
 - MIL-177: cocktail of 3 Mabs (same sequences as Zmapp)
 - Antiviral from Gilead

MARCH 2015






Favipiravir in patients with Ebola Virus Disease: early results of the JIKI trial in Guinea

(Inserm C1463 - EEUU H2020 666092)

Daouda SISSOKO, Elin FOLKESSON, M'lebing ABDOUL, Abdoul Habib BEAVOGUI, Stephan GUNTHER, Susan SHEPHERD, Christine DANIEL, France MENTRE, Xavier ANGLARET, Denis MALVY

Inserm U897, University of Bordeaux, France
Médecins Sans Frontières (MSF), Belgium
Alliance for International Medical Action (AIMA), France
Centre de Formation et de Recherche en Santé Rurale de Maféringah, Guinea
Bernhard-Nocht-Institut für Tropenmedizin, Germany
Inserm U1137, Paris Diderot University, France

All authors declared no conflict of interest







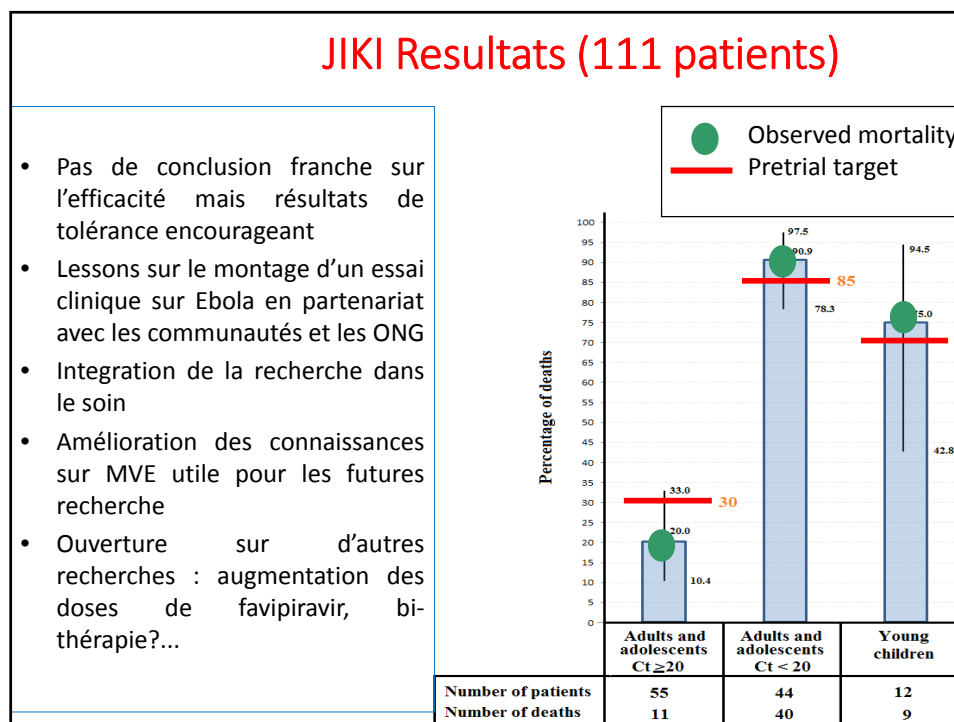


PLOS MEDICINE

RESEARCH ARTICLE

Experimental Treatment with Favipiravir for Ebola Virus Disease (the JIKI Trial): A Historically Controlled, Single-Arm Proof-of-Concept Trial in Guinea

PLOS Medicine | DOI:10.1371/journal.pmed.1001967 March 1, 2016



Clin Pharmacokinet
DOI 10.1007/s40262-015-0364-1

REVIEW ARTICLE

Ebola Virus Infection: Review of the Pharmacokinetic and Pharmacodynamic Properties of Drugs Considered for Testing in Human Efficacy Trials

Vincent Madelain^{1,2} · Thi Huyen Tram Nguyen^{1,2} · Anaëlle Olivo³ · Xavier de Lamballerie^{4,5} · Jérémie Guedj^{1,2} · Anne-Marie Taburet³ · France Mentré¹

ELSEVIER

Antiviral Research
journal homepage: www.elsevier.com/locate/antiviral

Favipiravir for children with Ebola

www.thelancet.com Vol 385 February 14, 2015
Naim Bouazza, Jean-Marc Treluyer, Frantz Foissac, France Mentré, Anne-Marie Taburet, Jérémie Guedj, Xavier Anglaret, Xavier de Lamballerie, Sakoba Keita, Denis Malvy, *Pierre Frange

Ebola virus dynamics in mice treated with favipiravir

Vincent Madelain^{a,b}, Lisa Oestereich^{c,d}, Frederik Graw^e, Thi Huyen Tram Nguyen^{a,b}, Xavier de Lamballerie^{a,b}, France Mentré^{a,b}, Stephan Günther^{c,d}, Jérémie Guedj^{a,b,e}

Dose regimen of favipiravir for Ebola virus disease

www.thelancet.com/infection Vol 15 February 2015
*France Mentré, Anne-Marie Taburet, Jérémie Guedj, Xavier Anglaret, Sakoba Keita, Xavier de Lamballerie, Denis Malvy

RESEARCH ARTICLE

Experimental Treatment with Favipiravir for Ebola Virus Disease (the JIKI Trial): A Historically Controlled, Single-Arm Proof-of-Concept Trial in Guinea

29

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea

J. van Griensven, T. Edwards, X. de Lamballerie, M.G. Semple, P. Gallian, S. Baize, P.W. Horby, H. Raoul, N. Magassouba, A. Antierens, C. Lomas, O. Faye, A.A. Sall, K. Fransen, J. Buyze, R. Ravinetto, P. Tiberghien, Y. Claeys, M. De Crop, L. Lynen, E.I. Bah, P.G. Smith, A. Delamou, A. De Weggheleire, and N. Haba, for the Ebola-Tx Consortium*

02.2016

THE NEW ENGLAND JOURNAL of MEDICINE

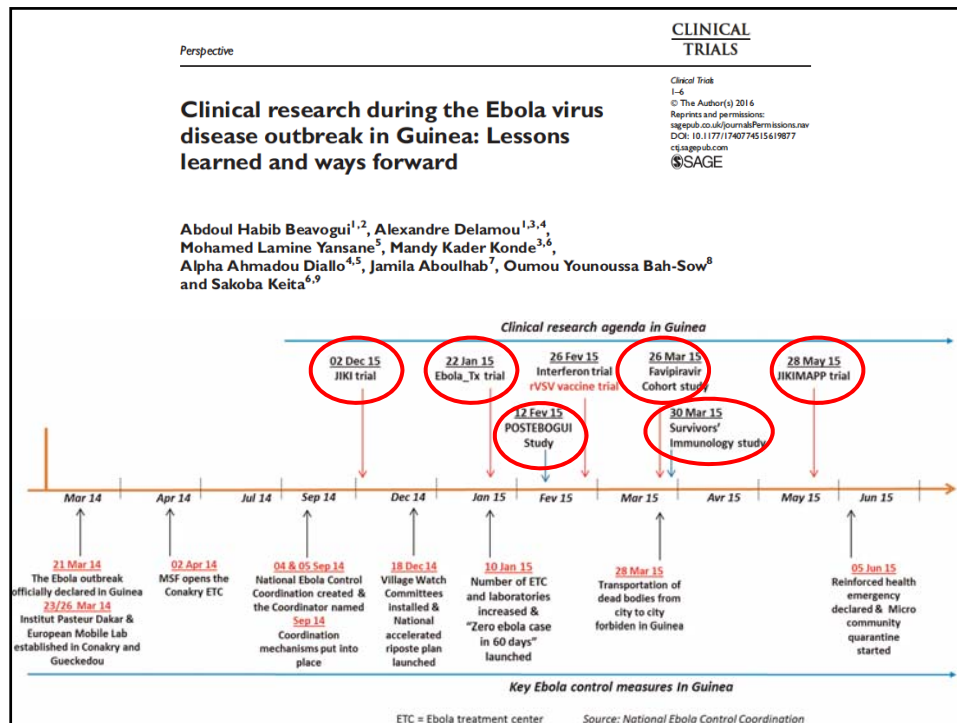
ORIGINAL ARTICLE

A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection

The PREVAIL II Writing Group, for the Multi-National PREVAIL II Study Team*

11.2016

REACTing



IRD Institut de recherche pour le développement

Inserm

POSTEBOGUI COHORT Guinea

M. Barry & S. Sow SMIT, CHU Donka, Conakry
E. Delaporte, IRD UMI233-INSERM U 1175

- To implement a cohort of adults and children declared free of EVD aiming at describing the:
 - Clinical and immuno-virological perspective**
 - Clinical symptoms and sequelae, co-infections
 - EBOV clearance in the different body fluids (blood, saliva, maternal breast milk, urines, feces, cervicovaginal secretions, semen)
 - Kinetics of IgM and IgG & Genetic factors
 - Psychological perspective**
 - Psychological consequences of Ebola disease (individual and family)
 - Social and anthropological perspective**
 - Analysis of social effects of EVD (through a description of stigma experience and typology of survivors' socio-sanitary impairment situations)
 - Subjective experience of illness and cure, impact on health workers
- To conduct an in-depth immunological ancillary study on a sub-sample of the main study (PostEbogui-Immuno, INSERM) REACTing

Cohorte de patients guéris, PostEbogui (Pr. Delaporte)

• L'objectif est

- d'étudier les conséquences cliniques, immuno-virologiques, psychologiques et socio-anthropologiques de la maladie sur une durée de 12 mois après la sortie
- et d'étudier chez les adultes les facteurs génétiques pouvant expliquer les différentes évolutions de la maladie à virus Ebola.
- **Cohorte** dynamique, ouverte, multicentrique, multidisciplinaire, observationnelle de type descriptive et analytique, constituée d'adultes et d'enfants/adolescents guéris confirmés après une phase aiguë d'infection à virus Ebola.
- Le recrutement des participants de la cohorte PostEboGui a été fermé le 11 juillet 2016.
- **Au total 802 personnes** participent à cette cohorte, pour une durée minimale de 2 ans, à partir de la date de leur entrée dans la cohorte.



The Journal of Infectious Diseases Advance Access published May 3, 2016

BRIEF REPORT

New Evidence of Long-lasting Persistence of Ebola Virus Genetic Material in Semen of Survivors

Mamadou S. Sow,¹ Jean-François Etard,² Sylvain Baize,³ N'Fally Magassouba,² Ousmane Faye,⁴ Philippe Mseleli,⁵ Abdoulaye II Touré,^{3,4} Ibimhima Savane,⁵ Moumié Barry,¹ and Eric Delaporte⁶; for the Postebogui Study Group*

¹Infectious Diseases Department, and ²Projet des fièvres hémorragiques de Guinée, Donka University National Hospital, Guinea; ³Institut de Recherche pour le Développement (IRD) UMI 233, Institut National de la Santé et de la Recherche Médicale (INSERM) U1175, Montpellier University, France; ⁴Chaire de Santé Publique, Département de Pharmacie, Université de Conakry, and ⁵Macenta Prefectural Hospital, Macenta, Guinea; ⁶IRD/UMI 233, INSERM U1175, Montpellier University, Montpellier, and ⁷Pasteur Institute/Unit of Biology of Emerging Viral Infections, International Center for Infectology Research, INSERM, CNRS, Lyon 1 University, Ecole Normale Supérieure de Lyon, France; and ⁸Institut Pasteur de Dakar, Senegal

Ninety-eight semen specimens were obtained for Ebola virus (EBOV) RNA screening from 68 men in Guinea during the convalescent phase of EBOV infection. Ten samples from 8 men were positive for EBOV up to 9 months after onset of the disease, with decreasing trends in the proportion of positive samples and the level of viral RNA. Safe sex practices should be observed after discharge from treatment centers.

Keywords. Ebola virus; survivors; semen; Guinea; virus persistence; outbreak.

(PCR) analysis (cycle threshold, 32) 199 days after onset of the disease [2]. The sexual transmission has been confirmed by genome sequencing [3].

In Guinea, as of 9 December 2015, 3351 cases have been confirmed, with 1268 survivors [4]. Here, we report new evidence of long-term persistence of Ebola virus RNA in semen of male survivors.

In March 2015, we started to enroll survivors in a follow-up study in Conakry and Macenta, Guinea, with a target cohort size of 450 patients and a follow-up duration of 1 year (referred to as the Postebogui cohort). Recruitment is ongoing, and enrollment is conducted at various times after discharge from Ebola treatment centers. After subjects provide informed consent, clinical examination, psychological assessment, and social assessment are performed, and semen specimens are obtained from adults for Ebola virus RNA detection. At Conakry/Donka National Hospital, a reverse transcription PCR (RT-PCR) developed by Weidman et al [5] and specific for Ebola virus nucleoprotein was used. In the Pasteur Laboratory in Macenta, both the RealStar Filovirus Screen RT-PCR kit 1.0 (Altona Diagnostics, Hamburg, Germany) and an additional in-house real-time RT-PCR kit, which has a higher sensitivity



Science*express*



Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak

- Le virus a diffusé à partir de l'Afrique Centrale par des animaux infectés au cours des 10 dernières années
- Puis transmission interhumaine



“In memoriam: Tragically, five co-authors, who contributed greatly to public health and research efforts in Sierra Leone, contracted EVD in the course of their work and lost their battle with the disease before this manuscript could be published. We wish to honor their memory.”



EBOV reservoir 2015-2106
Need for studies on EBOV at interface between wildlife and humans



In countries with know EBOV outbreaks and in countries estimated at risk

Role of bats: which species, how widespread?
bushmeat or faeces and/or saliva on fruit?

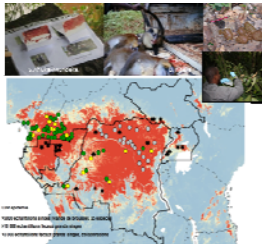
Role of bushmeat/hunting: primates, bats, antilopes etc..
EBV in bushmeat (monkeys, bats, etc..
EBV in faecal samples from apes

EBOV infections in humans involved in hunting and bushmeat

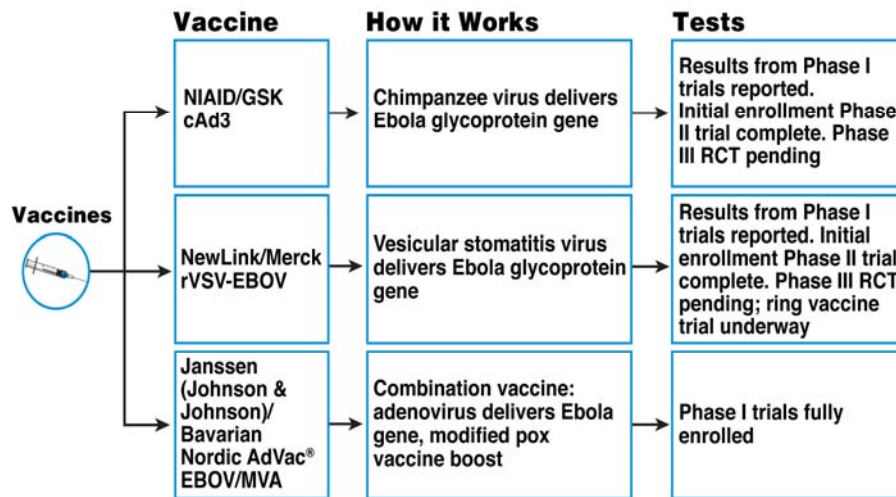
Previous studies on this samples:

Origin of HIV-1 in chimpanzees and gorillas (Science 2006, Nature 2006, PNAS 2015),
Origin of *Plasmodium falciparum* in gorillas and *Plasmodium vivax* in African apes

Martine Peeters, U1175/UMI233




Ebola Vaccine Candidate Pipeline



Phase 2 clinical studies in Europe (EBL2001) and in Africa (EBL2002) (Inserm coordination, Pr R. Thiébaud)



EBL2001: A Randomized, Observer-blind, Placebo-controlled, Phase 2 Study to Evaluate the Safety, Tolerability and Immunogenicity (humoral and cellular, gene expression) of Three Prime-Boost Regimens of the Candidate Prophylactic Vaccines for Ebola Ad26.ZEBOV and MVA-BN®-Filo in Healthy Adults (**n=612, 18-65 y**).

EBL2002: A Randomized, Observer-blind, Placebo-controlled, Phase 2 Study to Evaluate the Safety, Tolerability and Immunogenicity of Three Prime-boost Regimens of the Candidate Prophylactic Vaccines for Ebola Ad26.ZEBOV and MVA-BN-Filo in Healthy Adults, Including Elderly Subjects, HIV-infected Subjects, and Healthy Children in Three Age Strata (**n:1188, in BF, UG, Ky, Rw, IC**).



Partnership for Research on Ebola Vaccines in Liberia, Guinea and Sierra Leone –PREVAC-2017

Safety and immunogenicity of Ad26.ZEBOV/MVA-Bn-Filo and VSVΔG-ZEBOV in adults and children EBOLA (01-2017)

- **Multiple questions remain**
 - The immediacy and the durability of immune responses
 - the safety of the different vaccines in children
- **A need for additional effective vaccines**
- Two **randomized trials**, one in children and one in adults, that compares two vaccines (**Ad26.ZEBOV/MVA-Bn-Filo** and **VSVΔG-ZEBOV**) for immunogenicity & safety will be conducted)
- Guinea (2 sites), Liberia (1 site) and Sierra Leone (1 site)
- **Investigators:** Dr Beavogui (Guinea); Dr Kennedy (Liberia); Dr Wurie (Sierra Leone); Prof. Yazdan Yazdanpanah (Inserm); Prof. Cliff Lane (NIAID); Prof. Piot (LSHTM).



DEPARTMENT OF HEALTH & HUMAN SERVICES
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD



Inserm
Institut national
de la santé et de la recherche médicale

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Social and Human Sciences:

- Social Mobilisation and community engagement for the Ebola vaccine trial in Guinea and favipiravir trial
- Ebola Epidemic and social production of trust in Senegal; *IRD; CNRS; UCAD and Ministry of Health, Senegal*
- Rumors, disputes and controversies: perspectives from the digital world; *IRD; McGill University; Columbia University; WHO*



Ethical issues

La randomisation

Correspondence

Randomised controlled trials for Ebola: practical and ethical issues

2 months ago, when the numbers known to have died from Ebola in west Africa could still be counted in hundreds, WHO made an important statement about investigational drugs and vaccines. This crisis is so acute, WHO declared, that it is ethical to offer interventions with potential benefits but unknown efficacy and side-effects, though every effort should be made to evaluate benefits and risks and share

While we concur that RCTs provide robust evidence, and support their use where this is ethical and practical, we do not believe that either consideration is likely to be satisfied in the context of this epidemic. The priority must be to generate data about effectiveness and safety as swiftly as possible, so that the most useful new treatments can be identified for rapid deployment. Alternative trial designs have the potential to do this more quickly, and with greatest social and ethical acceptability.

The first objection to RCTs in which investigational drugs plus

The second objection is practical. Even if randomisation were ethically acceptable, it might not be deliverable in the context of health-care systems, and indeed wider social order, that are breaking down as in Liberia, Guinea, and Sierra Leone. Populations who are terrified by the progress of the epidemic, and who lack trust in health-care and aid workers, and in public authorities in the aftermath of civil wars, cannot be expected to offer informed consent to such randomised trials. It is also unclear that any capacity exists to impose controlled conditions during a raging epidemic.



Published Online
October 10, 2014
[http://dx.doi.org/10.1016/S0140-6736\(14\)61734-7](http://dx.doi.org/10.1016/S0140-6736(14)61734-7)

JF DELFRAISSY Lancet 2015

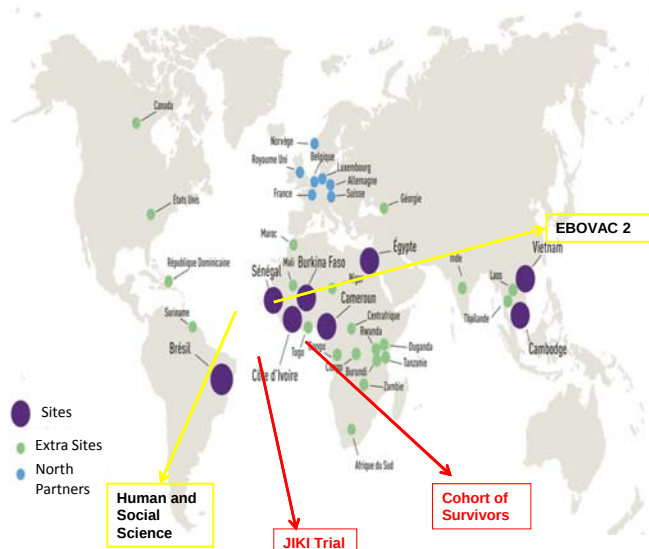
ANRS Research Sites involved in EBOLA

➤ Sub-Saharan Africa

Cameroon,
Burkina Faso,
Côte d'Ivoire,
Senegal

➤ South-East Asia

Cambodia,
Vietnam
➤ Egypt
➤ Brazil





Inserm
Institut national
de la santé et de la recherche médicale



aviesan
alliance nationale
pour les sciences de la vie et de la santé

Projets Zika France

Pr J-F. Delfraissy : ITMO I3M
Pr Y. Yazdanpanah : Reacting

Réunion de sécurité sanitaire
5 octobre 2016



REACTing



Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

MINISTÈRE
DES AFFAIRES SOCIALES
ET DE LA SANTÉ



BMJ 2016;352:i781 doi: 10.1136/bmj.i781 (Published 8 February 2016)

Page 1 of 2



EDITORIALS

Time for global action on Zika virus epidemic

Our response to infectious disease epidemics must be faster and smarter

Daniel R Lucey *adjunct professor of medicine*
Department of Medicine, Infectious Diseases, Georgetown University Medical Center, Washington, DC, USA

Association between Zika virus and microcephaly in French Polynesia, 2013–15: a retrospective study

Simon Cauchemez, Marianne Besnard, Priscilla Bompard, Timothée Dub, Prisca Guillemette Artur, Dominique Eyrolle-Guignot, Henrik Salje, Maria D Van Kerkhove, Véronique Abadie, Catherine Gard, Arnaud Fontanet*, Henri-Pierre Mallet*

Summary
Background The emergence of Zika virus in the Americas has coincided with increased reports of babies born with microcephaly. On Feb 1, 2016, WHO declared the suspected link between Zika virus and microcephaly to be a Public Health Emergency of International Concern. This association, however, has not been precisely quantified.

Published Online
March 15, 2016
[http://dx.doi.org/10.1016/S0140-6736\(16\)00651-6](http://dx.doi.org/10.1016/S0140-6736(16)00651-6)

www.thelancet.com Published online March 15, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)00651-6](http://dx.doi.org/10.1016/S0140-6736(16)00651-6)

Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study



Van-Mai Cao-Lormeau¹, Alexandre Blake², Sandrine Mossi, Stéphane Lestienne, Claudine Roche, Jessica Vanhommegien, Timothée Dubé, Laure Baudouin, Anita Teissier, Philippe Lemer, Anne-Laure Viol, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Wilton, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet³, Jean Neil⁴, Frédéric Chaveché⁵

Summary

Background Between October, 2013, and April, 2014, French Polynesia experienced the largest Zika virus outbreak ever described at that time. During the same period, an increase in Guillain-Barré syndrome was reported, suggesting a possible association between Zika virus and Guillain-Barré syndrome. We aimed to assess the role of Zika virus and dengue virus infection in developing Guillain-Barré syndrome.

Published Online:
February 29, 2016
[http://dx.doi.org/10.1016/S0140-6736\(16\)00562-6](http://dx.doi.org/10.1016/S0140-6736(16)00562-6)
DOI:10.1016/S0140-6736(16)00562-6

www.thelancet.com Published online February 29, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)00562-6](http://dx.doi.org/10.1016/S0140-6736(16)00562-6)

Acute myelitis due to Zika virus infection



Sylvie Mécharles, Cécile Harman, Pascale Poullain, Tuan-Huy Tran, Nathalie Deschamps, Grégory Mathon, Anne Landais, Sébastien Breurec, Annie Lannuzel

www.thelancet.com Published online March 3, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)00644-9](http://dx.doi.org/10.1016/S0140-6736(16)00644-9)

Zika virus detection in urine from patients with Guillain-Barré syndrome on Martinique, January 2016

B Rozé¹, F Najjoulah^{2,3}, J Fergé⁴, K Apetse⁵, Y Brouste⁶, R Césaire^{7,8}, C Faguer⁹, L Faguer⁹, P Hachédeu¹⁰, S Jeannin⁸, J Joux⁸, H Mehdaoui⁸, R Valentino⁸, A Signate⁸, A Cablé¹¹, on behalf of the GBS Zika Working Group¹²

1. Infectious and Tropical diseases Unit, University Hospital of Martinique, Fort de France, France
2. Laboratory of Virology, University Hospital of Martinique, Fort de France, France
3. Université des Antilles, EA 537, Fort de France, France
4. Intensive Care Unit, University Hospital of Martinique, Fort de France, France
5. Electrophysiological Department, University Hospital of Martinique, Fort de France, France
6. Emergency Department, University Hospital of Martinique, Fort de France, France
7. Diabetology Department, University Hospital of Martinique, Fort de France, France
8. Neurology Department, University Hospital of Martinique, Fort de France, France
9. INSERM CIC1428, Fort de France, France
10. The members of the group are listed at the end of the article

Correspondence: Benoît Rozé (benoit.roze@chu-fortdefrance.fr)

www.eurosurveillance.org

Projets de recherche – Zika 1^{er} trimestre 2016

- **Cohorte Arboviroses** dont des femmes enceintes (Andre Cabie /CM Nord)
- **Cohorte femmes enceintes symptomatiques** (ARS + Gynéco)
- **Suivi des enfants avec une malformation SNC** pendant l'épidémie de Zika aux Antilles-Guyane (Réseau de Diagnostic prénatal)
- **Cohorte nouveau-né/mère contaminée**: Suivi de nouveau-nés de mères infectées (Pédiatres)
- **Constitution de Biothèque** un prélèvement début grossesse et un prélèvement de fin de grossesse de tout femme enceinte aux Antilles-Guyane pendant la période épidémique. (Bruno Hoen/CM Nord)
- **Etude Cas-témoins** en Polynésie française (A Fontanet, IPP)



REACTing

A Global Alliance For Zika Virus Control And Prevention: ZIKAlliance



- Financement : EU / Inserm
- Lieu : Amérique du Sud, Caraïbes avec études ancillaires dans l'Océan Indien
- Piloté par l'Inserm (Pr Xavier de Lamballerie), le projet s'appuiera sur les équipes de différentes institutions de recherche en France, Inserm, IRD, Institut Pasteur ainsi que sur des équipes internationales, notamment d'Amérique Latine et Européenne (Brésil, Mexique, Colombie, Cuba, Equateur, Allemagne, UK, Pays-Bas, Belgique, Italie, Suisse, Espagne, Portugal, Norvège mais aussi Sénégal, Cambodge). Deux partenaires mexicains sont impliqués, l'Institut National de Santé Publique (INSP) et l'Institut Mexicain de Sécurité Sociale (IMSS).
- Etat d'avancement : Début Juillet 2016
- Budget : 10.000.000 EUR environ (dont 12 000 EUR de l'Inserm)



ZIKAlliance

**An interdisciplinary consortium for the study of
Zika disease**

Pr. Xavier de Lamballerie et al.



REACTing 2011-2016

éditorial

Virologie 2017, 16 (1) :3-5

Virologie

Bernadette Murgue¹

Jean François Delfraissy²

¹Adjointe, Institut de microbiologie et maladies infectieuses, Institut national de la santé et de la recherche médicale (Inserm), 101, rue de Tolbiac, 75654 Paris, Cedex 13, France
«bernadette.murgue@inserm.fr»
²Directeur de l'Institut de microbiologie et maladies infectieuses

Recherches en situation d'émergence infectieuse : la réponse à la crise se prépare dans l'intercriste

REACTing : the French response to infectious disease crises



Lancet, May 5 2016 (online) JF Delfraissy, Y Yazdanpanah, Y Lévy

« Quatrième priorité, la recherche dans toutes les disciplines, des sciences du vivant aux sciences humaines et à la démographie. »

Parce que l'anticipation en matière de recherche est cruciale et que les crises à venir se préparent dès à présent, la France a constitué un consortium mutualisant les moyens de ses instituts, baptisé REACTing : chargé de préparer la recherche sur les menaces sanitaires émergentes, ce consortium bénéficiera d'une allocation de 8 millions d'euros, pour mettre en œuvre un programme de recherche sur Zika et sur Ebola. Une dotation annuelle de 1 million d'euro lui permettra de fonctionner de manière pérenne. »

**Allocution du Président de la République, M. François Hollande
Conférence de Haut Niveau sur la Sécurité Sanitaire Internationale, Lyon – Mars 2016**

NUMERO SPECIAL DU LANCET

Towards a global agenda on health security



Lancet, May 5 2016 (online) F Hollande

France also acts in situations of acute crises, yesterday against Ebola in Guinea and today against Zika. We need to learn the lessons from these crises, in a spirit of responsibility and collective solidarity. During the closing of the High Level Conference on Global Health Security, on March 23, 2016, in Lyon, France, I fixed the following priorities:

- 1. Improve global mechanisms for surveillance, alert and diagnostics and plans for crises response**
- 2. Manage crises by reinforcing the role of civil society, local experts and affected populations**
- 3. Support research in life, human, and social sciences**
As the foresight in research is crucial, France has released €8 million for REACTing consortium, under the auspices of INSERM, with the mission to coordinate research on emerging health threats, such as Zika and Ebola
- 4. Apply the International Health Regulation with a strong and transparent global governance**



The need for global R&D coordination for infectious diseases with epidemic potential

*Marie Paule Kieny,
John-Arne Rottingen, Jeremy Farrar,
on behalf of the WHO R&D Blueprint team and the R&D Blueprint Scientific Advisory Group
www.thelancet.com Vol 388 July 30, 2016



World Health Organization

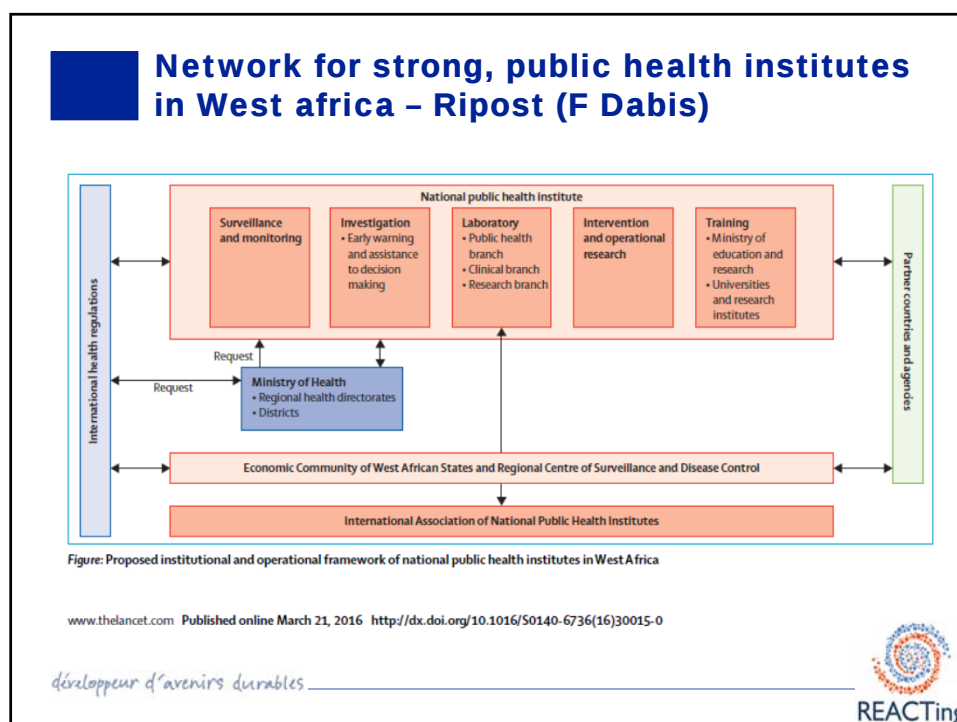
Blueprint WHO

GLOPID-R EU

Coordinating funding in public health emergencies

*Line Matthiessen, Walter Colli,
Jean-François Delfraissy,
Eung-Soo Hwang, Jeffrey Mphahlele,
Marc Ouellette, on behalf of GloPID-R members listed in the appendix
www.thelancet.com Vol 387 May 28, 2016





Le projet RIPOST en Afrique de l'Ouest (1/2)

- **Contexte post-Ebola** – Création à la demande de la CEDEAO d'un Centre de contrôle des maladies pour l'Afrique de l'Ouest – accompagnement des Etats par l'OOAS
- Finalité: **renforcer les capacités de santé publique des Etats francophones d'Afrique de l'Ouest**
- Un projet piloté par l'**Organisation Ouest africaine de la santé (OOAS)**
 - Budget de **5 M€** (3 M€ de crédits délégués par le MAEDI à l'AFD, et 2 M€ mobilisé par l'AFD sur le programme 209) – 5 ans
- **Objectifs :**
 - i) Renforcer les capacités des Instituts nationaux de santé publique de 6 Etats francophones de la CEDEAO (Bénin, Burkina Faso, Côte d'Ivoire, Guinée, Niger, Togo), ii) Renforcer les capacités de l'OOAS dans le domaine de la veille sanitaire et de la santé publique, iii) Soutenir le développement d'un réseau des Etats africains et des partenaires techniques sous l'égide de l'OOAS
- **Composantes principales :** i) Formation de professionnels de santé publique, ii) Mobilisation communautaire, iii) Appui technique à l'OOAS

développeur d'avenir durables



Le projet RIPOST en Afrique de l'Ouest (2/2)

- **Le rôle central des Etats de la région et de leurs INC** : Bénin, Burkina Faso, Côte d'Ivoire, Guinée, Niger, Togo
- Une dynamique régionale de **réseau entre Etats et partenaires techniques / financiers**, et une volonté de collaborer avec d'autres acteurs du secteur (CDC US, Banque Mondiale, GIZ/KFW...)
- **Un groupement d'acteurs franco-africains, experts en santé publique et sciences humaines**, recruté par AO international et composé de l'Agence de Médecine Préventive (chef de file), Santé Publique France, l'ISPED – Université de Bordeaux, l'IRD, IANPHI, l'ONG SOLTHIS (budget de 4 M€ sur les 5 financés par l'AFD à l'OOAS)
- **Une opportunité à la fois pour le renforcement de capacités des Etats ciblés, pour la valorisation de l'expertise française et pour la diplomatie sanitaire française dans la région**
- Mise en œuvre à compter de 2017

développeur d'avenir durables





ACKNOWLEDGMENTS

- Clinical and research teams
- Chairs of Coordinated working groups
- INSERM, ANRS staff
- Patients NGOs, more specifically ALIMA, MSF, Croix Rouge Française
- Institut Pasteur, IRD, CNRS, Hospitals
- Expertise France
- Pharmaceutical Industry
- WHO, NIH-NIAID, European Commission, WELCOME TRUST
- Patients
- GUINEA, Ebola Task Force

ANRS