The comprehensive response to Ebola and other Emerging Infections: the approach of the National Institute for Infectious Diseases "L. Spallanzani", Rome

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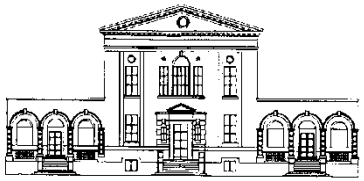

World Health Organization

WHO Collaborating Center for clinical care, diagnosis, response and training on Highly Infectious Diseases

Presentation outline

- The INMI “L. Spallanzani”:
  - brief historical introduction,
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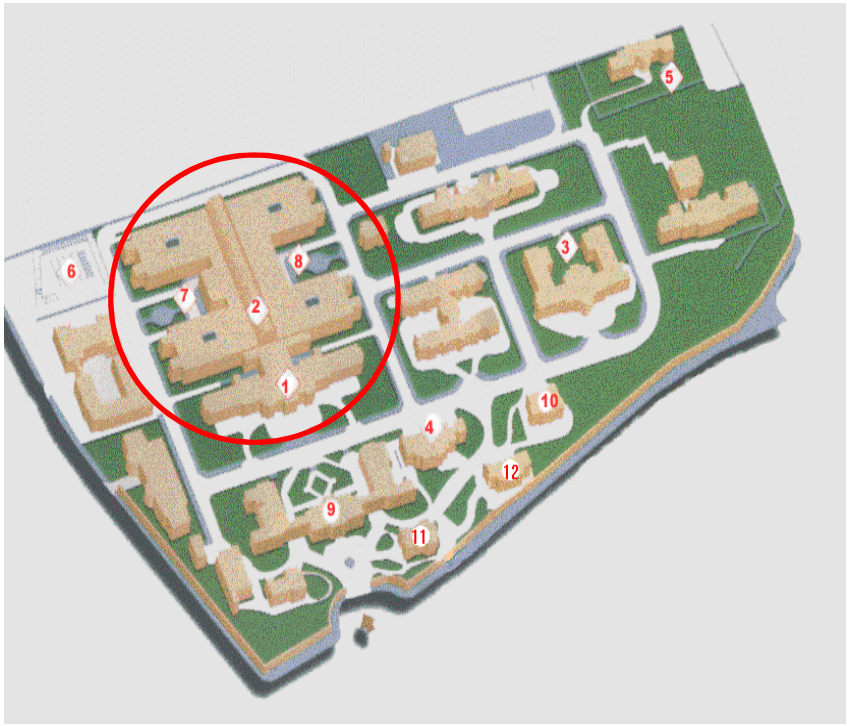
  - The activities “on the field”,
  - The research activities;
- Conclusion: the INMI vision

The National Insitute for Infectious Diseases (INMI) “L. Spallanzani”

- Located in Rome;
- Opened in the 1936, structured in pavilions;
- Completely renovated in 1992, according to modern standards for Health-Care settings;
- From 1996, recognized as National Institute for Research and Care of Infectious Diseases (IRCCS);



Pathway towards the establishment of INMI as a model of response to emerging IDs

Key words:

- Care
- Diagnosis
- Research
- Preparedness

1936 Opening IDs Center

1975 National Referral Center for Smallpox and dangerous IDs

1977 Isolation Unit for dangerous pathogens with Biocontainement Lab

1995 New Clinical Center (200 beds at negative pressure) and a BSL3 Lab
Ntl Referral Center for VHFs

1996 Concept proposed for 1 BSL4 and 2 BSL3 lab

2000 BSL4 and 2 BSL3 labs open
Agreement with NIH-NIAID

2001 Ntl Referral Center for Bioterrorism
Approval of an High Isolation Facility, new BSL4, 3 BSL3 labs and a biocontainment cryobank

2003
-BSL4-authorized
-2 BSL3 and cryobank open
-Ntl Referral Center for SARS
-GOARN partner

2005 Ntl Referral Center for Avian Flu

2006 Coordination of EU Networks on BSL4, HIDs units, training in EIDs emergencies, harmonization

2009 WHO Collaborating Center for clinical care, diagnosis, response and training on Highly Infectious Diseases

World Health Organization

2011 Infrastructure of Pan-European Interest identified by EC in the ESFRI on Highly Pathogenic Agents.

2015 High Isolation Facility

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…veramente due!!!

E’ arrivato!!!!!

Trasporto mediante un aereo KC 767
dell’Areonautica Militare.
Arrivo a Pratica di Mare, 24 nov 2014

LA STAMPA CRONACHE
+ Bossetti: “Prego ogni giorno per Yara”
+ Eternit, l’impegno di Renzi “Parte civile nel processo bis”
+ In un block notes i riti della ’ndrangheta
Ebola, l’arrivo allo Spallanzani del paziente italiano
(ANSA)

UNITÀ SPECIALE
DI BIOPROTEZIONE

Ebola at INMI: a successful story

- Evacuated from Sierra Leone;
- Admitted on November 25, 2014;
- Physician, male, 50 yrs old, working for Emergency (Italian NGO);
- Not clear how he became infected;
- Admitted in a High Isolation Unit (HIU) in a dedicated ward, then moved to another Isolation Unit with Intesive Care Capabilities (HI-ICU) and mechanically ventilated for 7 days;
- After Intensive Care support, his conditions progressively improved;
- After 38 days of hospitalization, the patient was discharged in fully recovery on 2 Jan 2015.

The INMI Spallanzani Model

- Managing Highly Infectious Diseases patients (such as patients with Ebola) require a strong preparedness activity;
- INMI has a 20-year-long background in hospital preparedness;
- All these previous activities resulted crucial in the safe and appropriate management of the Ebola patient.

The INMI Spallanzani Model

The model is based on many pillars:

- Logistic for effective and safe transport and isolation;
- Advanced diagnostic capabilities;
- High-level clinical and infection prevention and control (IPC) expertise;
- Long-term established international collaborations.

Management of the Italian imported case – The transport

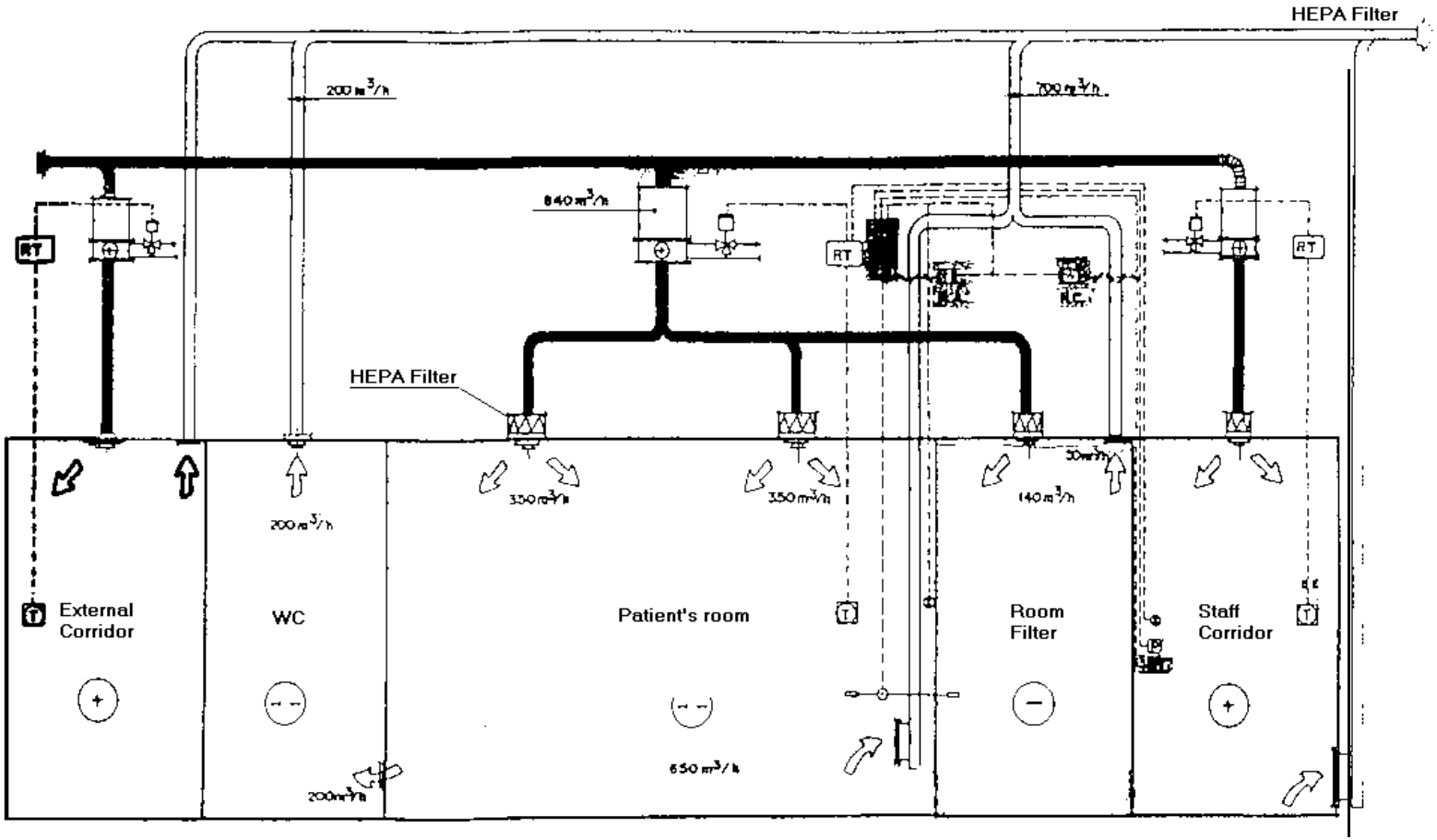
- Long-term collaboration with Aeromedical Evacuation Team of Italian Air Force;
- Several exercises in the past;
- Integration by the Air Transport Isolator (ATI) and the Stretcher Transport Isolator (STI)

Facilities for bio-containment transport at INMI

Controlled ventilation, negative pressure, HEPA filtration, intercom systems, and separation of driver's from patient's cabin

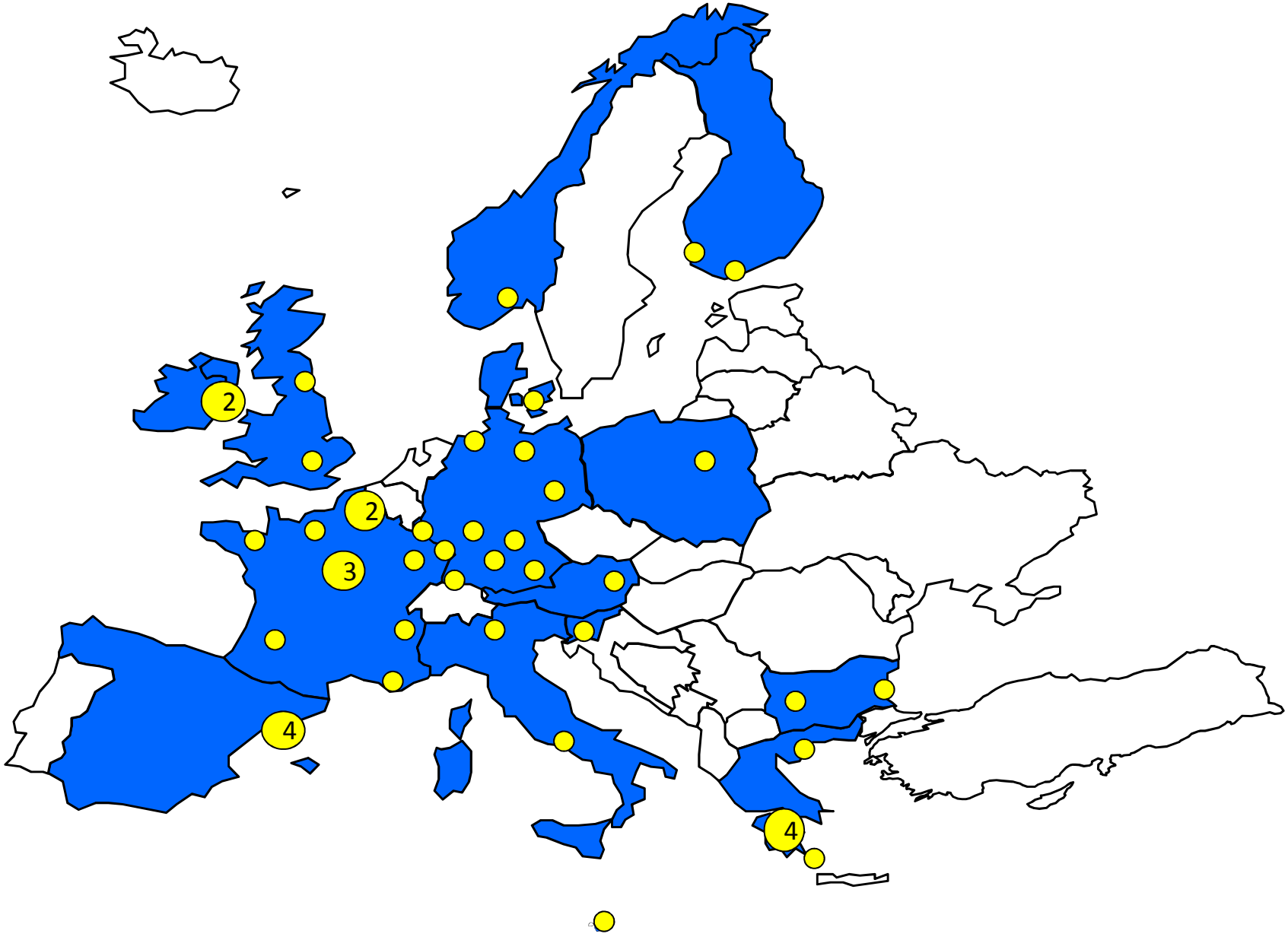
Facilities for patient isolation

- HIU: isolation room in a dedicated ward, equipped with dedicated pathway for patient entry, separate way-in and way-out for HCWs with anterooms for PPE doffing/donning, sealed doors and windows, negative pressure, HEPA filtration of exhausting air, observation windows and a web-cam system for patient monitoring;
- HI-ICU: isolation room integrated in (but functionally separated to) Intensive Care Ward, with the same feature as HIU, and in addition Intensive Care capabilities and a dunk-tank for specimen decontamination;
- A new High-Level Isolation Unit with 10 independent beds is ready to open;
- A BSL-3 autopsy suite is available, also.


HEPA Filter
200 m³/h
700 m³/h
840 m³/h
RT
RT
RT
HEPA Filter
350 m³/h
350 m³/h
140 m³/h
200 m³/h
External Corridor
WC
Patient's room
Room Filter
Staff Corridor
650 m³/h

HI-ICU

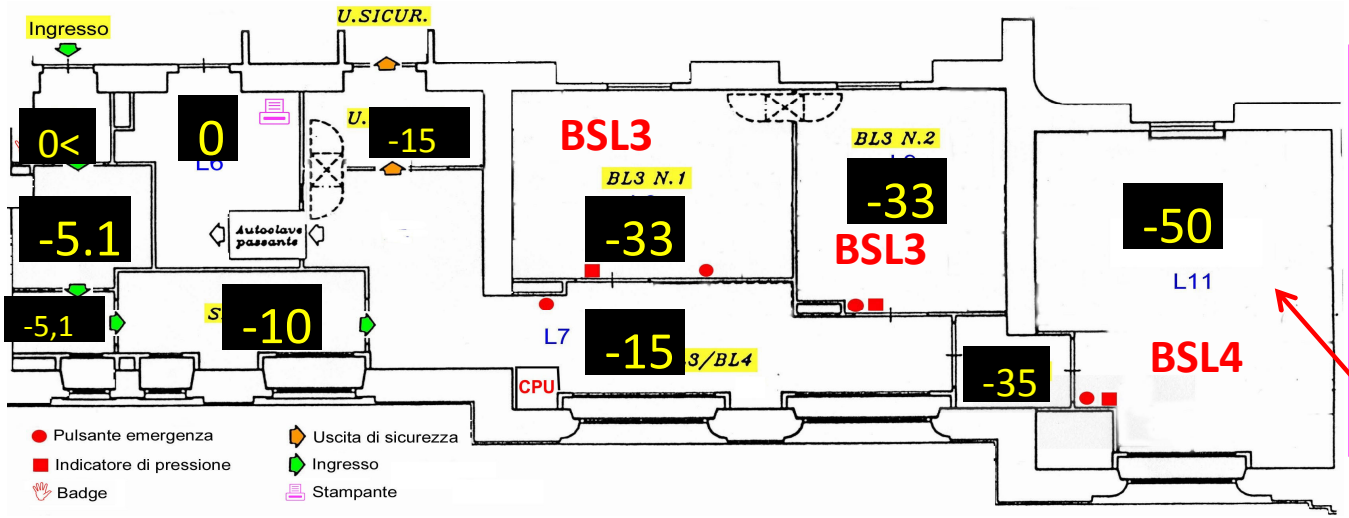
48 isolation facilities in 16 EU countries – 2009-10



EVD diagnosis: laboratory difficulties

- ✓ Need of a wide differential diagnosis
- ✓ Scarcity/absence of available reference materials for the development of diagnostic tools specific for EVD
- ✓ Scarcity/absence of validated commercial kit
- ✓ Need of accessory tests for the confirmation of the initial results, due to the poor PPV at low prevalence, as it is the case outside of the endemic areas
- ✓ Need to develop new methods
- ✓ Need of international networking in order to access: methods, materials, reagents, advice, confirmation of the results
- ✓ Need of high containment laboratory

Virus culture: BSL4



- The INMI has a strong experience and advanced diagnostic capabilities;
- One BSL-4 (based on cabinet line) is available, and some BSL-3 labs;

Capacità diagnostiche per Ebola allo Spallanzani

- Ricerca diretta del virus mediante metodi molecolari basata su un test iniziale di screening e vari test successivi di conferma
- Caratterizzazione molecolare mediante sequenziamento ed analisi filogenetica
- Ricerca diretta del virus mediante metodi colturali
- Ricerca diretta del virus mediante microscopia elettronica
- Ricerca degli anticorpi mediante Immunofluorescenza indiretta (IgM e IgG)
- Ricerca di anticorpi mediante test di neutralizzazione
- Diagnosi differenziale verso le principali eziologie alternative, nonché verso altre cause di sindromi emorragiche, incluse Lassa, Dengue, Alkhurma, febbre gialla, ecc.

Not only EBOV: many differential diagnosis capabilities available at INMI

- Malaria (especially falciparum malaria)
- Typhoid fever
- Other bacterial enteric infetions
- Leptospirosis
- Rickettsial infections
- Plague
- Viral hepatitis
- Dengue
- Chikungunya
- Yellow fever
- Rift Valley Fever
- Lassa fever
- Marburg hemorrhagic fever
- Severe influenza
- African trypanosomiasis
- Bacterial pneumonia
- Meningococcemia
- Other…

Clinical and Infection Control Expertise
Role of Training

- At INMI, a multidisciplinary task-force, including infectious diseases, epidemiology, intensive care and infection control expertise, is established since years;
- Since August 2014, the task-force members started an intensive re-training, mainly focused on PPE donning/doffing procedures;
- Similarly, a procedure covering all aspects of IPC has been drafted and continuously updated.

Procedure operative per la gestione di casi sospetti, probabili o confermati e contatti di malattia da virus Ebola (MVE)

Unità di Crisi MVE

Istituto Nazionale per le Malattie Infettive "Lazzaro Spallanzani"

IRCCS, Roma

Revisione 3/2014 del 10/11/2014

Indice

1. Premessa

2. Introduzione

    2.1 Brevi cenni generali sul virus Ebola

    2.2 Situazione epidemiologica attuale

    2.3 Attuali conoscenze sulla epidemia di MVE in corso in Africa Occidentale

    2.4 Definizioni di caso

3. Gestione del paziente presso l'INMI

    3.1 Triage in Accettazione

    3.2 Procedure per il ricovero del paziente

    3.3 Comportamenti durante il ricovero

    3.4 Aspetti di laboratorio

4. Altre procedure

   4.1 Modalità di disinfezione e sanificazione

   4.2 Modalità di trattamento e smaltimento dei rifiuti

   4.3 Modalità di gestione delle salme

   4.4 Modalità di sorveglianza sanitaria dei contatti

5. Sorveglianza sanitaria degli operatori esposti

6. Flussi informativi e disposizioni in materia di comunicazione

Allegati:

Allegato 1 – Procedure per la selezione dei DPI, vestizione e svestizione

Allegato 2 – Scheda raccolta dati MVE

Allegato 3 – Algoritmo diagnostico

Allegato 4 – Scheda paziente da allegare ai test diagnostici

Allegato 5 – Scheda informativa per i contatti

Allegato 6 - **E**sposizione accidentale dell'operatore sanitario nella gestione del caso di MVE

Allegato 7- **Modello notifica di caso**

Allegato 8 **Modulo comunicazione al Ministero della Salute e alla Regione Lazio**

Allegato 9 **Tabella sulla definizione di caso e contatto di MVE e flusso informativo**

Long-term established international networks and collaborations

- INMI works in close collaboration with European Commission, ECDC, and WHO, and is an active member of the Global Outbreak Alert and Response Network;
- The Institute coordinated several projects and networks in the field of preparedness and response to infectious diseases emergencies, and also participated in several projects as active member;
- These links has been used during the patient management, for example for rapid providing of experimental drugs.

Areas of interest of networks coordinated by INMI

- **Laboratory diagnosis and research**
  - The European Network of P4 Laboratories (Euronet-P4 and ENP4-Lab, 2005-2010; QUANDHIP and EMERGE 2011-now)
- **Training**
  - European Training in Infectious Disease Emergencies (ETIDE, 2006-2009)
- **Clinical and Infection Control management**
  - The European Network for Infectious Diseases (EUNID, 2004-2007)
  - European Network for highly infectious diseases (EURONHID, 2007-2010)

Areas of interest and networks coordinated by INMI

- Laboratory projects (EuroNet-P4, ENP4-Lab. QUANDHIP and EMERGE) created a unique umbrella for all BSL-4 operating in Europe, exchanging staff, data, specimens, reagents, and provide validation of diagnostic tests;
- The clinical and infection control project (EUNID and EuroNHID) developed standards for infection control, isolation, and High-level Isolation Units, and performed a survey of capabilities in EU countries;
- The training project (ETIDE) created a network of trained specialists which will facilitate communication and collaboration among European countries

Participation in several other networks

- ENIVD;
- ERINHA;
- European Mobile Lab;
- EVA and EVA-Global;
- Influenza networks;
- EpiSouth and EpiSouth-Plus;
- GVN
- Many other networks working in epidemiology, surveillance, preparedenss and response!

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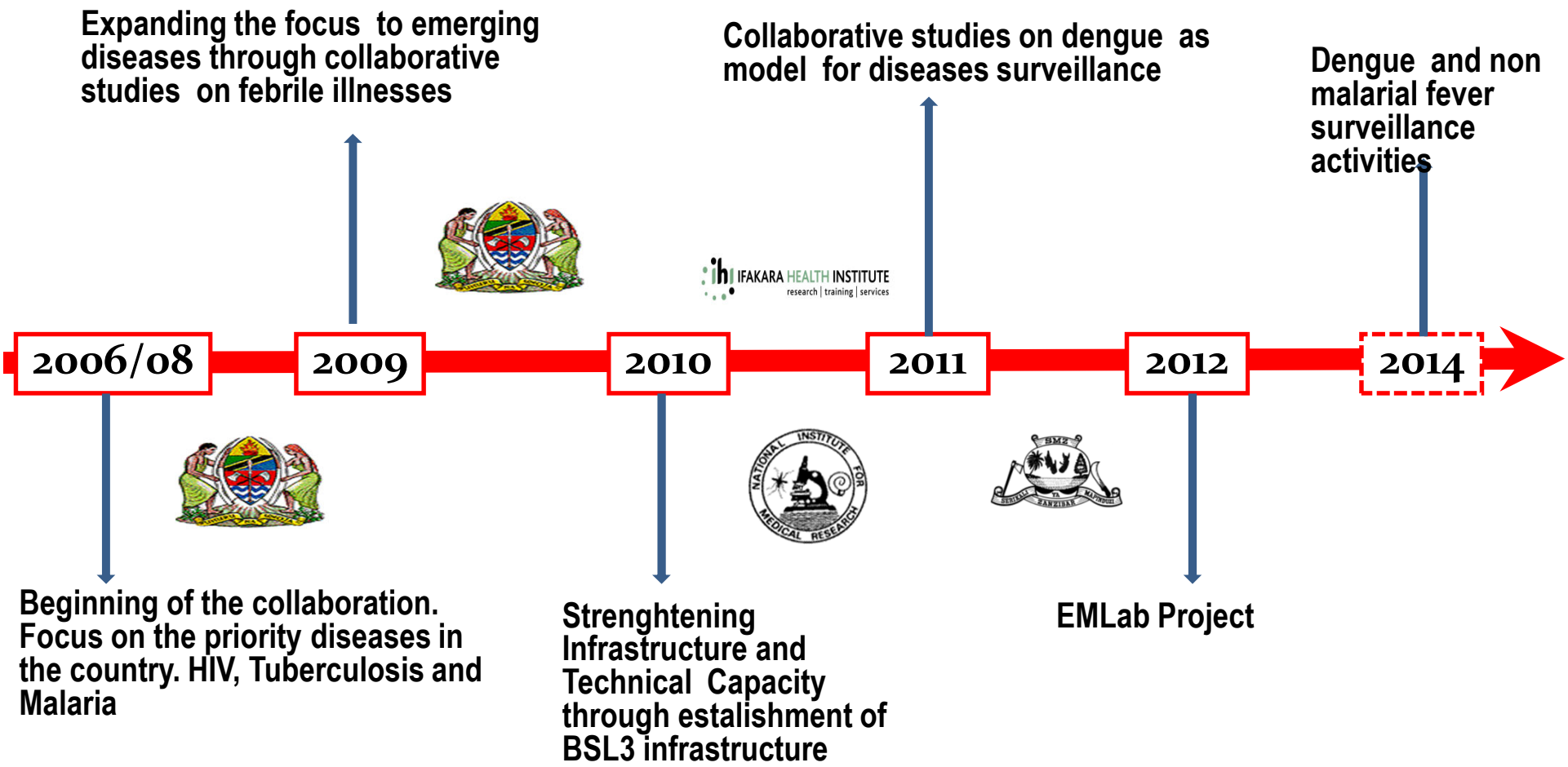
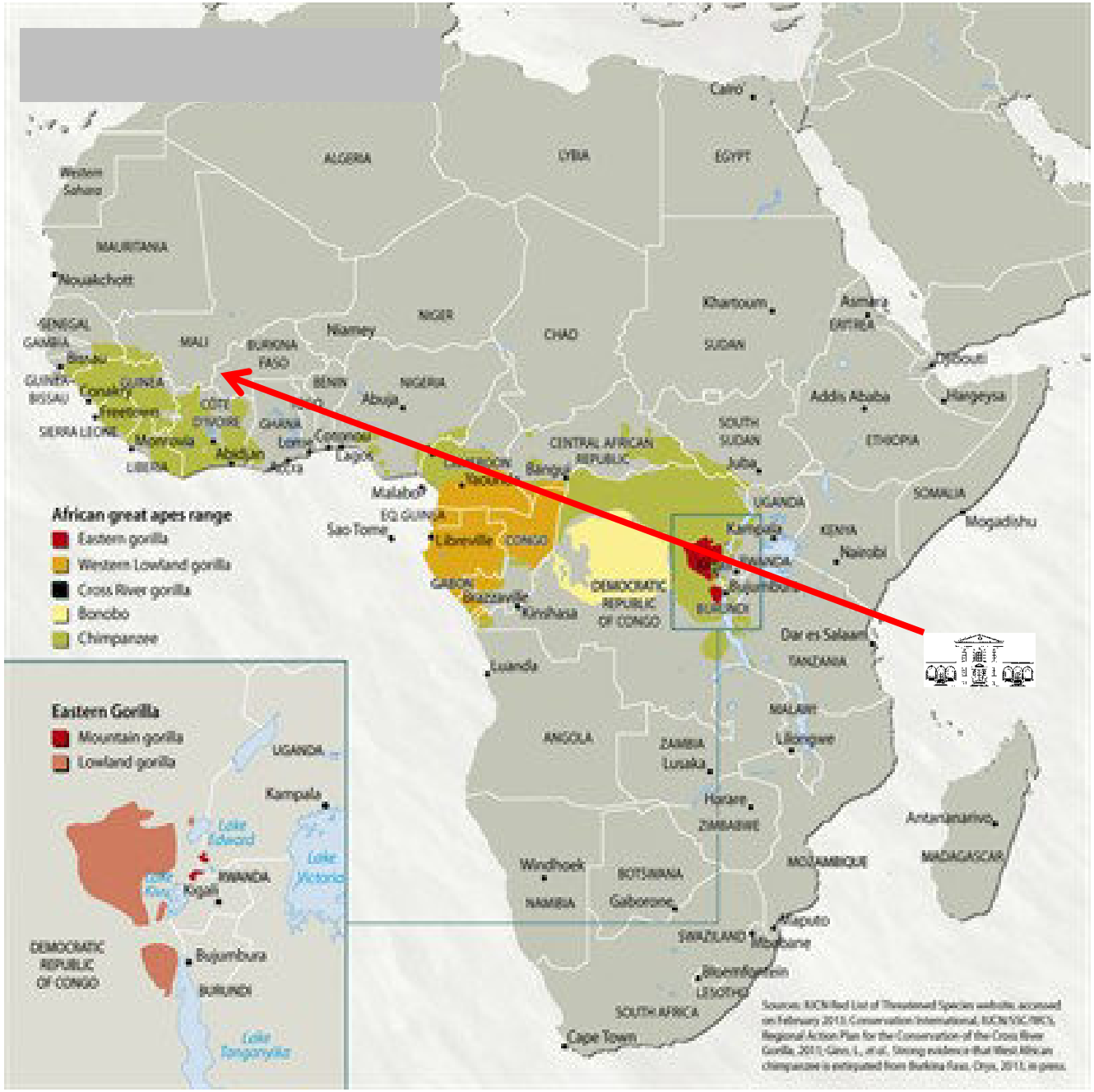
Long history of collaboration with Tanzania





After specific request from the Italian Ministry of Foreign Affairs, the Head of INMI Project in Tanzania moved to Sierra Leone, to coordinate the Italian interventions.

Specific Mandate from European Commission for Coordination of diagnostic activities (QUANDHIP)

Ref. Ares(2014)2939152 - 8/8

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Public health
Health threats

Luxembourg,
Sanco.dd(1.c)3 (2014) 3896585

Dr Roland Grunow, RKI

Dr Giuseppe Ippolito, INMI

Sent by e-mail only to
grunowr@rki.de
giuseppe.ippolito@inmi.it

Subject: WP 8 QUANDHIP activation

Dear Dr Grunow,

Dear Dr Ippolito,

Following the recent developments of the on-going Ebola Virus Disease (EVD) outbreak in West Africa and following the meeting of the EU Health Security Committee of 1 August 2014 at which work from QUANDHIP was presented and discussed, I am writing to ask you to activate the QUANDHIP network in order to be prepared to support an EU response in case of need.

The purpose is to provide assistance to national public health laboratories and reference virology laboratories in order to ensure access to adequate diagnostic capabilities for all EU Member States for confirming cases of Ebola Virus Disease infection.

In order to support those Member States who are temporarily in need of support we invite the QUANDHIP (2010021002) joint action, through the activation of its Work Package 8 (WP8), to support the following activities:

- connecting partner laboratories and alerting them of the need to be ready for requests for Ebola diagnostic testing analyses should the need arise;

- update guidance on the proper handling practices of clinical samples from patients suspected of Ebola virus disease in accordance with highest biosafety standards;

- facilitate access to diagnostic testing and in particular PCR testing for EVD in each of the EU-MS where diagnostic capacity is not available;

- put in place a system for on-call advice from EVD expert reference laboratories to national public health reference laboratories if needed;

- exploring means of shipping of samples from the mentioned Member States to the laboratories having the necessary capacity, if an urgent need will arise;

- establish close coordination and a reporting mechanism according to the Work Package 8 (WP8) procedure on QUANDHIP laboratories response to outbreaks due to Highly Infectious Pathogens.

In order to allow the smooth activation of the mechanism and to put in place all the arrangements to be ready to support the specific request, if it will be raised, we ask you to contact the Consumers Health and Food Executive Agency (CHAFEA) concerning administrative issues on the current execution of the WP 8 budget and to present the description what are the changes estimated on the budget to cover the transport of samples. Please describe the sample unit cost estimation, as previously done for the external quality assessment (EQA), as well as costs in terms of human resources needed to organize a 24/7 on-call service to coordinate activities and provide guidance.

Please do not hesitate to ask for additional information or to contact the Consumers Health and Food Executive Agency (CHAFEA) concerning administrative issues.

Thank you in advance for your collaboration.

Yours sincerely,

Herta Adam
Deputy Head of Unit

Copy: John F. Ryan, P. Gaglielmetti, C. Price, J Remacle (CHAFEA), C. Menel Lemos (CHAFEA), M. Sprenger (ECDC)

Commission européenne, 2920 Luxembourg, LUXEMBOURG – Tel. +352 4301-1
Office: HTC 03/069 – Tel. direct line +352 4301-32841

"Establishment of Mobile Laboratories for Pathogens up to Risk Group 4 in combination with CBRN Capacity Building in sub-Saharan Africa"

4 March 2009

Interim Feasibility Report on the Establishment of a European Mobile Laboratory for BSL4 Agents

Once upon a time…

October 2010:

The EuropeAid Cooperation Office (DevCo) of the European Commission designated scientists from EMP4Lab Project ***to write a contract*** for an European mobile laboratory project

December 2010:

Call for the European mobile laboratory project.

The EuropeAid Cooperation Office (DevCo) of the European Commission has set up the collaborative project **"Establishment of Mobile Laboratories up to Risk Group 4 in combination with CBRN Capacity Building in sub-Saharan Africa"** (EMLab project, 2012-2015) with a budget of 3.5 Mio EUR

The EMLab consortium includes several EU Biosafety level 4 laboratories and technical partners

15/12/2011 Project start date

European Mobile Lab Project

Background | Concept | Activities | Units | Partners | News & Events | F

Main partners

BNITM Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany

InstMikroBioBw Institute of Microbiology of the German Armed Forces, Munich, Germany

INMI National Institute for Infectious Diseases “L. Spallanzani”, Rome, Italy

External Advisory Board (EEAB)

WHO

ECDC

MSF

Partners and associated partners

Spiez, Switzerland

Marburg, Germany

Inserm, Lyon, France

Porton, Salisbury, UK

ISTH Irrua Nigeria

NIMR , Dar Es Saalam, Tanzania

IMI , Ljubljana, Slovenia

Berlin, Germany

NCE Budapest, Hungary

August 2013: first exercise in the Black Forest, Germany

February 2014: second exercise in Nigeria

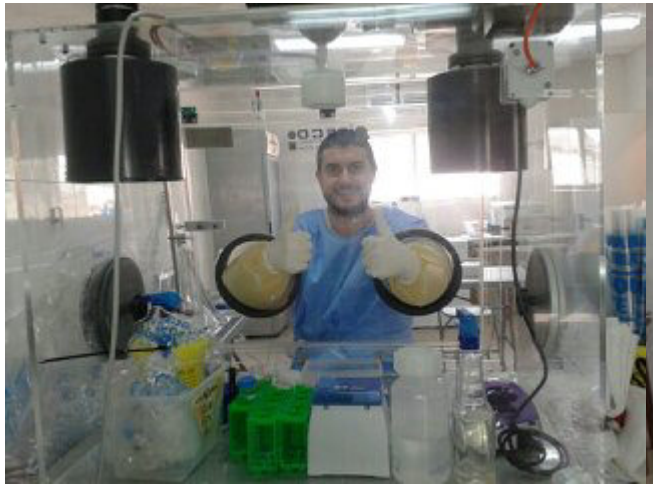
The deployment of European Mobile Lab to West Africa – March 2014

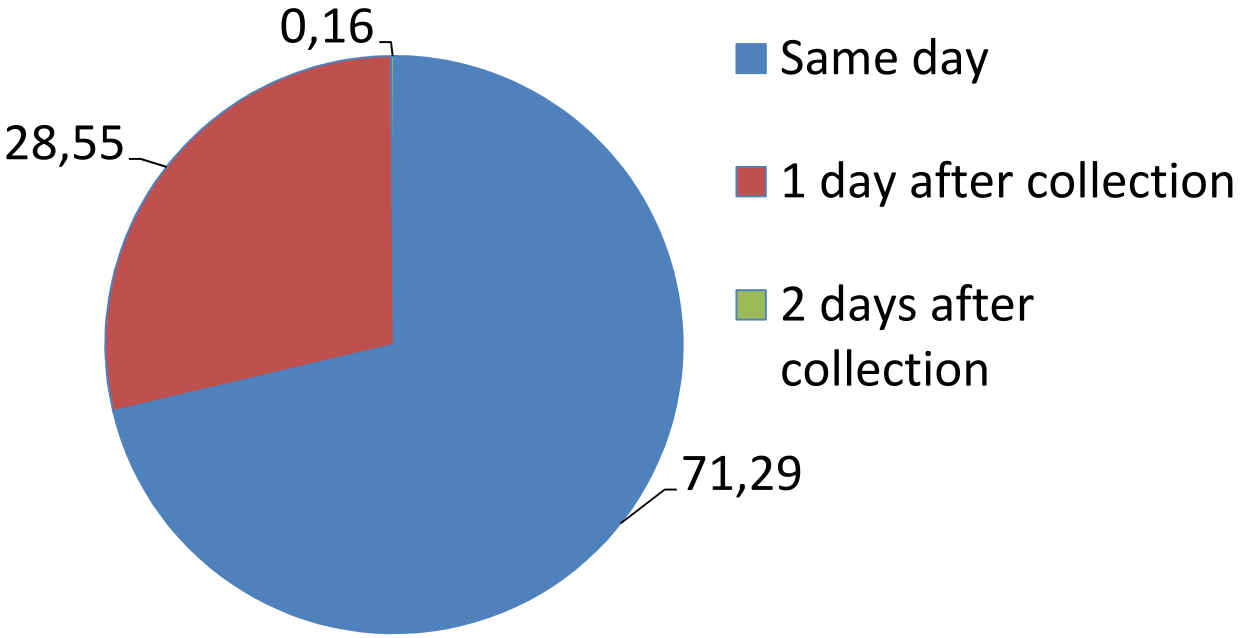
Mobile Lab working in Guinea

Mobile Lab working in Liberia

Italian Laboratory in Goderich Sierra Leone

- On 4 December 2014, INMI started the new advanced lab, located in the premises of the new treatment center managed by the Italian NGO Emergency.

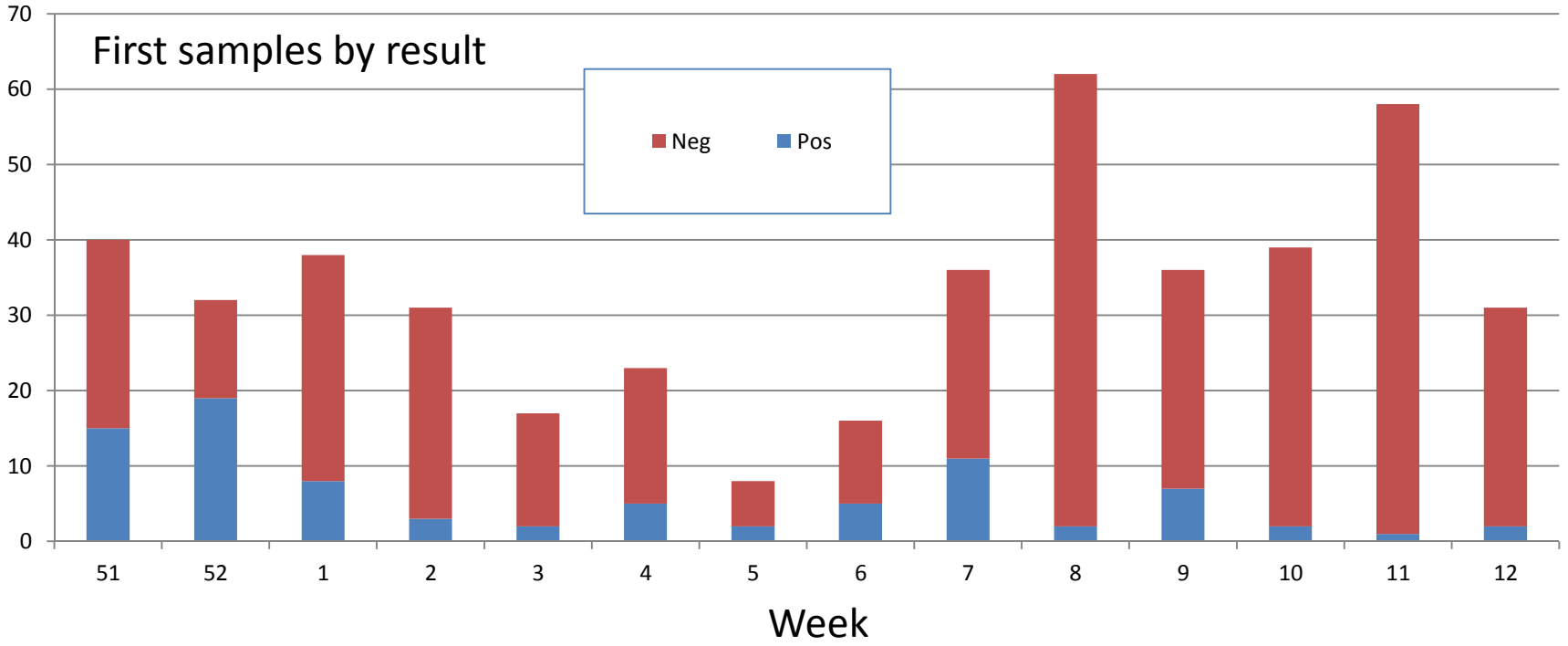




Istituto Nazionale per le Malattie Infettive "Lazzaro Spallanzani"

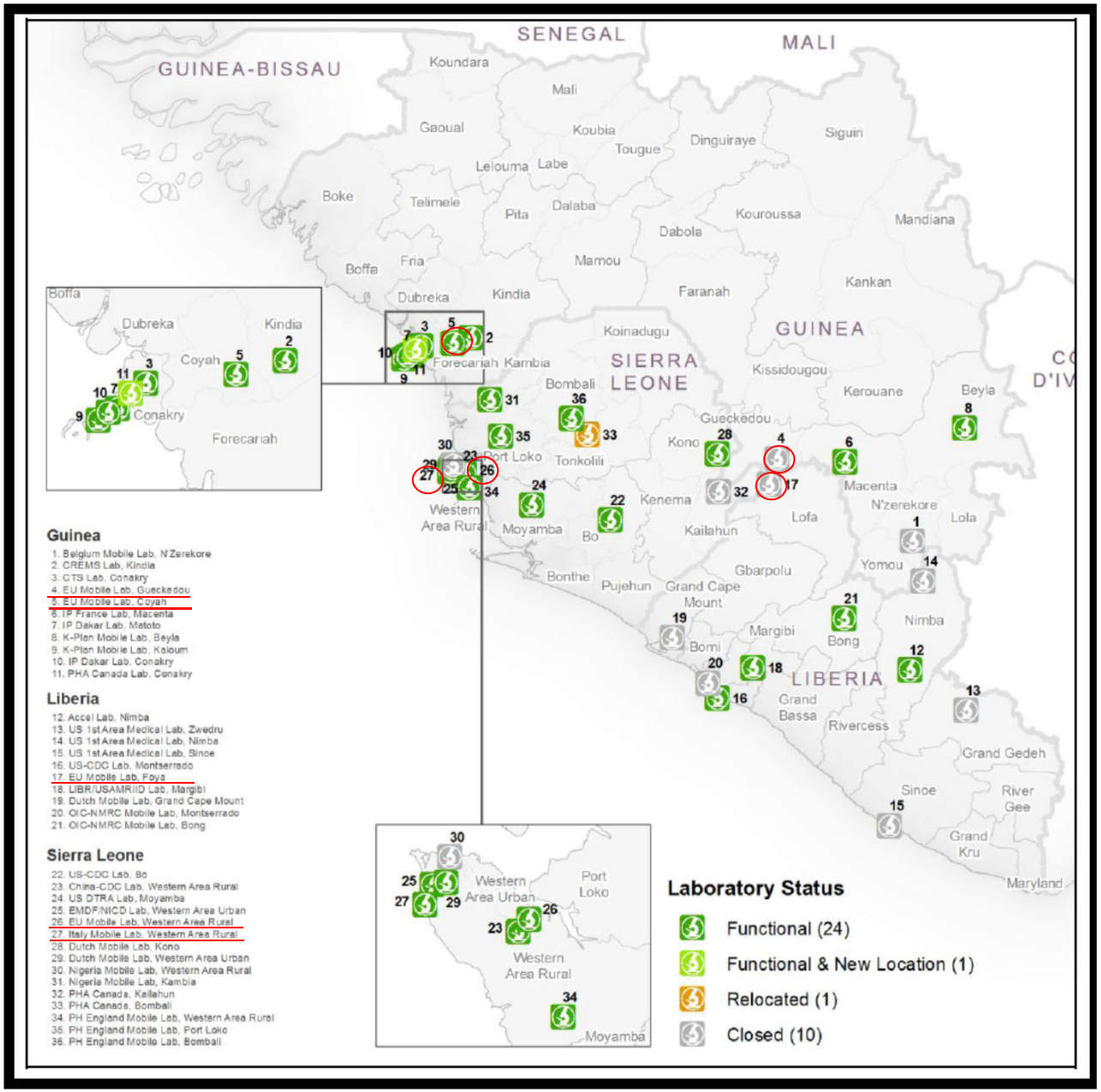
Cooperazione Italiana allo Sviluppo
Ministero Affari Esteri
Italian Development Cooperation

EMERGENCY



Providing capacity for prompt and accurate diagnosis of cases of EVD is an integral part of the response to the EVD outbreak

- 26 laboratories with the capacity to confirm EVD cases are operational today
- 9 operational laboratories in Guinea
- 4 operational laboratories in Liberia
- 13 operational laboratories in Sierra Leone
- Overall, 81-99% samples tested within 1 day



WHO situation report 22 April 2015

Participation into clinical response in Nigeria

Training and Infection Prevention and Control Expert Support in Sierra Leone

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EU funded projects on Ebola with INMI as partner

EVIDENT	Research on interactions between the Ebola virus and the host. This will provide urgently needed answers regarding the pathophysiology and transmissibility of the disease, and will help better guide the planned clinical trials on vaccines and potential treatments, as well as the management of patients with Ebola virus disease.
IF-EBOla	Study the safety and efficacy of using antibodies produced in horses against Ebola, as a passive immunity treatment for patients with Ebola virus disease.

Ebola+ Programme

Ebola and other filoviral haemorrhagic fevers

Innovative Medicines Initiative (IMI) launched the programme in response to the Ebola virus disease (EVD) outbreak that started in Western Africa in 2014

Rapid diagnostic test projects

There is an urgent need for fast, reliable tests to **detect Ebola Viral Infection**, as point of care (POC) systems for the safe, rapid, easy to use, specific and sensitive detection of Ebola Virus Infection

INMI is involved in three different projects:

- **IMI EbolaMoDRAD** (Ebola Virus: Modern Approaches for developing bedside Rapid Diagnostics)
- **IMI FiloDiag (**Ultra-fast Molecular Filoviruses Diagnostics)
- **IMI Mofína** (Mobile Filovirus Nucleic Acid Test)

General objectives:

- Evaluate and validate novel diagnostic tools, rapid and easy to use, first in BSL4 (analitical validation) and then in the field (clinical validation)
- Implement a strong capacity building program in West Africa with focus to rapid diagnostic, biosafety measures and outbreak management
- To create/develop a Bio-bank of residual samples collected during the current epidemics

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The INMI vision

Main pillars of our vision in the battle against Emerging Diseases:

- Strong integration between care and translational research;
- Networking and sharing of experience (One Health approach);
- Established programme with developing countries with mutual advantages;
- Key role of preparedness activities.

The INMI's motto is: 'deeds not words'.

Thanks to:
Giuseppe Ippolito
Vincenzo Puro
Maria Rosaria Capobianchi
Antonino Di Caro
Francesco Nicola Lauria
Mirella Biava
Concetta Castilletti
Simone Lanini
Silvia Meschi
Carla Nisii
Emanuele Nicastri
Silvia Pittalis
Francesco Vairo
Raffaella Pisapia
Many others…