European laboratory networks: the ultimate complement of national capacities for disease surveillance and alert?

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European Centre for Disease Prevention and Control, ECDC

7ème Séminaire des Centres Nationaux de Reference
Paris, 27 novembre 2015
**ECDC mandate and vision on microbiology**

**Task:**

“By encouraging cooperation between expert and reference laboratories, the Centre shall foster the development of sufficient capacity within the Community for the diagnosis, detection, identification and characterization of infectious agents which may threaten public health”.

...to provide timely and reliable information for infectious disease prevention and control at Member State and EU level

Source: Regulation (EC) 851/2004; ECDC Microbiology strategy
By 2020, ECDC has achieved:

• Consolidation of the capacity of the EU public health microbiology system for surveillance of communicable diseases and epidemic preparedness;

• System that assists Member States in monitoring critical microbiology laboratory capabilities;

• Integration of selected molecular typing data into European surveillance and epidemic investigations

• Integration of clinical laboratories and other public health laboratories in the surveillance and alert systems for human and zoonotic pathogens
The EU public health microbiology system

National and EU networks
  Data sharing
  Method harmonisation and quality

National Reference Laboratories
  Specialist diagnostics
  Pathogen characterisation

Clinical laboratories
  Diagnostics and drug susceptibility
  Typing
The EU-LabCap tool measures three levels of capabilities and capacity:

✓ Primary diagnostic microbiology services
✓ National reference microbiology services
✓ National and EU surveillance and preparedness networks
EULabCAP survey tool: 60 indicators

1. Primary diagnostic testing
   1.1 Provisions and regulation of clinical microbiology services
   1.2 Diagnostic testing guidelines
   1.3 Diagnostic testing and utilisation
   1.4 Antimicrobial drug susceptibility testing

2. NRL services
   2.1 Provision and regulation of reference microbiology services
   2.2 Reference diagnostic confirmation and pathogen identification
   2.3 Molecular typing for surveillance
   2.4 Antimicrobial drug resistance characterisation and monitoring

3. Surveillance/Response support
   3.1 National surveillance networks
   3.2 Active participation in EU disease networks
   3.3 National outbreak response support
   3.4 Emerging diseases laboratory preparedness and response support

3 dimensions

12 targets
(5 indicators/target = 60 indicators)
Microbiology system capacity level by country, EULabCap index 2013

Levels of system capability/capacity
- Low (0-5.9)
- Medium (6.0-7.9)
- High (8.0-10)

Data source: EULabCap on 2013 data
National microbiology capacity index by health expenditure, EU/EEA countries.

Source: Eurostat 2014
EULabCap 2013 capacity map

3 DIMENSIONS

1. Primary diagnostic testing
2. National reference laboratory service
3. Surveillance and response support

12 TARGETS

- EU median
- EU Q1
- EU Q3
Clinical microbiology laboratories obtained a licencing authorisation/registration by health authorities according to legal requirements that include regular participation to EQA exercises.
National laboratory surveillance network capacity index by country

Capability/capacity for national surveillance networks
- Low (0-5.9)
- Medium (6.0-7.9)
- High (8.0-10)

Countries

Data source: EULabCap on 2013 data
National outbreak response support capacity index by country

Capability/capacity for national outbreak response support

- Low (0.0-5.9)
- Medium (6.0-7.9)
- High (8.0-10)

Data source: EU LabCap on 2013 data
EU laboratory network participation capacity index by country

Data source: EU LabCap on 2013 data
ECDC Working with EU Disease Networks

15 disease networks including 11 laboratory networks

- Vaccine preventable (measles, mumps, rubella, etc.)
- Respiratory diseases (*Legionella*, influenza, tuberculosis)
- Sexually transmitted diseases, bloodborne infections, HIV
- Emerging, vector-borne and Imported viral diseases
- Invasive bacterial diseases
- Foodborne diseases
- Antimicrobial resistance and healthcare-associated infections

ECDC currently operates several European-wide disease-specific microbiology reference laboratory networks.
ECDC supported laboratory network activities, 2014 (N=14 network/projects)

<table>
<thead>
<tr>
<th>Type of work</th>
<th>No. of outputs</th>
</tr>
</thead>
<tbody>
<tr>
<td>External quality assessment</td>
<td>16</td>
</tr>
<tr>
<td>Technical guidance</td>
<td>7</td>
</tr>
<tr>
<td>Laboratory training courses</td>
<td>7</td>
</tr>
<tr>
<td>Technical capacity mapping</td>
<td>3</td>
</tr>
<tr>
<td>Cross-border testing services</td>
<td>4</td>
</tr>
<tr>
<td>Outbreak investigation support</td>
<td>4</td>
</tr>
</tbody>
</table>

- Source: ECDC Microbiology Activities Reports 2014
- 11 EU laboratory networks and 3 projects under the ECDC PHM programme
## EQA exercises by ECDC network, 2014

<table>
<thead>
<tr>
<th>Disease programme (Network)</th>
<th>Pathogens</th>
<th>Technical areas</th>
<th>Number of EU/EEA countries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Detection</td>
<td>AST</td>
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<tr>
<td>ARHAI (EARS-Net)</td>
<td>6 pathogens</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ARHAI (ECDIS NET)</td>
<td><em>C. difficile</em></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>EVD (ENIVD)</td>
<td>Chikungunya</td>
<td>X</td>
<td></td>
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<tr>
<td></td>
<td>MERS-CoV</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>FWD (FWD-Net)</td>
<td>Salmonella/Campylobacter</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Salmonella</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>STEC/VTEC</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td><em>Listeria monocytogenes</em></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>FWD ELDSNet</td>
<td><em>Legionella</em></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>HSH (Euro-GASP)</td>
<td><em>N. gonorrhoeae</em></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>VPD (IBD-LabNet)</td>
<td><em>N. meningitidis</em></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>H. influenzae</em></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>S. pneumoniae</em></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>TB (ERLTB-Net)</td>
<td><em>M. tuberculosis</em></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
Assessment by participants in the ECDC EQA schemes (2008-12, n=16 exercises)

- EQA help ¾ laboratories in obtaining quality accreditation
- More than half of respondents were able to detect capacity gaps and adopted measures to strengthen their capacities in these areas.

The role of WHO:
Global influenza surveillance and response

Global Influenza Surveillance and Response System (GISRS)

Global influenza virological surveillance has been conducted through WHO’s Global Influenza Surveillance and Response System (GISRS) for over half a century.

Formerly known as the Global Influenza Surveillance Network (GISN), the new name came into effect following the adoption of the Pandemic Influenza Preparedness (PIP) Framework in May 2011.

- WHO GISRS monitors the evolution of influenza viruses and provides recommendations in areas including laboratory diagnostics, vaccines, antiviral susceptibility and risk assessment.
- WHO GISRS also serves as a global alert mechanism for the emergence of influenza viruses with pandemic potential.

http://www.who.int/influenza/gisrs_laboratory/en/
Case study: Supporting laboratory preparedness for and response to Middle-East Respiratory Syndrome Coronavirus (MERS-CoV) and influenza A(H7N9) in Europe
The network was established in 1952. 138 National Influenza Centres, 6 WHO Collaborating Centres, 4 Essential Regulatory Laboratories

European Reference Laboratory Network for Human Influenza (ERLI-Net)

• Support to the European Influenza Surveillance Network
• Coordinated by ECDC
• Laboratory activities outsourced to PHE, NIMR and RIVM consortium
• Collaboration with WHO Europe influenza network

Source: Eeva Broberg, ECDC
European Network for Viral Imported Diseases (ENIVD)

Goal: early detection, surveillance and epidemic preparedness and support to emerging or re-emerging and vector-borne threats in Europe

Diagnosis capacity building:
• Sharing techniques, strains, specimens
• Evaluation and improvement of diagnostic techniques
• External Quality Assessment
• Ad hoc laboratory support in case of outbreak
• Technical training courses

Supported by ECDC
Links with WHO (GOARN), veterinary laboratories

Source: H.Zeller, ECDC
The Joint Action QUANDHIP

- “Quality Assurance Exercises and Networking on the Detection of Highly Infectious Pathogens” supported by Commission
- 38 laboratories from 23 European countries.
- Targets: high threat bacteria (Risk Group 3) and highly infectious viruses (Risk Group 4)
- Exchange of best diagnostic strategies, external quality assurance, training, and biosafety/biosecurity quality management.
- to support a joint European response to outbreaks of highly pathogenic infectious agents

http://www.quandhip.info/Quandhip/EN/Content/AboutUs/aboutus_node.html
Confirmed cases of MERS by month and probable place of infection, March 2012–13 October 2015 (n=1 616)

Source: ECDC Rapid Risk Assessment 21st update, October 2015

* Where the month of onset is unknown, the month of reporting has been used
** Data for October 2015 is incomplete
Joint WHO-ECDC surveys of laboratory capability for MERS-CoV detection in Europe, 2012-13

WHO surveillance guidance:
“Any probable or confirmed case ...should be reported to national authorities and be notified to IHR and EWRS.”

MERS-CoV screening and confirmation by RT-PCR assays

Network surveys by ECDC and WHO Europe
Survey I: Nov. 2012, Survey II: June 2013 of:
- NMFP (ECDC National Microbiology Focal Points)
- ENIVD
- ERLI-Net
- QUANDHIP

MERS CoV testing capability and practice, EU/EEA countries

Number of countries

<table>
<thead>
<tr>
<th></th>
<th>Nov-12</th>
<th>Jun-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening assays</td>
<td>19</td>
<td>28</td>
</tr>
<tr>
<td>Confirmation assays</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>Testing travel patients</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Testing contacts of cases</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
</table>

Number of patients tested for MERS Coronavirus, European Region, Sept 2012- June 2013

Source: Joint ECDC-WHO survey, Pereyaslov et al *EuroSurv* 2014
Distribution of confirmed MERS cases by place of probable infection, as of 13 October 2015 (n=1,616)

Source: ECDC Rapid Risk Assessment 21st update, October 2015
European regional laboratory response to emergence of avian influenza A(H7N9)

8 April 2013: Global alert
- WHO CC Beijing protocols for RT-PCR published
- Virus sequence sharing by China CDC through Global Initiative on Sharing All Influenza Data (GISAID)

European response
- 23 April 2013: Technical briefing on influenza A(H7N9) detection
- May 2013: GISRS sharing of virus/positive control materials to NICs
- Joint Survey on practices for identification of influenza A(H7N9)
Influenza A Subtyping capability by country in EU/EEA, May 2013

- No subtyping (N=3)
- H7 subtyping (n=27)
- H7 and N9 subtyping (N=21)

## European response to emerging diseases: agencies and laboratory networks

<table>
<thead>
<tr>
<th>Response step</th>
<th>MERS-CoV</th>
<th>Influenza A(H7N9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case definition</td>
<td>WHO</td>
<td>WHO/ ERLI-Net</td>
</tr>
<tr>
<td>Assay protocol</td>
<td>Eurosurveillance</td>
<td>ERLI-Net/WHO-CCs</td>
</tr>
<tr>
<td>Positive control:</td>
<td></td>
<td></td>
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<tr>
<td>• Source</td>
<td>U. Bonn</td>
<td>WHO-CC London</td>
</tr>
<tr>
<td>• Distribution</td>
<td>EVA/EMPERIE/ENIVD</td>
<td>GISRS/QUANDHIP</td>
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<td>Technical briefing</td>
<td>WHO</td>
<td>ECDC/WHO/ERLI-Net</td>
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<tr>
<td>Capacity mapping</td>
<td>ECDC/WHO/QUANDHIP/Eurosurveillance</td>
<td>ECDC/WHO/QUANDHIP/Eurosurveillance</td>
</tr>
<tr>
<td>Ext Quality Assessment</td>
<td>ENIVD</td>
<td>ERLI-Net</td>
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</table>
QUANDHIP project activation in response to the Ebola outbreak in West Africa

(i) updated and disseminated data about diagnostic capabilities for Filovirus in QUANDHIP laboratories (BSL4 and skilled BSL3);

(ii) developed directory of contact persons for laboratories with EVD diagnostic capabilities;

(iii) developed and disseminated “Brief instructions for handling and transport of samples from suspected cases and exposed contacts”, including referral for diagnostic confirmation

(iv) supported the EU Mobile Lab consortium providing skilled staff for activities in West Africa (Guinea, Liberia, Nigeria)

(v) consulted network organizations at national and European levels.

Source: F. Fusco, CHAFEA Workshop, Stockholm, 10 November 2015
EMERGE

Efficient response to highly dangerous and emerging pathogens at EU level

EMERGE is an EU funded Joint Action (CHAFEA n° 677 066), coordinated by the Robert Koch-Institut (RKI), and carried out in close cooperation with 34 associated partners and 3 collaborating partners: Altogether: **38 partner institutes from 25 European countries**.

Coordinator:
Robert Koch-Institut (RKI), Berlin, Germany
Contact persons: Roland Grunow / Daniela Jacob

Co-Coordinator:
L. Spallanzani National Institute for Infectious Diseases (INMI), Rome, Italy
Contact persons: Giuseppe Ippolito / Antonino Di Caro

Duration: 1st June 2015 – 31st May 2018 (3 years)
Total EU funding (60%): 3.5 Mio EUR

Source: F. Fusco, CHAFEA Workshop, Stockholm, 10 November 2015
Surveillance and alert of infectious diseases: role of European laboratory networks

- EULabCap shows robust microbiology capacity at EU and MS levels with specific areas of vulnerability
- EU public health networks strengthen laboratory capacity for surveillance and preparedness for emerging diseases
- Joint ECDC- WHO- Commission networks collaborate for deployment of detection capability for emerging diseases
- Capabilities for detection of emerging influenza and coronaviruses achieved rapidly across the EU/EEA
- Rapid risk assessment informs risk management by EU Health Security Committee
- Future strengthening of laboratory preparedness and emergency response systems led by European Commission
Acknowledgements

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ECDC Disease programmes and Disease networks experts

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QUANDHIP/EMERGE network coordinators and members
Merci!