



# **European Centre for Disease Prevention and Control**

**Updated**

**Public Health Microbiology Strategy**

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**Work Plan 2012-2016<sup>1,2</sup>**

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<sup>1</sup> Approved by ECDC [Management Board](#) (MB 23; 9<sup>th</sup>-10<sup>th</sup> November, 2011) and [Advisory Forum](#) (7<sup>th</sup>-8<sup>th</sup> December, 2011)

<sup>2</sup> Consulted with ECDC [National Microbiology Focal Points](#) (8<sup>th</sup> meeting; 27<sup>th</sup>-28<sup>th</sup> September, 2011 and via e-consultation 4<sup>th</sup>-23<sup>rd</sup> January, 2012)

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## Summary

1. ECDC has a mandate of 'encouraging cooperation between expert and reference laboratories' to 'foster the development of sufficient capacity within the Community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' (Founding Regulation, Article 5 point 3).
2. Accordingly, ECDC's Strategic Multi-annual Plan (2007-2013) Strategy 3.5 aims to promote and support the strengthening of microbiological support for communicable disease prevention, control and scientific studies in the European Union (EU). This strategy outlines a series of approaches, including networking with professional organisations and national laboratories to develop core competencies and unified molecular typing schemes, develop directories of national reference laboratories and map capacities, develop training schemes, promote EU-wide quality assurance systems for microbiological laboratories, analyse the needs for improved diagnostic technologies and reinforce links between human and veterinary laboratories.
3. In 2010, a mid-term review of progress has indicated substantial implementation of these strategic objectives but also identified a number of areas for improvement. To strengthen the public health microbiology system in the EU and clarify the respective contributions of the Commission and ECDC, a joint strategy for human pathogen laboratories has been developed.
4. The present document summarises the state of play of public health microbiology in Europe and outlines the rationale for priorities of work identified by ECDC to support Member States in this area in close partnership with the Commission and other stakeholders.
5. The updated ECDC microbiology priorities proposed for the next five years are: 1) To consolidate the capacity of the EU public health microbiology for European surveillance of infectious diseases and for epidemic preparedness; 2) To develop and implement a system for monitoring microbiology laboratory capabilities for European surveillance of infectious diseases and for epidemic preparedness; 3) To develop and implement a roadmap for integration of molecular typing into European surveillance and epidemic preparedness; and 4) To further develop the EU integrated surveillance and epidemic intelligence of antimicrobial resistance in human and zoonotic pathogens.

## Public health microbiology

6. Laboratory diagnosis, pathogen characterisation, susceptibility testing and typing, contribution of microbiology surveillance data, laboratory support to outbreak investigation, technology innovation and research are essential components of prevention and control of infectious diseases. Together with experts from the Member States, the European Centre for Disease Prevention and Control (ECDC) has developed a consensus definition of 'Public health microbiology' as 'a cross-cutting area that spans the fields of human, animal, food, water and environmental microbiology, with a focus on human health and disease. It requires laboratory scientists with the ability to work effectively across disciplines, particularly epidemiology and clinical medicine'. The following core functions of reference laboratories were recognised: reference diagnostics, reference material resource, scientific advice, collaboration and research and monitoring, alert and response.

7. Reliable capability of diagnostic and reference microbiology laboratory service is pivotal for ensuring adequate surveillance of communicable diseases and monitoring of drug resistance in human pathogens. It is also a prerequisite for enabling preparedness for future threats caused by emerging pathogens and epidemic disease, from local to global levels, as specified in the 2005 International Health Regulations.

8. The Annex I to the present document summarises the state of play of public health microbiology in Europe and the contribution of Commission and ECDC initiatives and activities to foster microbiology cooperation between Member States over the past decade.

## Position statement of the Commission and ECDC on human pathogen laboratories: a joint vision and strategy for the future

9. In 2010, the Management Board stated that the Commission and ECDC have to work even closer together to map and scrutinise their laboratory activities to ensure synergies. Such dedicated collaboration would eliminate duplication of work that remains since the establishment of ECDC and the gradual integration of laboratory networking initiatives (MB20/14).

10. To address the above challenges, the '**Position statement of the Commission and ECDC on human pathogen laboratories: a joint vision and strategy for the future**' was presented to the Management Board in 2011 (MB22/8; [link](#)). The position statement describes the joint vision of the Commission and ECDC in the area of human pathogen laboratories in the EU and indicates the strategic objectives as well as both partners' respective roles in achieving these objectives. The paper was endorsed by the Management Board with a request for further clarification and more detailed description of objectives and means to achieve them. The updated version of the position statement was revised accordingly and submitted for adoption to the Management Board (MB23).

## Updated ECDC Public Health Microbiology Strategy (2012-16)

### *Goal*

11. The overall goal of the Public Health Microbiology Programme is to strengthen the capacity of the EU public health microbiology system to provide timely and reliable information for infectious disease prevention and control at Member State and EU level.

### *Rationale for updating the strategy*

12. The ECDC Microbiology Laboratory Strategy (2007-2013) defined the general framework of strategic objectives that align laboratory projects to ECDC's mission of detecting, monitoring, assessing and supporting the prevention and control of infectious diseases. In 2010, the mid-term review of progress achieved indicated the need for ECDC to strengthen its microbiology work and update its Laboratory Strategy. In consultation with governing bodies and the Commission, ECDC was to identify priority areas of work toward strengthening the capacity of public health microbiology

systems at Member State and EU level. The present updated strategy proposal elaborates on the ECDC role towards implementing the Joint Commission and ECDC Laboratory Strategy (Annex II).

### ***Strategy 1: To consolidate the capacity of the EU public health microbiology for European surveillance of infectious diseases and for epidemic preparedness***

#### **Strengthening coordination of ECDC microbiology programme**

13. Under the new organisation of ECDC, the Microbiology Coordination Section of the Resource Management and Coordination Unit has the mandate to further support and coordinate the ECDC Public Health Microbiology Programme. This programme encompasses all microbiology activities of the Centre and aims to meet the objectives of the Multi-annual Strategic Programme and of the disease-specific surveillance and public health microbiology strategies. Coordination of laboratory work at ECDC will focus on activities with clear relevance to public health and promote better integration of functions across agencies and stakeholders.

14. The Microbiology Coordination Section will not execute this programme by itself but through joint work with the Disease Programmes and relevant sections in the Surveillance and Response Support Unit and the Public Health Capacity and Communication Unit. Internal communication will be strengthened through collaborations with the Internal Communication and Knowledge Management Section. Experts from microbiology coordination will participate in epidemic intelligence work and support the technical response to public health events.

15. The implementation of ECDC laboratory activities will be strategically aligned and supervised by the newly established Microbiology Steering Committee, composed of ECDC Heads of Unit with ad-hoc participation of Section Heads.

#### **Raising awareness of public health microbiology and strengthening liaison and coordination with key stakeholders**

16. ECDC will actively engage in health communication with the public, health professionals and public health authorities to raise awareness of the key functions fulfilled by public health laboratories in the Member States for epidemic preparedness and provision of timely and accurate information for disease surveillance and early warning. Its message to policy makers and professionals will underline the European added value of a sustainable and responsive public health microbiology system across the EU for informed public health action.

17. ECDC will liaise and share information on laboratory projects with the European Commission on a regular basis to ensure synergy and cohesion of all initiatives. Information on ECDC and Commission projects will be disseminated to the professional and general public through coordinated posting and cross-referencing of microbiology cooperation pages on ECDC's and the Commission's web portals.

18. Closer collaboration with the European Food Safety Authority (EFSA) will be developed to enable harmonisation of laboratory-based surveillance and molecular typing data collection across the human and animal health and food sectors. Agreement has been recently made between the Commission, ECDC and EFSA to investigate the feasibility of laboratories performing typing of zoonotic pathogens and indicator organisms from food, feed and animal samples to submit data to the extended TESSy system, in order to enhance comparability and linkage between strains from humans and potential sources and reservoirs.

19. ECDC will collaborate closely with competent bodies and expert communities in microbiology and epidemiology within Member States. It will do so by regular meetings and consultations of disease-specific EU networks and the forum of public health microbiology representatives, the National Microbiology Focal Points (NMFP).

20. Liaison with the WHO will be developed based on the ECDC-WHO collaborative agreements and roadmap to ensure good coordination of activities and avoid duplication of efforts.

21. Liaison was progressed in 2011 with the European Society of Clinical Microbiology and Infectious Diseases, European Society of Clinical Virology, European Society of Pediatric Infectious Diseases and European Federation of Parasitologists. ECDC will further explore cooperation with these societies in a number of areas of mutual interest, including: a directory of experts for scientific advice and technical assistance, outreach to health care and clinical microbiology professional membership reports via society newsletter and web links, contribution to scientific conferences and meetings, collaboration on professional training initiatives in microbiology and public health and link to professional quality assessment and technical guidance for laboratory methods.

### **Strengthening coordination of EU networks of national reference laboratories**

22. The microbiology coordination will support the disease programmes by facilitating internal sharing of best practice across disease networks. It will also develop general ECDC standards for microbiology calls for tenders to ensure consistency in terms of laboratory network coordination, documentation and reporting. The section will assist with technical advice and lead the work on issues of common concern such as guidance on establishing, maintaining and using strain collections and biobanks.

23. Microbiology outputs according to ECDC work plan will be implemented by the Microbiology Coordination and the network managers of each of the disease programmes. This Annual ECDC Microbiology Report will be reviewed by the Microbiology Steering Committee and form part of the reporting on the strategic performance indicator for surveillance target 3.5. Relevant information from this report, pertaining to capacity of laboratory-based surveillance, could also be contributing to the Annual Epidemiological report.

24. Capability monitoring of the EU networks of national reference laboratories will be gradually developed and implemented. Based on the monitoring results, priority actions to fill gaps and enhance these laboratories' surveillance, epidemic intelligence and alert functions will be jointly identified with the respective disease experts in consultation with ECDC governing bodies.

### **Support for training**

25. In cooperation with reference laboratory training sites in Member States, ECDC has initiated a two-year EU public health microbiology training programme (EUPHEM) which is closely linked to the European Programme for Intervention Epidemiology Training (EPIET) and promotes practical collaboration between public health microbiology and other core disciplines such as epidemiology. Both EUPHEM and EPIET are considered as specialist pathways of the 2 year ECDC fellowship programme for applied disease prevention and control. ECDC will further consult with Member States to enhance their recognition of these fellowships. ECDC will strive for EUPHEM involvement of each Member State, to contribute to harmonisation through operational training and joint projects.

26. The EUPHEM programme will be reviewed jointly with the EUPHEM Team and consensus definitions of core competencies in public health microbiology for EUPHEM trainees and for reference laboratories will be aligned in consultation with the NMFP and the EUPHEM Training Forum. The prioritisation of training activities in EUPHEM will be aligned with public health priorities as defined and recognised by ECDC. In addition, specific advanced training will be developed to support senior experts in public health microbiology, in particular the supervisors in the EUPHEM fellowship. Online training tools for public health microbiology will be further developed.

27. Many ECDC-funded training activities are implemented in the disease-specific networks, including laboratory technical courses hosted in partner institutes in the Member States. Microbiology Coordination will assist the disease programmes in defining technical training priorities linked to capacity gaps identified by EU public health microbiology capacity appraisal and monitoring. Likewise, the Microbiology Coordination Section will ensure 'bridging of information' to the Public Health Training Section about these distributed technical laboratory training activities.

28. Development of additional, short term professional training opportunities in public health microbiology will be explored, through exchange visits of expert staff from laboratories in the Member States. Such exchange programmes for continuing professional development could be linked to existing programmes for clinical microbiologists by learned societies through cooperation agreements with ECDC.

### **Promotion of quality assurance and bio safety measures**

29. ECDC will encourage adoption of EU and ISO quality assurance standards for reference laboratory services by its partners in EU laboratory networks, according to national arrangements and regulations

30. ECDC is supporting a large number of targeted External Quality Assessment (EQA) schemes with voluntary participation by reference or primary laboratories that are active members of EU surveillance networks. These surveys are complementary to national EQA systems and meant to contribute to enhanced EU wide comparability and reliability of laboratory-based data used for public health purposes. The ECDC microbiology section will harmonise eligibility criteria and quality standards for subcontracting services from EQA providers. It will also reinforce the corporate reporting format of EQA results to improve consistency of reports and recommendations of corrective actions. The possibility for ECDC to issue "certificates of proficiency" or "certification of laboratory capability" to successful participants in ECDC EQA surveys will be explored.

31. The ECDC microbiology section will continue to promote awareness of laboratory biosafety standards, for enhanced compliance with good practice throughout the EU, in coordination with other agencies with responsibilities in this area. . Guidance on international shipment of biological material and etiological agents according to international bio safety and bio security regulations will be addressed based on lessons learned from recent epidemic investigations and recommendations from EU laboratory coordination exercises led by the Commission.

### **Support to technical guidance, harmonisation and standardisation of laboratory methods**

32. ECDC will encourage microbiology experts participating in disease-specific EU networks to develop and maintain evidence-based technical guidance on appropriate sampling and microbiological testing for diagnosis of infection and further characterisation of human pathogens of public health relevance.

33. Minimum testing requirements for informative laboratory-based surveillance will be further elaborated over the coming years to include all pathogens/diseases under EU surveillance based on Decision 2000/96/EC.

34. Harmonisation of laboratory methods will be encouraged for ensuring capacity to report accurate and comparable microbiology data to the EU disease surveillance system in compliance with case definitions and surveillance protocols. Further standardisation of primary or reference testing methods will be supported whenever this is critical to producing comparable results or in areas where EQA schemes indicate inconsistent or inaccurate test results likely to introduce significant bias in surveillance data. This work will be performed in coordination with the development of the European Case Definitions and revision of the diseases under EU surveillance. A paramount example is the sine qua non adoption of common laboratory testing standards and definitions (EUCAST) for surveillance of antimicrobial resistance to enable data comparability.

35. Whenever feasible, ECDC will provide assistance with coordinated access to and distribution of non-commercial reference materials and specialised reagents for characterisation of human pathogens or confirmation of cases according to EU case definitions. This will be especially relevant to provide extended capability and surge capacity to trace emerging pathogens with novel strain characteristics in case of major epidemic spread across the EU.

### **Support to development, assessment and application of innovative laboratory methods**

36. ECDC will advocate the public health benefits of innovative microbiology testing with enhanced accuracy and the key role of disease specific EU laboratory networks in developing and assessing such technical innovations in public health microbiology. Jointly with the disease programmes, the ECDC microbiology coordination will support activities to technically validate innovative microbiology technologies and appraise their public health effectiveness through systematic literature reviews.

37. It will likewise encourage the development of evidence-based guidance on their appropriate application in public health microbiology. It will support Member State access to and implementation of improved diagnostic and molecular typing technologies by organising technical training workshops and including these assays in external quality assessment schemes.

### **Communication and information dissemination**

38. The ECDC microbiology coordination will strengthen its work together with the External Communication section in advocating the key role of public health microbiology in disease surveillance and control through development and dissemination of key messages accessible to the general public and clinical practitioners. It will inform about public health microbiology projects and activities supported by the Centre, the Commission, the Member States and international bodies, including the WHO and learned medical societies. This communication will address the general public by means of the ECDC web portal as well as press releases on major breakthroughs. ECDC will join forces with European learned societies in coordinating communication on public health microbiology issues to reach out to their medical and scientific expert constituencies.

39. It will also provide dedicated extranet communication platform for access to technical information and consultation for the Competent Bodies and NMFPs. Moreover, NMFPs will be encouraged and supported in advocating public health microbiology benefits and disseminating information in their countries about their joint work with ECDC and the Commission.

40. EU mapping surveys of national reference laboratories were conducted by ECDC in 2008 and by the Health Protection Agency (HPA) in 2011. Building upon these surveys as well as on information on file from ECDC and Commission-supported networks, a searchable directory of expert and reference laboratories that are available in the EU for all human pathogens, will be developed and maintained. It will describe their expertise, offer of services and list their contact information. In case of emergency, this inventory should assist Competent Authorities in gaining rapid access to state-of-the-art expertise and advanced laboratory testing not available at national level, following the model established by the European Network of Imported Viral Diseases (ENIVD)

41. **Timelines: the strategy 1 is proposed to be developed and implemented over the next five years** (See Table 1 - Proposed Public Health Microbiology Work Plan 2012-2016).

### ***Strategy 2: To develop and implement a system for monitoring microbiology laboratory capabilities for European surveillance of infectious diseases and epidemic preparedness***

42. ECDC's mission is 'to foster the development of sufficient capacity for diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' (Regulation 851/2004, Article 5.3). To fulfil this mission, ECDC will first develop a common approach to reach consensus with experts from the Member States to define the needs and establish which capacity and capability level of public health laboratory systems is sufficient to meet the requirements of EU legal and International Health Regulation for European surveillance of infectious diseases and epidemic preparedness. The scope of requirements is covering capacity at Member State and EU level from a system approach. Second, ECDC will develop and validate a set of appraisal criteria and indicators for monitoring public health microbiology capability and capacity level at Member State and EU network systems with regard to generic functionalities and disease/pathogen specific needs. These standards and indicators will be regularly updated according to state of the art practice. Third, ECDC will collect data from Member States and ECDC supported laboratory networks to monitor these capability indicators and priorities for capacity building initiatives at Member States and EU levels. Therefore, the primary user of capability monitoring results will be ECDC itself, in order to prioritise and evaluate the benefits of its laboratory support activities. In addition, input will be sought from the Member States to define tools for evaluation of national public health microbiology system according to their country needs and contribution to EU preparedness for cross-border threats. The added value for Member States would be to access standard measuring tools for self-assessment of capability of public health microbiology system as well as benchmarking their preparedness level against agreed requirements and range of country practices.



43. The development of agreed standards and minimal requirements for public health microbiology systems as well as capability measurement tools will be developed over the coming years through an iterative process of extensive consultation with Member States and guidance from public health and disease experts. This process will involve regular consultation and input from the NMFP, AF, disease network experts and professional bodies. In 2011, ECDC has initiated a pilot project to develop draft definitions and measurement tools of sufficient laboratory capacity by function and by pathogen, as required for EU surveillance, alert and response to relevant diseases (call for tender "*Development of Methods and Tools for Appraisal of Laboratory Capabilities for European Surveillance of Communicable Diseases*". Ref.: OJ/27/05/2011-PROC/2011/045"). Quality indicators will build upon the results and conclusions from the EURLOP project as well as inputs from other communicable disease capacity building projects of the Commission.

44. The first step will entail defining (a) generic elements of core laboratory capacity pertaining to the laboratory system, infrastructure and functions; (b) specific elements of sufficient capability per disease; (c) criteria for priority ranking of diseases and pathogens according to maximal EU public health gain of laboratory capability. These laboratory capability indicators will be aligned to the disease-specific 'Objectives for strengthening the surveillance of communicable diseases in the European Union' (AF15/2).

45. The sufficient level of laboratory capability will be defined with reference to currently available EU or international laboratory practice guidance and disease-specific minimum requirements for EU reporting and preparedness, as agreed by participants to EU disease surveillance networks. The second step will aim at determining quality indicators and measurement tools for appraising generic and specific laboratory capabilities at Member State and EU level. To ensure added value, an inventory of international technical guidance will be made and WHO experience with laboratory guidance and self-assessment tools for implementation of IHR will be integrated, in liaison with WHO-Lyon and WHO-EURO.

46. In the pilot phase, these appraisal instruments of core laboratory capacity will be developed, tested and validated for 3 priority diseases for which EU standards or international consensus guidance on good practice and EU data on mapping laboratory practice are already available

47. Following the pilot phase, laboratory capability indicators and appraisal tools will be further developed by the ECDC microbiology team, Epidemiological Methods section and disease-specific programme experts in consultation with the Commission, Advisory Forum and NMFPs as well as disease experts in the Member States. The pilot tools and indicators will be expanded in scope over the following four years via a three-phase stepwise process of development and validation. They will thus gradually include a larger proportion of the diseases and health issues listed under Commission Decision 2119/98 and subsequent revisions. It is expected that this instrument will allow monitoring of laboratory capacity for three diseases in phase 1, for six diseases in phase 2 and for 12 diseases in phase 3

48. [Timelines: the strategy 2 is proposed to be developed and implemented over the next five years](#) (See Table 1 - Proposed Public Health Microbiology Work Plan 2012-2016).

### ***Strategy 3: To develop a roadmap for integration of molecular typing into European surveillance and epidemic preparedness***

49. The concept paper on integrating molecular typing in surveillance (2008), as updated and further developed in 2011 in consultation with the Advisory Forum (AF26 Working Group) will form the basis for developing a roadmap for integration of molecular typing into European surveillance and epidemic preparedness. This roadmap must take into account any significant scientific and technological progress and innovative IT solutions. To identify the most versatile, affordable and robust genotyping strategies, it would be desirable to consult basic microbiologists in addition to public health epidemiologists.

50. The following steps are proposed to further develop this roadmap:

- 1) Systematic reviews of the public health effectiveness of typing technologies for specific viral and bacterial pathogens will ascertain and better delineate the areas of potential added value of gathering typing data at EU level for surveillance and international outbreak investigations.

- 2) ECDC will organise external consultations of scientists with a broad range of expertise in human pathogen population genomics, 'resistomics', evolutionary genetics, bioinformatics and molecular epidemiology. They will review bacterial and viral molecular typing techniques and database management used by ECDC-supported laboratory networks. Finally, they will appraise mid-term applicability and potential added value of next-generation sequencing for typing pathogens under EU surveillance and threat monitoring.
- 3) The ECDC Microbiology Coordination and Epidemiological Tools sections will jointly analyse with disease programme experts the added value, feasibility and cost implications for ECDC and Member States of integrating genotyping data analysis across a range of pathogens, sampling strategies and typing method scenarios. Based on this analysis, options will be developed for a 5-year roadmap towards an affordable and cost-effective integration of molecular epidemiology data into enhanced EU surveillance and epidemic intelligence systems. This typing integration roadmap as well as user access and data management policies for TESSy 3.0 enhanced surveillance system will be further reviewed in consultation with NMFP and AF members and key stakeholders, namely the typing experts from respective disease surveillance networks and the EFSA.

51. [Timelines: the strategy 3 is proposed to be developed and implemented over the next five years](#) (See Table 1 - Proposed Public Health Microbiology Work Plan 2012-2016).

### **Strategy 4: To further develop integrated surveillance and epidemic intelligence of antimicrobial resistance in human and zoonotic pathogens**

52. ECDC will contribute to raise awareness that antimicrobial resistance is not confined to hospitals and that combating this cross-sectoral phenomenon needs an holistic approach prioritised according to public health relevance. To improve the current system in terms of scope, accuracy, comparability, resolution and timeliness, a cross-cutting EU integrated surveillance and epidemic intelligence of antimicrobial resistance (AMR) in human and zoonotic pathogens will be jointly developed by the Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) programme and other ECDC disease programmes, members and coordination group of the European Antimicrobial Resistance Surveillance Network (EARS-Net), microbiology coordination team, surveillance and epidemic intelligence experts in close consultation with National AMR Focal Points, the Advisory Forum and the Commission.

53. The objectives are:

- a) to support European Committee on Antimicrobial Susceptibility Testing (EUCAST) in further developing expert guidance for early detection of resistance and in harmonising clinical antimicrobial breakpoints and susceptibility testing methods for all pathogens under EU surveillance of AMR;
- b) to encourage antimicrobial susceptibility testing laboratories throughout the EU and beyond to gradually adopt ISO standard testing methods and EUCAST or equivalent breakpoints for pathogens under EU surveillance of AMR, in collaboration with National AMR Focal Points, EUCAST network of antimicrobial susceptibility testing committees and the Transatlantic Task Force on Antimicrobial Resistance;
- c) to promote the wide adoption by virology laboratories throughout the EU and beyond of the EISN guidance for testing and reporting antiviral resistance of influenza viruses in humans
- d) to develop, test and evaluate the EPIS/EWRS information sharing tools in a stepwise manner for early detection, verification and warning of emerging resistance and international spread of multidrug and extensively drug-resistant bacterial and viral pathogens, in order to allow timely public health response;
- e) to develop guidance on the design of structured prevalence surveys of drug resistance in key bacterial, fungal and viral pathogens of public health significance, in collaboration with microbiology experts from the relevant ECDC-supported disease networks and experts from other organisations involved in the surveillance and study of AMR; to support studies in the

area of antimicrobial resistance of major fungal pathogens and better understand determinants of antimicrobial resistance in the community

- f) to consider and evaluate options for developing new and complementary EARS-Net data collection modules to address gaps in timely monitoring of incidence and cross-border dissemination of extensively drug-resistant bacterial pathogens;
- g) to develop technical guidance on harmonized detection of antimicrobial resistance mechanisms and identification of epidemic resistant clones of public health importance, in collaboration with microbiology experts from the relevant ECDC-supported disease networks and experts from other organisations involved in the surveillance and study of AMR;
- h) to develop a roadmap for integration of surveillance data into TESSy Version 3 for monitoring the distribution over space and time of epidemic prone multidrug-resistant clones and genetic determinants. An important step will be the international agreement on common definitions of antimicrobial resistance and typing nomenclature between the veterinary and human domains
- i) in collaboration with EFSA and EU reference laboratories, to harmonise laboratory methods and implement EUCAST breakpoints in public health, veterinary and food safety microbiology laboratories to enable integration of AMR surveillance in zoonotic and foodborne pathogens from humans, food and food-producing animals and plants;
- j) to develop integrated epidemiological reporting on AMR surveillance in human pathogens in the EU through the TESSy system

54. [Timelines: the strategy 4 is proposed to be developed and implemented over the next five years](#) (see Table 1 - Proposed Public Health Microbiology Work Plan 2012-2016).

**Table 1 - Proposed Public Health Microbiology Work Plan 2012-2016**

Work plan	2012	2013	2014	2015	2016
<b>STRATEGY 1. To consolidate capacity of the EU public health microbiology system</b>					
- Internal microbiology coordination	Core activity				
- Stakeholder liaison & Communication	Core activity				
- EU laboratory network support & activity monitoring	EQA standards	Strain collection standards	To be defined based on network needs and capacity gap analysis		
- Microbiology training, quality and biosafety promotion	EUPHEM-PHM laboratory core competencies alignment Technical laboratory training based on capacity gaps	EUPHEM core competencies training in 30% MS Coordinated EQA schemes Technical laboratory training based on capacity gaps	EUPHEM core competencies training in 40% MS Coordinated EQA schemes Technical laboratory training based on capacity gaps	Joint educational programmes with learned societies EUPHEM core competencies training in 50% MS Coordinated EQA schemes Technical laboratory training based on capacity gaps	Joint educational programmes with learned societies EUPHEM core competencies training in 60% MS Coordinated EQA schemes Technical laboratory training based on capacity gaps
- Methods harmonisation and standardisation, evaluation and guidance	Promotion of EUCAST AMR definition and test methods (target: 90 % MS for 75 % pathogens by 2016) Other methods: Topic based on technology advances and capacity gap analysis				

Work plan		2012	2013	2014	2015	2016
<b>Phase</b>	<b>STRATEGY 2. To develop a system for monitoring of EU microbiology laboratory capabilities</b>					
<b>1</b>	- Development of draft generic and specific capacity appraisal tools, core capability requirements and criteria for disease priority setting					
	- Pilot testing on 3 diseases and revision of phase 1 generic and specific appraisal tools					
	- Consultation of AF/NMFP and revision of phase 1 generic and specific appraisal tools for 3 diseases					
<b>2</b>	- Development of phase 2 specific capacity appraisal tools scaled up for 6 diseases from 3 disease programmes					
	- Consultation of AF/NMFP on phase 2 tools					
	- Application of phase 2 tools for generic capacity and for 6 diseases					
<b>3</b>	- Development of phase 3 tools for specific capacity appraisal scaled up for 12 diseases from 5 disease programmes					
	- Consultation of AF/NMFP on phase 3 tools					
	- Application of phase 3 tools					
Annual monitoring report on EU laboratory capability			Generic + 3 diseases	Generic + 6 diseases	Generic + 12 diseases	

Work plan		2012	2013	2014	2015	2016
<b>Phase</b>	<b>STRATEGY 3. To develop a roadmap for integration of molecular typing in EU surveillance</b>					
<b>1</b>	- Development of systematic review of public health effectiveness of typing and evidence based guidance on pathogen and laboratory methods of potential EU added value					
	- Expert consultation on technological feasibility and typing network priorities and public health benefits of molecular typing					
<b>2</b>	- Development of roadmap for integration of molecular typing in EU surveillance					
	- Consultation of AF/NMFP & other key stakeholders					
<b>3</b>	- Implementation and annual review of roadmap					

Work plan		2012	2013	2014	2015	2016
<b>Phase</b>	<b>STRATEGY 4. Development of integrated surveillance and epidemic intelligence of antimicrobial resistance</b>					
<b>1</b>	- Development of integrated surveillance methods and reporting of antimicrobial resistance in zoonotic and foodborne bacterial pathogens					
	- Promotion of AMR testing standardisation in Europe by general adoption of EUCAST and EISN antiviral test methods and breakpoints by antimicrobial testing laboratories					
<b>2</b>	- Development of enhanced surveillance strategy for timely monitoring of epidemic carbapenemase-producing and extensively drug-resistant bacterial pathogens - consultation of AF/NMFP/AMR FP/Commission for endorsement of strategy					
<b>3</b>	- New AMR surveillance objectives and feasibility assessment of new EARS-Net data collection modules - Consultation of AF/NMFP/AMR FP/Commission for endorsement of strategy					
<b>4</b>	- Development of strategy for integration of EU surveillance of antimicrobial resistance in viral, bacterial and fungal pathogens of public health importance - Consultation of AF/NMFP/AMR FP/Commission for endorsement of strategy					
<b>5</b>	- Development of methodology guidance on microbiological AMR prevalence surveys					

## **Annex I: Background and milestones in EU public health microbiology, 2007-2011**



## Background

1. Human pathogens cause a considerable disease and economic burden globally, ranging from acute infections transmitted from person to person (e.g. influenza and respiratory viruses), healthcare-associated infections (e.g., *Clostridium difficile*, *Staphylococcus aureus*), foodborne infections (e.g. Salmonella and enteropathogenic viruses), vector-borne infections (e.g. malaria, Chikungunya and West Nile viruses) to chronic infections (e.g. tuberculosis, HIV) and infection-induced cancer (e.g. HPV, EBV, *Helicobacter pylori*). Management of infectious diseases is increasingly threatened by accumulation of antimicrobial resistance determinants among bacteria through mutations and horizontal genetic transfer selected by antimicrobial use. Acquired mutational resistance to antiviral, antifungal and antiparasitic agents is likewise an increasing public health problem.
2. Continuing expansion in international food trade, travel and cross-border care amplify opportunities for epidemic dissemination of human pathogens and drug resistance determinants. This was recently illustrated by the global spread of extensively drug-resistant enteric bacteria, producing New-Delhi metallo-beta-lactamase-1 (NDM-1) and the foodborne outbreak of multidrug-resistant Shiga-toxin-producing *Escherichia coli* O104:H4 in Europe. In addition, population migration, expansion of eco-tourism, as well as climate change are just examples of many factors increasing the probability of emergence and importation of zoonotic and vector-borne diseases in the European Union (EU).
3. Endemic infectious diseases such as vaccine-preventable diseases and foodborne infections are targets of prevention interventions and public health policies at national, EU and international levels. Diseases of epidemic potential can cause rapid and large scale increase in morbidity and mortality, social and economic disruption, and are therefore of significant international concern. The 2005 International Health Regulations mandate each country to develop capability to detect and contain such threats. Robust and well integrated epidemiological and microbiological surveillance and alert systems are key elements of preparedness for these threats.
4. Scientific and technological advances in microbial genomics, proteomics, diagnostics and typing create tremendous new opportunities for public health microbiology. Rapid microbial and drug resistance detection tools are now reaching the point-of-care diagnostic market. High-throughput next generation sequencing technology is making global microbial population genomics and 'resistomics' available for every major human pathogen. Comparative and functional whole genome analysis, beyond tracing evolution and spread of microbial pathogens, can rapidly uncover novel markers of virulence, drug resistance and potential for epidemic transmission. This was illustrated by this year's whole genome analyses revealing, within a few days, the hybrid pathotype Enterohaemorrhagic-Enteroblast Aggregative *E.coli* EHEC-EAEC O104:H4 responsible for the largest ever outbreak of haemolytic-uraemic syndrome in Europe.
5. In this fast moving field, there is a largely unmet need to critically assess the accuracy and public health added value of new laboratory testing methods and the characterisation of novel pathogen biological markers. In addition, national reference laboratories need access to external quality assurance schemes for emerging diagnostic and typing technologies to ensure comparability of data used for EU surveillance. The use of new technology for disease management and control pathways needs to be prospectively evaluated by large scale studies which are increasingly supported by national- and Commission- funded programmes. ECDC has played a central role in advising the Commission on relevant research programmes and has undertaken systematic literature reviews appraising the scientific evidence of public health effectiveness of new diagnostic and typing methods.

## Public health microbiology in the EU

6. Across the EU, Member States operate healthcare, public health and national surveillance systems that differ in their legal foundations, organisational models, funding sources and regional devolution of authority. Likewise, primary diagnostic and secondary reference laboratory services vary significantly between Member States in their organisational models, use of diagnostic testing

methods, referral rates of specimens for advanced characterisation at secondary level, use of reference testing methods and participation in national and international surveillance networks.

7. Since 1999, in recognition of the need for EU coordination of response to cross-border health threats, the Network of Communicable Diseases (Decision 2119/98/EC) links public health authorities in the EU Member States, the Commission and international partners, coordinating EU-wide surveillance and the early warning and response system (EWRS) (Decision 2000/57/EC). The system includes 49 communicable diseases, healthcare-associated infections and antimicrobial resistance, the list of which is updated periodically according to Decision 2000/96/EC as new diseases emerge.

8. Since 2005, ECDC has been fulfilling its mission to identify, assess and communicate current and emerging threats to human health from communicable diseases (Founding Regulation 851/2004). Epidemiological surveillance of infectious diseases, epidemic preparedness and scientific advice for infection control are all critically dependent on appropriate microbiological testing. In this context, the Centre has a mandate, 'by encouraging cooperation between expert and reference laboratories, to foster the development of sufficient capacity for diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' (Article 5.3).

9. The ECDC Long-term Surveillance Strategy (2007-2013) paved the way for building up a strong, centralised, integrated European surveillance system in close partnership between ECDC and epidemiology and microbiology experts from the Member States, organised in disease networks and their coordination groups. The Surveillance Objectives paper (AF15/2) gave a practical roadmap for implementation of the long-term surveillance strategy. In 2011, the first phase of the strategy was successfully completed by transferring the management of 16 Dedicated Surveillance Networks (DSN) to ECDC and integrating epidemiological surveillance data into TESSy for 14 of them. This achievement has significantly enhanced the efficiency, accessibility and comparability of surveillance data and ensured the sustainability of the European surveillance system.

10. When ECDC was established, there were 17 DSN focusing on specific diseases or health issues, such as EWGLINET, EARSS, EuroHIV. These networks had been developed "bottom up" by public health and microbiology experts of specific diseases after obtaining grant support from the Public Health Programme of the Commission. After ECDC had evaluated the DSNs in 2007-08, relevant operations of the networks were progressively integrated into ECDC's work with funding of the corresponding microbiology activities. The transition phase involved the development of new professional partnerships between the ECDC experts who had been recruited to work in each disease programme and the former DSN members with top expertise in their field and decades of experience in international collaboration. This new partnership followed a learning curve to build mutual trust and strike a careful balance between ensuring the continuity of surveillance and supporting innovative capacity building initiatives under ECDC coordination. Several of the network microbiology projects have predictably required adjustment when new criteria to prioritise support included not only the opinion of network experts but also the EU added value as reviewed by ECDC together with its governing bodies.

11. The ECDC Strategic Multi-annual Plan (SMP, 2007-2013) includes Surveillance Strategy 2.1. It aims to establish EU-wide reporting standards and an integrated data collection network for surveillance including all Member States and covering the communicable diseases and health issues included in Decision 2119 with the necessary detail according to their priority. This strategy envisages the development and use of standard case definitions and integration of laboratory data into TESSy, including data derived from molecular typing. Scientific Advice Strategy 3.5 aims to promote the strengthening of microbiological support for communicable disease prevention, control and scientific studies in the EU. This strategy outlines a series of approaches, including networking with professional organisations and national laboratories to develop core competencies and unified molecular typing schemes, develop directories of national reference laboratories and map capacities, develop training schemes, promote EU-wide quality assurance systems for microbiological laboratories, analyse the needs for improved diagnostic technologies and reinforce links between human and veterinary laboratories.

12. Over the past 5 years, these strategies have been implemented to a substantial degree. In 2008, ECDC started with a 2 year fellowship for training in Public Health Microbiology (EUPHEM), strongly linked to the established EPIET training network. The General Strategy and Framework of Actions for ECDC Cooperation with Microbiology Laboratories and Research Institutes in the EU

(2007-2013) established a forum of National Microbiology Focal Points (NMFP) nominated through the Management Board members by the national authorities. This forum endorsed the objectives of SMP strategy 3.5 that was followed up by ECDC's Microbiology coordination team. The EU situation was analysed and the national reference laboratory systems for communicable diseases in the Member States were mapped. Stakeholders were consulted on laboratory quality systems, biosafety and biosecurity and efforts were joined with professional organisations to promote good practice in this area across the EU. A consensus definition of public health microbiology and core public health functions of national reference laboratories has been published.

13. Based on a mid-2011 survey of ECDC microbiology activities, 13 disease specific networks supported by ECDC currently have a microbiology component, comprising 21 ECDC-funded projects on 22 diseases outsourced to the Member States. Of these, 11 projects integrate molecular typing data for surveillance on 16 pathogens. In addition, there are 12 ongoing external quality assessment schemes including 23 pathogens and 14 laboratory training projects on diagnostic testing, antimicrobial susceptibility testing and molecular typing (see Annex II).

### EU laboratory capacity

14. In keeping with the EU Health Strategy, every Member State should have access to routine and emergency diagnostic and reference laboratory services to detect, identify, characterise and subtype human pathogens of public health significance, either locally or through cooperative agreement, as required for informing disease management, control and prevention measures. Clinical microbiology laboratories, beyond their primary function to inform patient management, have an important role to play in ensuring local surveillance of healthcare-associated infections and antimicrobial resistance and notifying laboratory test results to surveillance networks. Reference laboratories should design and operate their services in close coordination with experts in epidemiology within the public health authorities. Their staff should be prepared to participate in the detection and investigation of and response to outbreaks. They should also maintain links and provide technical guidance to clinical laboratories, veterinary laboratories and laboratories testing environmental samples, water and food. In particular, they can play a significant leadership role supporting the development of adequate quality and reliable diagnostic services.

15. The ECDC Strategies for Disease-specific Programmes (2010-2013) identified areas or improvement in pathogen-specific laboratory capacity as source of data for EU surveillance. A common theme is the large and variable degree of disease under-ascertainment by country related to variations in provision, access and quality of primary diagnostic services. Laboratory capacity gaps are related to sub-optimal diagnostic and reference testing for some disease agents, e.g. limited access to accurate laboratory methods, lack of awareness of clinical practitioners about best diagnostic practice, underutilisation of microbiology testing, lack of standardisation or deficient quality control of laboratory methods. ECDC disease programmes have begun to address some these deficiencies through ongoing projects to validate laboratory methods, perform external quality assurance schemes and organise microbiology training (Annex II, page 5). These projects are coordinated by the leading reference microbiology groups within each network and mobilise their pooled expertise and operational experience. Several networks (FWD-Net, ELDSNet, EARS-Net, ENIVD-CLRN, ERLN-TB) have developed EU guidance on good laboratory practice and defined pathogen-specific minimal diagnostic requirements for reliable surveillance and threat monitoring. For tuberculosis, no network of laboratories was in place in the EU prior to 2005. ECDC has therefore established a fully-fledged European laboratory network (ERLN-TB) which has already built microbiology capacity to support the EU Framework Action Plan on Tuberculosis.

16. Europe is facing serious threats to laboratory capacity due to financial cutbacks in health services, shortage of trained medical specialists, and decreased interaction between microbiologists and clinicians following consolidation of microbiology services into large private laboratories. These challenges underline the need for encouraging collaboration between clinical and public health microbiology services. They also highlight the importance of maintaining the laboratory capability at primary, secondary and tertiary levels that is required for effective surveillance, alert and response to infectious disease threats throughout Europe.

17. As part of its Decision 1350/2007/EC, the Commission encourages the development of a tertiary system of EU reference laboratories for human pathogens to ensure preparedness and rapid

cross-border response against communicable disease and other biothreats. To this end, the Public Health Programme has funded the EURLOP project (European Reference Laboratories System for Human Pathogen Options Project) aimed at defining the functions of a responsive EU reference laboratories system, appraise the gaps in the existing capacity across the EU through NRL and EU laboratory networks and define strategic options and models to fill in the gaps. It will be crucial for Member States, Commission and ECDC to take stock of the results and conclusions of this project (to be available by September 2011) for further public health microbiology capacity building initiatives.

## EU surveillance of antimicrobial resistance

18. Antimicrobial resistance (AMR) affects a wide range of viral, bacterial, fungal and protozoal pathogens. It increases the morbidity and mortality of many infectious diseases and compromises chemotherapeutic control measures. ECDC's Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) programme is coordinating the European Antimicrobial Resistance Surveillance Network (EARS-Net) which provides core surveillance data on AMR in bacterial pathogens of public health importance. The ARHAI programme also assesses the risk of emerging multidrug-resistant pathogens affecting the EU. These activities are developed and carried out in close collaboration with the nominated National AMR Focal Points, National AMR Surveillance Contact Points and the Commission. In addition, drug resistance of clinical and public health relevance in a number of viral and bacterial pathogens is monitored by other ECDC disease programmes and EU surveillance networks (e.g. influenza, tuberculosis, foodborne bacterial infections, gonococcal infections). Therefore, AMR surveillance and epidemic preparedness is a cross-cutting microbiology issue relevant to many European networks and ECDC disease programmes.

19. Since 2002, the European Committee on Antimicrobial Susceptibility Testing (EUCAST), working under the auspices of ESCMID and supported by ECDC since 2007, has achieved extensive standardisation of antimicrobial susceptibility testing breakpoints. EUCAST has also led improvements of quality, comparability and clinical predictive value of antimicrobial resistance monitoring in human pathogens of public health relevance. However, EUCAST resistance breakpoints and validated test methods are not yet available for all pathogens under EU surveillance of AMR.

20. Formerly called EARSS and coordinated by RIVM until its transfer to ECDC in 2010, EARS-Net is a world class international surveillance network for antimicrobial resistance which includes over 900 clinical microbiology laboratories from 28 European countries. It provides extensive population coverage throughout the EU and focuses on a limited set of drug classes and epidemiologically significant bacterial pathogens causing invasive human infections. The network has been remarkably successful in gradually adopting common technical standards for resistance detection with support from EUCAST guidance and an external quality assurance scheme. By providing robust and reliable resistance data that allow benchmarking between Member States and monitoring of secular trends over more than a decade, the system has fostered awareness of AMR and triggered public health prevention and control programmes in Member States.

21. However, EARS-Net has intrinsic limitations in the surveillance and alert functions that are needed for informing AMR control policies. Its data collection process is restricted to invasive isolates and follows an annual cycle of cumulative data aggregation from primary laboratories. This process is too slow and insensitive to serve as an early detection and warning system for emerging resistance or cross-border clusters of infections caused by multidrug-resistant clones. As a result, recent EU-wide health threats caused by regional and international dissemination of extensively drug-resistant bacteria, such as carbapenemase-producing *Klebsiella pneumoniae* and *Acinetobacter baumannii*, have not been recognised in a timely manner by this system. Research studies have investigated these AMR epidemic threats by using further microbiological characterisation, including molecular typing and analysis of resistance determinants and their genetic vectors. These molecular data are essential to detect, ascertain and delineate AMR epidemics and inform control measures. ECDC is piloting a study with a network of expert laboratories to evaluate the feasibility and public health benefits of integrating this type of molecular data for EU surveillance of meticillin-resistant *Staphylococcus aureus*.

22. AMR epidemiological data on influenza virus, *Salmonella*, *Campylobacter*, *Mycobacterium tuberculosis* and *Neisseria gonorrhoeae* are collected, analysed and reported separately by ECDC.

Cross-disease harmonisation of surveillance sampling frames, testing methods and analysis strategies as well as integration of data reporting at EU level have not yet been achieved.

23. To enhance comparability of epidemiological surveillance of AMR worldwide, ECDC has recently published international expert consensus definitions of multidrug, extensive drug and pan-drug resistance phenotypes in bacterial pathogens of public health relevance. The successful application of these epidemiological categories will depend on harmonisation of testing by clinical and public health laboratories of an extensive and consistent range of antimicrobial drugs. The feasibility of this approach will require further study.

24. Besides ECDC programmes, academic investigators and the pharmaceutical industry conduct pan-European and global surveys of AMR in human pathogens. These studies apply state-of-the-art methods of quantitative susceptibility testing and mechanism of resistance identification that allow detailed analysis of geographic distribution and spread of resistance determinants and multidrug-resistant clones in human populations. AMR surveys funded by Member States and DG Research are often conducted by or in cooperation with members of ECDC-supported laboratory networks. Such surveys provide microbiological data that are necessary for developing risk assessment and guidance on detection and control of emerging antimicrobial resistance at national and European level. There would be advantages for ECDC to interact more closely with researchers on AMR. It would be helpful to develop general guidance on the design of prevalence surveys of drug resistance in key bacterial, fungal and viral pathogens of public health significance.

Since 2011, the ARHAI programme, together with epidemic intelligence experts, is developing an Epidemic Intelligence System (EPIS) platform module for rapid exchange of information on possible antimicrobial resistance threats, such as cross-border outbreaks of extensively drug-resistant bacteria. This tool will need to be carefully piloted and fine-tuned to help early assessment and verification of complex AMR threats across the EU. A challenge will be to engage expert laboratories on the detection frontline to share advanced microbiological information and unpublished findings with public health authorities in the Member States. It remains to be seen how this tool or other data collection approaches can allow monitoring of cross-border outbreaks of extensively drug-resistant bacteria.