



Summary of work activities

Sabrina Weiss

European Public Health Microbiology Training Programme (EUPHEM), 2014 cohort

Background

According to Articles 5 and 9 of ECDC's founding regulation (EC No 851/2004) 'the Centre shall, encourage cooperation between expert and reference laboratories, foster the development of sufficient capacity within the community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health' and 'as appropriate, support and coordinate training programmes in order to assist Member States and the Commission to have sufficient numbers of trained specialists, in particular in epidemiological surveillance and field investigations, and to have a capability to define health measures to control disease outbreaks'.

The ECDC Fellowship Training Programme therefore includes two distinct curricular pathways: Intervention Epidemiology Training (EPIET) and Public Health Microbiology Training (EUPHEM). After the two-year training EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. Both paths that provide competency based training and practical experience using the 'learning by doing' approach in acknowledged training sites across European Union (EU) and European Economic Area (EEA) Member States.

European preparedness for responding to new infectious disease threats requires a sustainable infrastructure capable of detecting, diagnosing, and controlling infectious disease problems, including the design of control strategies for the prevention and treatment of infections. A broad range of expertise, particularly in the fields of epidemiology and public health microbiology, is necessary to fulfil these requirements. Public health microbiology is required to provide access to experts in all relevant communicable diseases at the regional, national and international level in order to mount rapid responses to emerging health threats, plan appropriate prevention strategies, assess existing prevention disciplines, develop microbiological guidelines, evaluate/produce new diagnostic tools, arbitrate on risks from microbes or their products and provide pertinent information to policy makers from a microbiological perspective.

According to the European Centre for Disease Prevention and Control (ECDC) Advisory Group on Public Health Microbiology ('national microbiology focal points'), public health microbiology is a cross-cutting area that spans the fields of human, animal, food, water, and environmental microbiology, with a focus on human population health and disease. Its primary function is to improve health in collaboration with other public health disciplines, in particular epidemiology. Public health microbiology laboratories play a central role in detection, monitoring, outbreak response and the provision of scientific evidence to prevent and control infectious diseases.

This report summarises the work activities undertaken by Sabrina Weiss, cohort 2014 of the European Public Health Microbiology Training Programme (EUPHEM) at Public Health England (PHE), London, UK.

All EUPHEM activities aim to address different aspects of public health microbiology and underline the various roles of public health laboratory scientists within public health systems.

Pre-fellowship short biography

Sabrina studied medical Biotechnology in Berlin, Germany, and did her diploma thesis about retroviral envelopes in the laboratory of Marc Sitbon at the Institute of Genetic and Molecular Medicine (IGMM) in Montpellier, France. She then returned to Germany to pursue her doctoral studies in the laboratory of Fabian Leendertz at the Robert Koch-Institute (RKI) in Berlin. In 2013 she earned her PhD from the Technical University Berlin with "summa cum laude" for her work on *Identification and characterisation of emerging viruses in free-ranging bats from sub-Saharan Africa*. Sabrina continued working at the RKI as a postdoctoral researcher and project coordinator before joining the EUPHEM programme in 2014.

Fellowship assignment: Public health Microbiology (EUPHEM) path

Methods

This report accompanies a portfolio that demonstrates the competencies acquired during the EUPHEM fellowship by working on various projects, activities and theoretical training modules.

Projects included epidemiological investigations (outbreaks and surveillance); applied public health research; applied public health microbiology and laboratory investigation; biorisk management; quality management; teaching and public health microbiology management; summarising and communicating scientific evidence and activities with a specific microbiological focus.

The outcomes include publications, presentations, posters, reports and teaching materials prepared by the fellow. The portfolio presents a summary of all work activities conducted by the fellow, unless prohibited due to confidentiality regulations.

Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the EUPHEM scientific guide¹.

1. Epidemiological investigations

1.1. Outbreak investigations

A. An outbreak of Verocytotoxigenic Escherichia coli (VTEC) O55 in a nursery in England, October - December 2014

Supervisor: Sooria Balasegaram

Whilst investigating an ongoing outbreak of VTEC serotype O55 in the South of England three new cases occurred in children and staff attending the same nursery. Microbiological and epidemiological investigation revealed a total of twelve nursery-associated cases for which no common exposures could be identified aside from nursery attendance. Molecular typing and phylogenetic analysis showed that isolates from the nursery cases were identical or differed by a single nucleotide polymorphism (SNP) and comprised a distinct cluster differing by three SNPs from non-nursery cases in the wider outbreak. Control measures implemented in the nursery after identification of the sub-cluster were deep cleaning of premises, screening, and exclusion of cases until microbiological clearance. No new cases were identified thereafter. The fellow contributed to data cleaning, data analysis, and communication of the results (report) to the relevant stakeholders.

B. Outbreak of OXA-48 Carbapenem-resistant organisms linked to the use of one endoscope in a hospital in London, between March and June 2015.

Supervisors: Charlotte Anderson, Paul Crook

During April and June 2015 seven inpatients attending the same ward in a hospital in London have tested positive for OXA-48 Carbapenemase-producing organisms (OXA-48 CPO). Cases were detected through routine screening of all patients and root cause analysis by the hospital identified that all had been exposed to the same endoscope during endoscopic retrograde cholangiopancreatography. The endoscope in question has been removed from use,

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2013. Available from: <http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf>

examined and sampled but no OXA-48 CPO was detected. A case-control study was suggested to test the hypothesis of transmission via the endoscope, and the PHE Field Epidemiology Service (FES) agreed to support the investigation. The fellow was seconded to FES to assist in the outbreak investigation and to conduct a case control study to test the null hypothesis that exposure to the specific endoscope was not associated with CPO colonisation. The fellow was leading on writing the study protocol and developing the questionnaires. For internal reasons, the hospital eventually decided not to proceed with the study.

C. Training modules

EPIET/EUPHEM Introductory Course, September-October 2014, Spetses, Greece: The course familiarised participants with the principles, techniques and logistical aspects of outbreak investigations. Fellows were taught the principles of intervention field epidemiology and the function and importance of public health microbiology. Outbreak Module, December 2014, Berlin, Germany: The module focused on how to apply theoretical knowledge on outbreak investigation in practise using various software packages. Participants were trained in essential data management skills and in how to perform descriptive and analytical studies, including cohort and case control studies, in an outbreak investigation.

Multivariable Analysis Module, March 2016, Vienna, Austria: The module provided the knowledge and tools necessary to understand the principles of multivariable analysis and to identify analysis situations that require the use of multivariable analysis. Fellows were trained in identifying the relevant variables to build up an optimal regression model, to control for confounding and effect modification at the analytical level, and to interpret the results of a regression model.

Educational outcome: The fellow had hands-on experience within outbreak investigations and participated in multidisciplinary outbreak control team meetings; prepared study protocols and formulation of appropriate hypotheses; designed data collection forms and questionnaires; collaborated and communicated with external colleagues; in addition to report writing. Sabrina also served as the link between the laboratory and epidemiologist in an outbreak setting both nationally and internationally.

1.2. Surveillance

A. Ebola Virus Outbreak in Guinea, March-April 2015 (international mission)

Supervisor: Aftab Jasir

Following a call for assistance by the Global Outbreak Alert and Response Network (GOARN) the fellow was deployed to Boffa, Guinea. The overall objective of the mission was to support the World Health Organisation (WHO) country office and the Ministry of Health by contributing to the rapid control of the outbreak and prevention of further spread by breaking the cycle of transmission in the community and health care facilities. Together with a second epidemiologist from ECDC the fellow joined a team of six Guinean doctors already placed in Boffa via the WHO, one infection, prevention and control consultant from DRC and two consultants recruited from Cameroon. Specific activities were focused on active case finding, case investigation, mapping chains of transmission, contact monitoring, surveillance, and analysis of epidemiological data. These data were reported daily and weekly to the central level. Training and technical assistance provided to the team included support in the design and operation of the alert system, active surveillance protocols and case/contacts databases as well as software training. Since reticence towards activities of WHO and the Red Cross was prominent in the prefecture of Boffa, specifically the island of Kito, the team was involved in sensitisation campaigns and in supporting contacts and affected families, conducted in liaison with other response partners such as the World Food Programme (WFP) or UNICEF. Despite that widespread acceptance of secured burials remained an issue, sensitisation activities and efficient support were successful in lifting most of the reticence. Follow-up of contacts proved successful and no new cases were reported from the area after the team had left.

B. Assessing Whole Genome Sequence based SNP analysis as a tool for national epidemiology and surveillance of MRSA

Supervisors: Bruno Pichon, Angela Kearns

The national surveillance system of methicillin-resistant *Staphylococcus aureus* (MRSA) in England is restricted to cases of bacteraemia and the referral of isolates for typing and characterisation is not mandatory. Hospitals send samples to Public Health England (PHE) for surveillance and to assist with outbreak investigations, but traditional techniques have limited discriminatory power to distinguish between strains of the same lineage. The aim of the project was to test the utility and feasibility of whole genome sequencing (WGS) as tool for routine surveillance of EMRSA-15 (CC22-SCCmecIV), the dominant healthcare-associated clone in the UK. A total of 505 EMRSA-15 isolates received from 61 hospitals across England between 2010 and 2014 were subjected to whole-genome sequencing. Phylogenetic analysis was undertaken with the objectives of facilitating the detection of phylogenetic clusters and possible transmission events. Notably, phylogeographic analysis showed evidence of regional EMRSA-15 clusters. While it was possible to refute certain suspected transmission events based on the phylogenetic analysis, the data did not allow for a fixed single nucleotide polymorphism (SNP) threshold that alone could be used for ascertainment clusters. However, results generated in this study provide a genomic framework and serve

as long term resource for contextualizing novel sequences and inferring possible origins. When SNP based data are analysed in conjunction with epidemiological information, phylogenetic analysis will prospectively allow for distinction between linked and sporadic cases that are difficult to discern through traditional methods. This will facilitate rapid, targeted public health action where appropriate. The fellow was the main investigator for this project and performed all *in silico* analyses. The results of this study are currently summarised to be submitted for publication in a peer-reviewed journal.

C. Training modules

EPIET/EUPHEM Introductory Course, September-October 2014, Spetses, Greece: The course familiarised the fellows with the principles of surveillance and how to develop, validate, evaluate and operate a surveillance system.

Rapid Assessment and Survey Methods, June 2015, Athens, Greece: The module introduced participants to techniques for surveillance in complex emergency situations as well as sampling techniques and morbidity and mortality surveys.

Vaccinology Module, May 2016, Paris, France: The module focused on the surveillance of vaccine-preventable diseases, including surveying vaccine coverage and vaccine efficacy.

Educational outcome: Analysis of combined syndromic and laboratory surveillance data in a complex situation (Ebola outbreak); microbiological support on surveillance systems; application of combined microbiological and epidemiological knowledge in outbreaks, surveillance and participation in an outbreak investigation with having one or more PH microbiology tasks. This included the analysis of molecular typing data in conjunction with epidemiological data; working in an acute outbreak situation; teaching and moderating discussion for international and interdisciplinary teams; writing scientific reports; formulation of specific public health recommendations; analysing WGS data derived from Next Generation Sequencing (NGS) using bioinformatics tools; applying phylogenetic knowledge in a new context (bacterial genomes); interpretation of classic bacterial typing results (PFGE, spa-typing, ribotyping); field epidemiology: case finding, case investigation, mapping chains of transmission, contact monitoring, surveillance, analysis of epidemiological data

2. Applied public health microbiology research

A. Elucidating *Clostridium difficile* pathogenicity from the epigenome to the proteome

Supervisor: Raju Misra

Predicting strain pathogenicity from genomic data is an important tool for strain characterization and allows for quickly identifying outbreaks or the emergence of novel strains. At present many genomic markers for *Clostridium difficile* are predictions, often borne from comparative genomic studies. However, genomically similar *C. difficile* strains often exhibit marked phenotypic variability, in particular when compared with antimicrobial resistance patterns. Integrated genomic, epigenetic, and proteomic data were analysed and compared to a microbiologically-derived antibiotic resistance data. In total, a database comprising genomic, epigenetic and protein expression data of ten selected *C. difficile* strains was composed by the fellow. Comparative analysis show marked differences in methylation and protein expression patterns between different strains, but also between three strains originating from the same outbreak. In depth-analysis of the derived dataset might enable to phenotypically validate markers for CDI diagnosis, epidemiological surveillance, outbreak detection and antibiotic treatment.

B. MLST of *Leptospira* species to inform the global epidemiology and disease burden in UK

Supervisor: Victoria Chalker

Leptospirosis is a zoonotic bacterial disease affecting more than 1 million people per year globally, particularly in impoverished populations in tropical climate countries. Also epidemics are increasingly reported and in these settings rapid typing is essential to identify potential clusters and transmission pathways. Diagnosis of leptospirosis is primarily clinical or, if possible, by real-time PCR, but typing still requires bacterial isolates. However, culturing fastidious leptospires is time consuming and often unsuccessful, hampering routine typing. The aim of the project was to modify an existing MLST scheme to lower the limit of detection, allowing for amplification of alleles directly from clinical specimens, including non-invasive urine samples. The developed assay enables rapid identification of clusters during outbreaks. It allows alleles to be sequenced using two standard primers which significantly reduces costs. Further, the provision of a simple and relatively cheap way of typing *Leptospira* might enhance worldwide surveillance. When combined with phylogenetic analysis single alleles are sufficient to retrieve species information. Because of its specificity the assay may be further explored to be used as diagnostic assay in low-income countries, where leptospirosis is common but real-time PCR is not available. The fellow was the main investigator for this project and performed all experiments and analysis. The assay is currently being implemented in the routine reference service undertaken by the *Leptospira* reference laboratory for England and Wales. Results from this study were published in PLoS Neglected Tropical Diseases. Typing information of pathogenic *Leptospira* spp. could therefore, be obtained directly from a variety of clinical samples using this modified MLST assay. This assay

negates the need for time-consuming culture of *Leptospira* prior to typing and will be of use both in surveillance, as single alleles enable species determination, and outbreaks for the rapid identification of clusters.

C. Training modules

Phylogeny and Bioinformatics Module, November 2014, Stockholm: The module provided the knowledge and tools for participants to perform robust maximum likelihood phylogenies and to reliably interpret the results. It further served as an introduction into common software packages and bioinformatics platforms for participants to build on.

Educational outcome: Ability to plan and organising courses and in doing so moderate case studies, give lectures and perform pedagogical teaching. Communicate effectively with persons from a multidisciplinary background, authorities, the public in the form of publications, reports and oral presentations. Key examples were working with huge datasets using bioinformatics tools and developing programming skills (python, R); working on epigenetic and proteomic data; understanding the process involved in implementing a new test into routine use; writing scientific reports; communicating with peer-reviewed journals; understanding limitations of laboratory methods and the appropriate use of diagnostic algorithms; time management

3. Applied public health microbiology and laboratory investigations

A. Diphtheria in Indonesia

Supervisor: Androulla Efstratiou

Diphtheria caused by toxigenic strains of *Corynebacterium diphtheriae*, *C. ulcerans*, or *C. pseudotuberculosis* continue to play a major role as lethal resurgent infectious diseases and remain a serious health problem within many regions of the world, especially South East Asia. The microbiological diagnosis of the disease, the identification of contacts and carriers, and the appropriate clinical management of patients are therefore crucial. In 2011, a laboratory workshop was held in Balai Besar Laboratorium Kesehatan (BBLK), Surabaya, Indonesia, in response to an ongoing diphtheria epidemic in East Java. A follow-up workshop was held at BBLK on 3-4 June 2015 to review the current status of the epidemic and identify immediate and long term needs to strengthen epidemiological and microbiological surveillance. To present and discuss the results at this workshop the fellow analysed molecular typing (ribotyping) data that was generated at BBLK between 2010 and 2012. Samples originated predominantly from cases in East Java (148/161, 92%), however, few cases came from Sulawesi (n=7) and Kalimantan (n=6). Patient data was available for 111 cases (69%). Of these, 67 (60%) were female. The majority of cases (n=60, 54%) occurred in children below 10 years of age. No temporal or spatial patterns could be identified based on the dendrogram derived from the data. During the workshop numerous discussion groups took place highlighting the current practises that are in place throughout the country and contributing towards a better understanding of the present situation. The workshop contributed towards improvements in the understanding of the current practice for diphtheria case management and diagnostics and led to the development of multiple recommendations regarding sampling, diagnostics, and dissemination of information in the general public. The fellow was responsible for data analysis, presentation of the results during the workshop, and moderation of discussion groups during the workshop. In preparation of the workshop the fellow was involved in writing a comprehensive book chapter together with the supervisor on microbiological, epidemiological and clinical aspects of diphtheria.

B. Understanding serological cross-reactivity between and host responses to emerging enterovirus types to enhance public health responses

Supervisor: David Allen

Non-polio enteroviruses (NPEVs) are an important cause of illness in neonates below 90 days of age. Currently mostly sequence-based methods are used for detection and characterisation of enteroviruses. As UK Reference Virology Laboratory, ECDC partner, and WHO National Polio Laboratory, the Enteric Virus Unit (EVU) in the Virus Reference Department of Public Health England needs to be able to respond fast and smart to public health threats from emerging enterovirus strains (e.g. EV-D68, EV-A71, EV-CA21). The aim of the project was to contribute to a curated bank of NPEV strain isolates for characterisation, provision of reference materials, and quality assurance panels for use in method development and validation. Based on the aforementioned three emerging NPEV types the fellow grew and titrated virus stocks for each. She developed neutralisation assays to be used for examining cross-reactivity between and to determine the presence of neutralising antibodies against those viruses. The assays allow for serological characterisation of the targeted NPEVs and contribute towards a better understanding of circulating NPEV strains.

C. Training in Diphtheria laboratory diagnostics

Supervisors: Ginder Mann

The fellow received training on reference laboratory techniques for the detection and characterisation of potentially toxigenic *Corynebacterium sp.* Methods covered included culture and isolation on specialised media, confirmation and typing of species via biochemical tests, determination of toxigenicity status via the Elek-test and detection of toxin genes with PCR.

Educational outcome: Identify training needs, plan and organising the workshop, moderate working group discussions, give lectures and perform pedagogical teaching to a diverse scientific audience overseas on laboratory methods for characterisation of bacteria and the detection of diphtheria toxin, understanding limitations of laboratory methods; developing neutralisation assays

4. Biorisk management

A. Study on preparedness of the UK toward Ebola virus disease

In early 2015 the fellow did a study on the preparedness of the UK towards an imported case of Ebola virus disease. The results were presented to the Director, the Chief Microbiologist, and the Chief Scientist of ECDC during the Module on Initial Public Health Management.

B. Field mission during Ebola virus outbreak

During the deployment to Guinea to support the Ebola virus outbreak response the fellow followed necessary biosafety measures. These included appropriate hygiene and sanitation techniques and social distancing, especially during field visits, including case investigations and contact follow-up.

C. Training modules

Biorisk Management, February 2015, Stockholm, Sweden: The module provided participants techniques for biosafety assessment and risk mitigation, including WHO recommendations on biosafety management in laboratories and a visit to a biosafety level 4 (BSL4) facility. One day focused on the International Civil Aviation Organization (ICAO) regulations for the transport of dangerous goods and was completed with a WHO certificate of International Transport of Infectious Substances.

Educational outcome: understanding biosafety regulations, applying biorisk mitigation methods in theory and practise in laboratory and field settings, learning appropriate measures for the safe transport of hazardous substances and pathogenic specimens

5. Quality management

A. Euro-GASP External quality assessment (EQA) scheme, 2015 for *Neisseria gonorrhoeae* antimicrobial susceptibility testing

Supervisor: Michelle Cole

In October 2015, an EQA scheme for antimicrobial susceptibility testing in *Neisseria gonorrhoeae* was distributed to 27 laboratories in 25 participating countries as part of the European gonococcal antimicrobial susceptibility programme (Euro-GASP). Ten gonococcal isolates were selected by Public Health England (PHE) and distributed by the United Kingdom National External Quality Assessment Service (UK-NEQAS). Isolates chosen were representative of a range of different antimicrobial susceptibility profiles and selected from well characterised and recently isolated clinical strains. Participating laboratories were requested to test the panel using local methodology and breakpoints against a range of antimicrobial agents and results were submitted to UK-NEQAS who issued individual laboratory reports. PHE decoded and further analysed the results based on the categories of susceptibility and the minimum inhibitory concentrations (MICs) assigned. Twenty-six laboratories (24 countries) returned EQA results. The majority of laboratories used E-tests and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints. Overall, the inter- and intra-laboratory concordances were demonstrating comparability between different testing methodologies and allowing for confidence in Euro-GASP decentralised testing. The EQA results also highlighted the need for five centres to receive further guidance to help reach the recommended target (95% of MICs within two dilutions of the modal MICs) to ensure reliable antimicrobial susceptibility testing results for *N. gonorrhoeae* across the network. The fellow was responsible for data compilation, which she expedited by the creation of scripts (in python), data analysis and wrote the final report.

B. Laboratory audit

The fellow did an internal audit of the National Legionella Reference Laboratory (NLRL) at PHE as part of the Quality Management Module.

C. Training modules

Quality Management, February 2015, Stockholm, Sweden: The module provided an overview of quality management concepts in diagnostic laboratories, according to the ISO 15189 standard. Topics covered included factors influencing quality in laboratories, internal and external quality control, norms and accreditation,

assessments and audits, documentation and record keeping, sample management, stock purchase and inventory management, management of equipment and temperature-controlled devices, process improvement, customer service and international health regulations.

Educational outcome: involvement in external quality assurance (EQA); participation in a European network; familiarisation with the concept of antimicrobial susceptibility testing; performing an internal audit; learning about accreditation processes and required laboratory standards

6. Teaching and pedagogy

A. Lecturing during Biorisk Module

The fellow amended and delivered a lecture on factors influencing quality in a laboratory. Title: "Introduction-Laboratory Quality Management System".

B. Teaching during international mission

Part of the objectives during the fellow's deployment to Guinea was training and technical assistance for the local team. Together with her partner the fellow prepared, delivered, and facilitated on software workshops, and provided support in the design and operation of the alert system, active surveillance protocols and case/contacts databases.

C. Lecturing and facilitation of group discussions during Diphtheria workshop

A workshop on Clinical, Microbiological, and Public Health Aspects of Diphtheria in Indonesia was held in Surabaya, East Java, Indonesia, in June 2015. Besides the presentation of scientific data the objectives of the workshop included teaching aspects. To that end the fellow gave a lecture entitled "Review of novel diagnostics and typing methods for Diphtheria".

D. Facilitation of case study on Ebola contact tracing

The fellow facilitated a case study on Ebola virus contact tracing. The case study was delivered to participants of the Rapid Assessment and Survey Methods module held in June 2015 in Athens.

E. Organisation and management of the Lab4Epi Module

The fellow co-organised this two-day module held at PHE in January 2016 together with a fellow from the UK field epidemiologist training programme. While the module is open to external participants it is aimed to provide trainee field epidemiologists with a functional overview of the public health laboratory's role in outbreak investigations and surveillance of infectious disease. Lectures and discussions during the day included hot topics in antimicrobial resistance, molecular epidemiology in outbreak investigations and the challenges of applying whole genome sequencing to public health microbiology. Further, it included sessions on the distinct role of the food and water laboratory in outbreak investigations and two case studies. The fellow contributed to setting up the programme, facilitated the case studies, and moderated throughout the two days.

F. Update and facilitation of a case study on MERS-CoV

The fellow updated and facilitated a case study on Middle East Respiratory Syndrome Coronavirus (MERS-CoV) that was delivered during the Lab4Epi module in January 2016.

G. Lecture on immunology and immunological tests during Vaccinology Module

The fellow amended lecture on immunology and extended it by a part describing different test systems used in serological diagnostic. The lecture was delivered by the fellow to participants of the Vaccinology Module held in May 2016 in Paris.

Educational outcome: plan and organise lectures, facilitate case studies, identify specific learning objectives for diverse audiences, teaching people with diverse backgrounds, organise and moderate meetings and workshops, develop learning materials

7. Public health microbiology management

A. Public health microbiology management components as part of regular projects

Public health microbiology management was an integral component of all projects and activities during the fellowship. Working successfully on outbreak investigations relied on effective communication with people from various backgrounds like microbiologists, physicians, laboratory technicians, epidemiologists, statisticians, logisticians, government officials, and public health officers. Ethical and integrity considerations had to be taken

into account as well as team building aspects and coordination. Specifically in international contexts like the Indonesia workshop and the Ebola outbreak mission the management of cultural differences while strengthening team work was absolutely necessary for fruitful communication and collaboration.

Laboratory investigations as in the *Leptospira* and Enterovirus project required good time-managing skills to plan and conduct practical lab work using shared machines and workspaces. Time management and organisational skills were further trained by working on multiple projects at a time. The co-organisation of the Lab4Epi module required good planning and organising skills to ensure a successful workshop.

B. Training modules

Initial Management in Public Health, February 2015, Stockholm, Sweden: The module focussed on the understanding of roles and responsibilities in public health management. Topics included the identification of different management styles, team roles and team evolution, the delegation of tasks and the provision of structured feedback.

Educational outcome: gain experience of working in multidisciplinary national and international public health teams; understand team management; understand roles and formal responsibilities in public health microbiology; plan, schedule and organise research projects; managing multiple projects at the same time.

8. Communication

A. Publications

1. Weiss S, Menezes A, Woods K, Chanthongthip A, Dittrich S, Opoki-Boateng A, Kimuli M, Chalker V. An extended multilocus sequence typing (MLST) scheme for rapid direct typing of *Leptospira* from clinical samples. PLoS Negl Trop Dis. 2016 Sep 21;10(9):e0004996. doi: 10.1371/journal.pntd.0004996.
2. Weiss S, Efstratiou A. Diphtheria. In: Infectious Diseases and Antimicrobial Agents. 2015;1-9. <http://www.antimicrobe.org/b99.asp>
3. Weiss S, Spiteri G, Tripodo F, Amato-Gauci AJ, Cole M on behalf of the EURO-GASP network participants. ECDC technical report: Euro-GASP External quality assessment (EQA) scheme, 2015 for *Neisseria gonorrhoeae* as antimicrobial susceptibility testing. Submitted to ECDC for publication on ECDC website (in progress)
4. International SOP for direct MLST on *Leptospira* to provide to the community (offered to the International Leptospira study group/WHO Leptospira Reference Laboratories websites/ the PHE Leptospira website)

B. Reports

1. The outbreak investigation team. Interim investigation report: An investigation of an outbreak of Verocytotoxigenic *Escherichia coli* O55 in England, July to November VTEC. March 2015
2. Weiss S. GOARN Mission Report: Ebola Response in Guinea (Boffa). 2015
3. Weiss S, Anderson C, Mook P, Crook P. Outbreak investigation and case-control study protocol: Outbreak of OXA-48 Carbapenem-resistant organisms in a hospital, London, between March and June 2015.
4. Efstratiou A, Weiss S, De Zoysa A, Bracebridge S, Hughes G, Husada D, Kes, RM, Ambarwati W, Irawan E. Report from the Workshop on Clinical, Microbiological, and Public Health Aspects of Diphtheria in Indonesia. June 2015

C. Conference presentations

1. Weiss S, Mikhail A, Balasegaram S, McCarthy N, Bolt H, Dabke G, Kingsbridge S, Chattaway M, Godbole G, Dallman T, Jenkins C, Rawlings C, McFarland N on behalf of the outbreak control team. An outbreak of Verocytotoxigenic *Escherichia coli* (VTEC) O55 in a nursery in England, October - December 2014. E-poster presentation, ESCAIDE 2015, Stockholm, Sweden.
2. Weiss S, Menezes A, Woods K, Chanthongthip A, Dittrich S, Opoku-Boateng A, Kimuli M, Chalker V. An extended MLST scheme for rapid direct typing of *Leptospira* from clinical samples. E-poster, ECCMID 2016.
3. Weiss S, Doumith M, Kearns A, Pichon B. Using Whole Genome Sequencing as a tool for rapid identification of EMRSA-15 clusters. Poster presentation at ISSSI 2016, Seoul, Korea.
4. Weiss S, Spiteri G, Tripodo F, Seaton S, Fagan E, Cole M. External quality assessment (EQA) for *Neisseria gonorrhoeae* antimicrobial susceptibility among 26 European laboratories. E-poster presentation at ESCAIDE 2016, Stockholm, Sweden.
5. Weiss S, Doumith M, Kearns A, Pichon B. Using Whole Genome Sequencing as a tool for MRSA national surveillance. Oral presentation at ESCAIDE 2016, Stockholm, Sweden.
6. Weiss S, Menezes A, Woods K, Chanthongthip A, Dittrich S, Opoku-Boateng A, Kimuli M, Chalker V. Use of multi locus sequence typing (MLST) to obtain discriminatory information and *Leptospira* species directly from clinical specimens. E-poster presentation at ESCAIDE 2016, Stockholm, Sweden.

D. Other presentations

1. Weiss S. Introduction – Laboratory Quality Management. Lecture given during the Quality Management Module. February 2015.
2. Weiss S., De Zoysa A. Molecular typing of Diphtheria in East Java. Oral presentation at the workshop on Clinical, Microbiological, and Public Health Aspects of Diphtheria in Indonesia. June 2015
3. Weiss S., De Zoysa A. Review of novel diagnostics and typing methods for Diphtheria. Lecture given during the workshop on Clinical, Microbiological, and Public Health Aspects of Diphtheria in Indonesia. June 2015
4. Weiss S. EUPHEM – year one activities. Presentation during the PHE ECDC site visit and mid-term evaluation of the fellow(ship). August 2015
5. Weiss S. An extended MLST scheme for rapid direct typing of *Leptospira* from clinical samples. Oral presentation during the one year review of the National Leptospirosis Service. March 2015
6. Weiss S., Williams C. Immunological basis of vaccines and immunization. Lecture given during the EPIET Vaccination Module. May 2016
7. Weiss S. European Public Health Microbiology Fellowship: my two-year programme at PHE and beyond! Presentation at the end of the Fellowship presented at PHE. September 2016

E. SOPs

1. PHE Standard Operation Procedure for direct MLST of *Leptospira* on clinical specimens.
2. PHE Standard Operation Procedure for micro-neutralisation tests for non-polio enteroviruses

9. EPIET/EUPHEM modules attended

1. Introductory course, Anargyrios and Korgialenios School of Spetses, Spetses, Greece (3 weeks)
2. Outbreak Module, Robert Koch-Institut, Berlin, Germany (one week)
3. Initial Management in Public Health Microbiology, ECDC, Stockholm, Sweden (one week)
4. Biorisk and Quality Management, ECDC, Stockholm, Sweden (one week)
5. Rapid Assessment and Survey Methods, National Institute of Public Health, Athens, Greece (six days)
6. Project review module, Lisbon, Portugal (2 x one week)
7. Bioinformatics and Phylogenetics, National Institute of Public Health, Stockholm, Sweden (3 days)
8. Multivariable analysis, Austrian Agency for Health and Food Safety Ltd., Vienna, Austria (one week)
9. Vaccinology Module, Public Health France, Paris, France (one week)

10. Other training

1. WHO certificate for International Transport of Infectious Substances
2. An introduction to Stata (1 day)
3. Bioinformatics – Programming for Biologists (2 days; 11 CPD)
4. Bioinformatics – Introduction to Galaxy – an online bioinformatics platform (0.5 days)
5. Bioinformatics – Next Generation Sequencing data analysis (2 days; 11 CPD)

Discussion

Coordinator's conclusions

One of the main goals of the EUPHEM programme is to expose the fellows to different public health experiences and activities, thus enabling them to work across various disciplines. This portfolio includes laboratory and epidemiological projects covering bacterial and viral pathogens across a variety of disease programmes, such as vector-borne diseases, sexually-transmitted diseases, food and waterborne diseases, respiratory tract infections, vaccine-preventable disease and antimicrobial resistance. All projects here described were in line with the 'learning by doing' and 'on-the-job' training service approach of the EUPHEM programme and followed the core competency domains described by professionals in mid-career and above.

Outbreak and surveillance activities ranged from local outbreaks to the analysis of national databases and outside of Europe, international missions to Indonesia and Guinea. All contributed to the understanding of important public health issues. During the two-year fellowship, the fellow, supervisors and training site have demonstrated the capability of addressing communicable disease threats in a structured joint approach between public health microbiology and epidemiology such as the use of whole genome sequencing based SNP analysis as a tool for national epidemiology and surveillance of MRSA.

Projects involved different professional groups, such as physicians, laboratory technicians, epidemiologists, statisticians, government officials, public health officers and logisticians, strengthening the fellow's ability to work in a multidisciplinary team. Those activities were complimented by nine training modules providing theoretical

knowledge. Projects had a clear educational outcome, with results communicated in scientific journals and at conferences.

The coordinator team concludes that the fellow has succeeded in performing all her tasks to a very high standard and with a professional attitude.

Supervisor's conclusions

The EUPHEM programme was a great opportunity for Sabrina and has provided her with the unique tools to find her niche in the field of public health microbiology and epidemiology whilst working with colleagues from very diverse disciplines, both nationally and internationally. For the host institution, it has provided the opportunity to build new bridges and strengthen collaboration between the different sectors within public health on both a national and international level. It has been a pleasure to mentor Sabrina for the past two years and it has been a sheer delight to see her develop within the programme and acquire many new skills, particularly within the field of bioinformatics and the application to public health. Her projects covered all core domains within the programme and showed that she was able to work on these projects independently, only occasionally consulting colleagues and peers for advice. One of her greatest strengths is her desire to work internationally in areas of public health and she was given the opportunity to do this via her missions to Indonesia (East Java) and Guinea. Sabrina also presented her findings and outputs from her projects at various national and international meetings ranging from local PHE Meetings to International Congresses, for example the International Symposium on Staphylococci and Staphylococcal Infections (ISSSI) in South Korea. Her scientific knowledge, technical and organisational skills and team spirit has been very much appreciated by all supervisors along with her open-mindedness, positivity, diligence and goal-oriented personality. It was a great pleasure to have Sabrina as a EUPHEM fellow within PHE and we highly appreciate her contribution and achievements within the fellowship programme. I wish Sabrina every success for the future and shall follow her career with interest.

Personal conclusions of the fellow

The prevention and control of infectious diseases relies, among other players, on microbiologists who can effectively communicate and collaborate with people from different disciplines, especially epidemiologists and medical microbiologists. Based on its "learning-by-doing" approach, the objective to perform projects across different disciplines, and the multitude of training modules provided, the EUPHEM fellowship provides an excellent foundation to perform these tasks.

The projects I have undertaken during those two years not only allowed me to diversify my microbiological knowledge and to develop new skills in previously unfamiliar areas, it also provided me with a good basis of epidemiological skills due to the close interaction with the EPIET path and the interdisciplinary character of the projects. As a result, the fellowship broadened my view and taught me to tackle problems from different perspectives. It also helped me to further develop my scientific network at an interdisciplinary and international level, which is a great basis for future collaborations that are so important for efficient disease prevention and control. I believe the fellowship provided me with the skills necessary to approach solutions towards national and international public health problems in a proficient way. I hope to successfully apply these skills in the future to help protect and improve people's health.

Acknowledgements of the fellow

Foremost, I would like to thank my supervisor at PHE, Androulla Efstratiou, for her excellent supervision, her continuous support and encouragement throughout those two years. She always found the right balance between guiding me towards the fellowship's objectives and giving me the freedom to pursue my own ideas. Special thanks go to all my project supervisors on site that gave me the opportunity to work on all these interesting and challenging projects and to all their staff who continuously supported me on a day-to-day basis.

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