

The main title 'Summary of work activities' in a bold, white, sans-serif font, set against a blue background.The author's name 'Theresa Enkirch' in a white, sans-serif font, set against a blue background.The subtitle 'European Public Health Microbiology Training Programme (EUPHEM), 2016 cohort' in a white, sans-serif font, set against a blue background.The section header 'Background' in a bold, blue, sans-serif font.

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.

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 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'.

Moreover, Article 47 of the Lisbon Treaty states that 'Member States shall, within the framework of a joint programme, encourage the exchange of young workers. Therefore, ECDC initiated the two-year EUPHEM training programme in 2008. EUPHEM is closely linked to the European Programme for Intervention Epidemiology Training (EPIET). Both EUPHEM and EPIET are considered 'specialist pathways' of the two-year ECDC fellowship programme for applied disease prevention and control.

This report summarises the work activities undertaken by Theresa Enkirch, cohort 2016 of the European Public Health Microbiology Training Programme (EUPHEM) at the Public Health Agency of Sweden.

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.

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Pre-fellowship short biography

Theresa graduated from the University in Heidelberg (Germany) as biologist in 2007. She continued her education in Heidelberg with a PhD in virology studying the use of lentiviral vectors for gene therapy and the envelope proteins of paramyxoviruses. She then undertook two postdoctoral positions, one at the Paul-Ehrlich-Institute (Federal Institute for Vaccines and Biomedicines) in Langen, Germany and one at Duke-NUS Medical School in Singapore. During her postdoctoral positions, Theresa mainly worked on respiratory viruses, their characterisation and respective novel treatment approaches. In 2015, she worked in a mobile laboratory during the Ebola outbreak in Guinea which strengthened her wish to pursue a career in the public health sector. She undertook the EUPHEM programme in order to develop competencies in public health microbiology and gain first experiences in epidemiology.

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 projects or activities (on-job services) 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

Outbreak of EIEC gastroenteritis at a hotel and conference venue in Halland, Sweden, 2017

Supervisors: Adam Roth, Cecilia Jernberg

On 13 and 14 November 2017, the Environmental Health Unit of Falkenberg and the Communicable Disease Control Unit in Halland County, Sweden, received phone calls from three individuals who had visited a hotel and conference venue during 8 to 10 November, all of whom displayed symptoms of gastroenteritis. An outbreak investigation team was established with members from the Public Health Agency of Sweden, the Environmental Health Unit of Falkenberg, the Communicable Disease Control Unit in Halland County, and the Swedish National Food Agency. To investigate the extent of the outbreak and to identify the source, a questionnaire was sent out to all individuals that had visited the conference centre during the period 8 to 10 November 2017.

Stool samples collected from three cases were tested positive for *Shigella*/enteroinvasive *E.coli* (EIEC) at the local clinical laboratories and further analysis using whole genome sequencing (WGS) performed at the Public Health Agency of Sweden confirmed EIEC as the etiological agent in this outbreak.

83 cases were identified using the questionnaire, all of whom had experienced gastrointestinal illness after visiting the venue. The epidemiological investigations suggested contaminated leafy greens to be the transmission vehicle. The public health response to this outbreak involved communication with the public and government sectors, contact tracing of cases and will lead to further studies on differentiation between EIEC and *Shigella* sp. within the National Reference laboratory (NRL) network.

The fellow was part of the team that analysed the results from the cohort study, wrote the outbreak investigation report and also contributed to the communication with other authorities, the hotel and conference venue. Furthermore, she co-authored a manuscript reporting on this outbreak and the problematic of laboratory differentiation between EIEC and *Shigella* sp.

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2017. Available from: <http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf>

An ongoing hepatitis A outbreak linked to frozen strawberries identified through sequencing, Sweden, June 2018

Supervisors: Josefine Lundberg Ederth, Lena Sundqvist

In beginning of June 2018, five cases of hepatitis A virus (HAV) infections were notified in county 1 in Sweden. All cases reported to have consumed smoothies containing strawberries. Several days later, the numbers increases to nine cases in county 1. Additionally, single cases were reported from three more counties (county 2, 3, and 4). In County 2, two residents of the same elderly home were diagnosed with HAV infections. Molecular characterization was carried out by sequencing the HAV VP1/2A genome region, comparison with reference strains and phylogenetic analysis. Sequencing demonstrated that all cases had an identical HAV genotype IB strain, suggesting a common source. As of 28 June 2018, the outbreak comprises 12 cases, ten confirmed and two probable. Epidemiological investigations including telephone interviews and a standard questionnaire distributed to five individuals showed that all cases had consumed strawberries in the 30 days before disease onset. No other food-item except for strawberries was reported as consumed in high frequencies among cases.

The identified HAV genotype IB strain has not been reported so far. The most closely related sequences (98% similarity) were involved in a HAV outbreak related to travelers returning from Egypt in 2013 and from the HAV outbreak affecting the Nordic countries in October 2012 to June 2013 which was caused by frozen berries.

The Environmental Health Office and the Swedish Food Agency traced the strawberries back to producer X residing in Poland. Left over strawberries from the elderly home were sent in to the National Food Agency for sequencing in close collaboration with the Swedish Public Health Agency. The presence of the HAV IB outbreak strain in the strawberries was confirmed and the respective batch was withdrawn from the market. Other control measures included HAV testing of staff and contact persons, preventive vaccination and immunoglobulin treatment.

This report highlights the importance of fast collaborations between different agencies and sequencing of HAV samples. Without the sequence information, the single cases in counties 2, 3 and 4 wouldn't have been linked to the cluster of cases in county 1. Furthermore, sequencing confirmed frozen strawberries as the source of this outbreak.

The fellow was involved in all steps of the outbreak investigation, from the identification of the outbreak through sequencing, the first teleconference with the counties and different agencies, the descriptive data analysis and reporting. The fellow also sequenced the HAV outbreak samples and coordinated the sequencing from the strawberries with the Swedish Food Agency.

Training modules

During the EPIET/EUPHEM introductory course, participants were familiarised with the methods and logistical aspects of outbreak investigations. Additional, training during the 'Outbreak Investigation Module' taught essential data management skills (entering, validating and cleaning data), dataset management and how to perform case-control studies, descriptive and cohort studies, including stratified analyses in STATA. Likewise this module familiarized fellows with different tools for bioinformatics and phylogenetic analysis for outbreak investigations. Building on these courses, during the 'Multivariable analysis Module', fellows discussed the principles, application and interpretation of multivariable analysis (linear regression, conditional logistic regression, Poisson and cox regression) and its role in field epidemiology.

Educational outcome: To apply microbiological and epidemiological knowledge in outbreak situations; participation in a multidisciplinary outbreak team and involvement in outbreak investigations (case definition, case-finding, data collection, data analysis, laboratory typing methods, communication); dataset management; writing of report presentations and formulation of recommendations; scientific publication.

1.2. Surveillance

Improving preparedness to respond to cross-border hepatitis A outbreaks in the European Union/European Economic Area: towards comparable sequencing of hepatitis A virus

Supervisors: Ettore Severi, Katrin Leitmeyer

Sequence-based typing of hepatitis A virus (HAV) is an important tool for outbreak detection, investigation and surveillance. In 2013, a large EU-wide outbreak related to frozen berries was detected and sequencing was of central importance in the outbreak investigation. However, as the sequenced HAV genome regions were only partly comparable between countries, results were not always conclusive. In 2014, the European Centre for Disease Prevention and Control (ECDC) distributed an on-line survey on HAV sequencing and related surveillance practices in EU/EEA countries in order to assess the variation in sequencing procedures. The survey results were used as a basis for an expert consultation to conclude on harmonized procedures for effective response to cross-border

outbreaks. In 2016, a follow-up survey was performed to assess the uptake and use of the recommended sequencing protocol.

The response rates were 74% (23/31) and 87% (27/31) in 2014 and 2016, respectively. The number of countries with central collection and storage of HAV positive samples subjected to sequencing increased from 11 in 2014 to 15 in 2016, and 17 countries performed sequencing in 2016, two more than in 2014 (n=15). Variation still existed in laboratories sequencing practices and amplicon length.

Analysis of both surveys demonstrates that many EU/EEA countries have a good capacity for sequence-based typing of HAV but variation still existed in sequencing methods and amplicon length. To fully utilize sequencing techniques for strengthening preparedness and accelerating public health responses in Europe, comparability of sequencing practices across all sectors need improvement.

The fellow analysed and validated the data, and drafted the manuscript which was submitted to Eurosurveillance, 19th July 2018. The work will be presented at ESCAIDE 2018 (poster presentation).

Characteristics of *C. difficile* in community-associated (CA) or healthcare-associated (HA) infections in Jönköping County, Sweden

Supervisors: Kristina Rizzardi, Thomas Åkerlund

Clostridium difficile (*C. difficile*) is one of the most common causes of nosocomial diarrhoea worldwide with associated substantial morbidity and mortality. During recent years, *C. difficile* infections (CDI) have emerged as an increasingly important infectious disease. Common reservoirs for this pathogen are hospitalized patients or patients with a history of antibiotic exposure, contaminated hospitals or other healthcare facilities. However, community-associated infections have also been described (approximately 28 % of CDI cases) and CDI have emerged in the community in populations previously considered low risk.

The aim of this project is to compare characteristics of *C. difficile* that are mainly associated with community-associated (CA), healthcare-associated (HA) and recurrent CDIs. Therefore, samples of CDI infections in Jönköping county, Sweden, and demographic data will be collected over a period of 6 months and analysed. Specific PCR ribotypes and/or antibiotic resistance profiles will be identified and the prevalence of different *C. difficile* types for CA, HA and recurrent CD infections will be compared. Whole genome sequencing (WGS) will be used to identify virulence genes and genetic markers involved in antimicrobial resistances in order to identify risk factors for CDI. Phylogenetic analysis will be performed in order to determine whether transmission between patients and healthcare settings has occurred (CA vs. HA).

The project is still ongoing and at this point, demographic data of the CDI patients were retrieved from the patient journals, all samples were ribotyped and the majority of the samples was analysed using WGS.

The project will show the dynamic nature of *C. difficile* prevalence in the population in Jönköping in order to implement respective public health measurements. These can be for example advising clinicians in the use of antibiotics or adapt hygiene measurements. Furthermore, the results of this study will strengthen knowledge building within the community in order to prevent CDIs.

The fellow was involved in developing the study, getting ethical approval, communication with Jönköping county, the data collection process, the analysis of the epidemiological and laboratory data and will draft a manuscript.

Evaluation of the laboratory-based surveillance of Rubella in Sweden

Supervisors: Hélène Englund

The elimination of Measles and Rubella in the European Region is a target formulated by the WHO Regional Committee for Europe and will also lead to elimination of congenital rubella syndrome (CRS). In Sweden, no endemic case of CRS has been reported since 1985, and endemic transmission ceased following the introduction and widespread implementation of a two-dose vaccination schedule in 1982. In 2017 the European Regional Verification Commission for Measles and Rubella Elimination declared that rubella had been eliminated in Sweden. However, the Commission had raised doubts concerning the quality of the rubella surveillance. Over 1700 Rubella tests were requested in Sweden in 2017 but the indication behind is unknown. Suspected cases are notifiable but usually not notified. The aim of this project is to evaluate the laboratory-based surveillance and more specifically to investigate the reasons for testing and quantify the number of suspected rubella cases by another method, in order to confirm the elimination of rubella in Sweden. The results will be used by the Public Health Agency of Sweden in their yearly report to the Scandinavian Verification committee, and might also lead to recommendations for further improvements to the relevant authorities and laboratories.

A questionnaire about diagnostic procedures and reasons for rubella testing will be distributed to the laboratories. Clinical suspicions of Rubella among the requests for Rubella testing sent to the laboratories will be identified and rubella laboratory capacities in Sweden mapped.

A pilot study was initiated and a questionnaire was sent to one of the biggest laboratories in Sweden. The laboratory reported to receive mostly electronic requests on which the general practitioners (GPs) choose between Rubella IgG only or IgG and IgM combined. The request form also contains the option for pregnancy/fertility screening which includes Rubella diagnostics (for immunity, IgG). Around 50 % of the received request forms contain clinical information which is mostly not used by the laboratory to decide on the diagnostic test to perform. Usually, the laboratory only performs the test specifically ordered by the GP. In the rare cases when the GP lets the laboratory decide about the diagnostics based on the clinical information, the laboratory performs rubella, morbilli- and parvovirus tests and follows a SOP describing how to decide on testing for rubella IgG only or IgG and IgM. This pilot study gave an insight into the work flow of a laboratory performing rubella diagnostics but does not allow to draw conclusions concerning the aim of the study. More information is needed and the questions of the survey need to be more specified.

This is an ongoing study together with the EPIET fellow Fanny Chereau. The fellow was involved in drafting the study protocol and formulating the questions for the survey of the pilot study.

Training modules

During the EPIET/EUPHEM introductory course, participants were familiarised with the the different types of surveillance systems, the attributes of a surveillance system and the development of questionnaires and surveys. Additional, training during the 'Outbreak Investigation Module' taught essential data management skills (entering, validating and cleaning data), dataset management and how to perform descriptive studies. Besides, fellows were familiarized with different tools for bioinformatics and phylogenetic analysis for outbreak investigations. These skills were equally useful and relevant for the analysis of surveillance data.

Educational outcome: Design and implement a survey to assess surveillance practices (questionnaire design, pilot survey, data analysis), public health management and communication, analysis of surveillance data (epidemiological and microbiological information), phylogenetic analyses to inform on pathogens circulating, writing of reports, scientific publications and presentations at conferences.

2. Applied public health microbiology research

Characterization of shiga toxin-producing Escherichia coli isolates found in human samples leading to haemolytic uremic syndrome in Sweden, 2010-2017

Supervisors: Cecilia Jernberg, Ingela Hedenström, Catarina Flink

Shiga-toxin-producing *Escherichia coli* (STEC) can lead to intestinal infections of varying severity in humans, including life-threatening haemolytic uremic syndrome (HUS). The ability to cause outbreaks with high disease burden make STEC an important target for surveillance and infection control. In order to characterize STEC infections leading to HUS in Sweden, we identified risk factors associated with HUS development compared to non-HUS cases.

We described serogroups, virulence profiles, and demographic characteristics of STEC isolates submitted to the Public Health Agency of Sweden between 2010-2017 (n=2210). We compared these variables between HUS (n=70) and non-HUS (n=2140) cases and calculated univariate and adjusted odds ratios (OR) with 95% confidence intervals (CI) using logistic regression modelling.

Numbers of STEC isolates increased from 170 in 2010 to 267 in 2017, most frequent serogroups in HUS patients were O157 (38.6%), O26 and O121 (15.7% each). The majority of HUS cases was <5 years old (52.9%), had domestically-acquired infections (82.9%) and yielded STEC with *stx2* (75.2%) and *eae* (87.1%). Multivariate analysis demonstrated that age <5 years (OR=4.3; 95% CI: 1.7-10.7), domestically-acquired infection (OR=2.7; 95% CI: 1.2-5.9), *stx2* (OR=3.5; 95% CI: 1.4-8.6) and *eae* (OR=3.4; 95% CI: 1.0-11.1) were independently associated with an increased risk of HUS development. Although O157 (OR=3.3; 95% CI: 1.8-5.8) and O121 (OR=7.5; 95% CI: 3.5-16.2) were associated in the univariate analysis, they were not independent risk factors.

Our study identified HUS risk factors in concordance with other European countries. However, while serogroup O157 is predominantly HUS-associated in Europe, the majority of Swedish HUS cases were caused by non-O157 types. We recommend further analysis including other virulence genes to optimize the molecular risk assessment for HUS development.

The fellow wrote the study protocol, analysed the data, drafted the manuscript and gave an oral presentation about this work at the Public Health Agency of Sweden during a work and progress meeting.

Serogroups and virulence factors in STEC isolates found in food items and human samples in Sweden, 2010-2017

Supervisors: Cecilia Jernberg, Ingela Hedenström, Catarina Flink

Shiga-toxin producing *Escherichia coli* (STEC) are serious foodborne pathogens with cattle being the main reservoir. Therefore, meat and milk products pose a risk for human infections. The aim of our study was to characterize STEC strains from beef and in-line milk filters and compare them to human isolates. The results will provide insights into the risk associated with consumption of beef and raw milk products in Sweden.

STEC isolates from beef (28) and in-line milk filters (36) from Swedish dairy farms collected by the Swedish Food Agency (2010/11, 2015) were analysed through whole genome sequencing (WGS) and compared to human isolates (2210) submitted to the Swedish Public Health Agency 2010-2017. Serogroups and virulence genes (*stx1*, *stx2*, *eae*) were identified and analysis of single nucleotide polymorphisms (SNP) was performed on WGS results.

Twenty-three serogroups were detected from beef and milk filters, 18 of those were also identified in humans. Most prevalent serogroups were O145 and O26 (7.8% each), which were also common in humans (4.2% and 19.4%). *stx1* prevalence was similar in milk filter (47.4%) and human isolates (43.3%), *stx2* only (59.1%) or together with *stx1* (36.4%) dominated in beef isolates (35.1% and 18.5% in humans). *eae* distribution differed between milk filter (41.7%), beef (17.9%) and human isolates (71.5%). One milk filter isolate (2015) was related to four human cases in 2017 (32 SNPs difference) but no epidemiological link was found.

The isolate categories share several serogroups but vary in virulence gene distribution. No genotyping link between samples was detected, concluding that our food isolates were not associated with human infections. Nevertheless, further monitoring is needed for risk assessment of human infections coming from food-associated strains.

The fellow wrote the study protocol, analysed the data, drafted the manuscript and will present this work at ESCAIDE 2018 (poster presentation).

Training modules

During the EPIET/EUPHEM introductory course, participants were trained in writing a study protocol and discussing study designs, including exercises on scientific writing. Furthermore, the 'Outbreak Investigation Module' together with the 'Multivariable analysis Module' taught essential data management skills (entering, validating and cleaning data), dataset management and how to perform uni- and multivariable analysis. Additional, fellows were familiarized with different tools for bioinformatics and phylogenetic analysis. During the 'Initial Management in Public Health Microbiology Module', participants were trained in time and person management and communication, which are important aspects in research activities.

Educational outcome: Preparation of a study protocol, adherence to ethical principles, gaining expertise in data analysis with STATA, data mapping, analysis of ribotyping, whole genome sequencing data and phylogenetic analyses, communication with different parties, presentations at conferences and writing scientific publications.

3. Applied public health microbiology and laboratory investigations

Epidemiology and diagnostics of schistosomiasis in travellers in Sweden – can we improve advice on travel risks and diagnostics?

Supervisors: Tore Lier, Charlotta Rydgård

Schistosomiasis, also known as bilharzia, is one of the most important neglected tropical diseases, affecting more than 240 million people worldwide and being endemic mostly in sub-Saharan Africa. In Sweden, individuals who are diagnosed with schistosomiasis are travellers or migrants from endemic countries. As tourism to endemic countries has risen during the last decades more people have been exposed to the parasite through fresh water contact during recreational activities. In Sweden, a large number of serologically positive cases were reported to Public Health Agency of Sweden (PHAS) in 2015. At Karolinska hospital the diagnosis of schistosomiasis in returning travellers is done using microscopy to detect eggs in faeces and urine samples. In addition, samples are sent to PHAS for confirmation of diagnosis using serological methods like immunofluorescence and ELISA. Patients with positive serology will be diagnosed as infected. The aim of this study was to assess the epidemiological and clinical characteristics in patients with suspected schistosomiasis in Sweden, 2012-2016, and to draw conclusions on improving diagnostics. Since microscopy is known to be less sensitive than serology, the results of this study will aid in evaluating the need of microscopy as routine diagnostics for schistosomiasis.

Patient data were retrieved from PHAS and the clinical journals of Karolinska hospital after ethical approval. So far, data from 213/393 individuals between 2012 and 2014 were collected. A preliminary analysis showed that 18-39 year old individuals were mainly affected (50.7 %), most of them were exposed to the parasite in Sub-Saharan Africa (61.5%). Of the 213 individuals, 31.0 % were migrants born in an endemic country whereas 54.6% were Swedish travellers or migrants from non-endemic countries and 23.5% were confirmed to have schistosomiasis.

This is the first time that information on the epidemiology of schistosomiasis in travellers in Sweden is provided. To draw conclusions on the need of microscopy for diagnostics, more data are needed. Since tourism to endemic countries is increasing and many travelers are accepting the risk to acquire schistosomiasis, the disease and its diagnostic deserves more attention.

The fellow became familiar with the laboratory workflow of schistosomiasis diagnostics and travel-related epidemiology of schistosome infections in Sweden. She contributed to the ethical approval, the study protocol and collected the data from PHAS and several of the patient journals and did a preliminary analysis. Due to the large numbers of patients and variables collected and the high amount of time that is needed to go through the patient journals, the study could not be finished and will be continued as a joint project with the local MS track EUPHEM fellow Nina Lagerqvist.

Whole genome sequencing of Hepatitis B virus to support outbreak investigations

Supervisors: Tatjana Tallo, Mia Brytting

Molecular surveillance of acute Hepatitis B conducted at the Public Health Agency of Sweden (PHAS) is currently performed using Sanger sequencing of the Hepatitis B virus (HBV) S gene, which is relatively conserved within genotypes. Since 2013, numbers of HBV cases in Sweden increased and sequencing revealed two ongoing outbreaks. Transmission routes were unknown and no link between cases could be determined. Since whole genome sequencing (WGS) data allow better differentiation between strains, the aim of this study is to investigate the current outbreaks through establishing WGS of HBV in order to provide information for transmission events.

Despite its small genome size of ~3.2 kb, HBV presents several challenges to establish WGS like the circular genome, its high secondary structure and its sequence variability. Primers were designed to amplify whole HBV genomes of different genotypes and a WGS protocol (IonTorrent) was established. A subset of patient samples from the two outbreaks (10/129) submitted to PHAS between 2013 and 2016 was chosen according to year, geographic distribution and genotype. Samples were sequenced and phylogenetic tree topology was compared between S gene sequences (Sanger) and WGS.

Sequence analysis revealed differences in outbreak strains between Sanger and WGS. The S gene is much conserved but one sample showed 36 SNPs detected with WGS outside the S gene region. Phylogenetic analysis of the samples using S gene sequences (~1170 bp) or WGS (~3200 bp) revealed differences in tree topology.

The WGS data provide more detailed sequence information and the differences in tree topology suggest more than two outbreaks. The results allow prioritization of targets for HBV infection control such as contact tracing and risk group vaccination. To investigate exact numbers of outbreaks, WGS should be applied to all acute HBV samples. Since the results demonstrated an added value to outbreak investigations, the WGS protocol will be adapted to use it routinely.

The fellow was responsible for designing the primers, analyzing the WGS data and creating phylogenetic trees. The project was presented during the Nordic Mini Project review module in Helsinki, 2017, and during the Microbiology forum at the Public Health Agency of Sweden, 15.09.2017.

Evaluation of whole genome sequencing for drug susceptibility testing of Mycobacterium tuberculosis, Sweden, 2016/17

Supervisors: Mikael Mansjö, Jim Werngren

Mycobacterium tuberculosis one of the most common cause of death from an infectious agent in the world and the emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant (XDR-TB) strains is of major concern. The gold standard to test drug susceptibility of TB strains are culture-based assays which are sensitive but due to the slow growth of Mycobacteria, very time consuming. Whole genome sequencing might replace phenotypic drug susceptibility testing (DST) in the future due to its faster turnaround time and it's becoming more affordable. The aim of this project is to compare whole genome sequencing (WGS) data of *Mycobacterium tuberculosis* with phenotypic drug susceptibility testing (DST) for the implementation of routinely applied WGS for the prediction of drug resistances of tuberculosis (TB) infections in Sweden. The two objectives are to describe mutations found in TB isolates in Sweden and to compare the WGS data with phenotypic DST to predict the resistance phenotype from the genetic sequence.

Isolates (n=877) sent to the Public Health Agency of Sweden between 2016 and 2017 were characterised phenotypically (Mycobacteria Growth Indicator Tube, MGIT) and genotypically (WGS) for first-line drug

susceptibilities. WGS data were analysed using a tool developed in house. Sensitivity and specificity and positive/negative predictive values of genotypic compared with phenotypic drug susceptibility were calculated. The sensitivity of the in-house tool to analyse WGS data to predict any resistance among strains against first-line drugs ranged from 97.3 % to 99.9 %, depending on the respective resistance mutation, and was very similar amongst individual drugs. The specificity was between 92.9 % (Ethambutol) and 100.0 % (Rifampicin).

The results of this study will support the introduction of WGS into routine diagnostics which then would replace phenotypic typing of isolates to predict resistance against common TB drugs. Molecular determination of resistance offers a rapid, potentially cost effective, and safer alternative.

The fellow was introduced to the BSL3- laboratory to work with *Mycobacteria tuberculosis* and learned the different techniques to test the drug susceptibility of TB strains. She did the data analysis and evaluated the relevance of the WGS approach as a diagnostic tool.

Training modules

During the 'Outbreak Investigation Module', fellows were familiarized with essential data management skills (entering, validating and cleaning data), dataset management and how to perform descriptive studies. Likewise this module familiarized fellows with different tools for bioinformatics and phylogenetic analysis for outbreak investigations. These skills were equally useful and relevant for the analysis of surveillance and laboratory data for both the schistosomiasis, the hepatitis B and the tuberculosis project. Additional, training during the 'Biorisk and Quality Management Module' taught essential quality management practices which were applied when the fellow undertook laboratory investigations.

Educational outcome: Application of virology, bacteriology, and immunology concepts to the discipline of public health discipline; understanding the use and limitations of diagnostic and typing methods and their interpretation; developing expertise in analysis of next generation sequencing data and microbiome analysis; development and assessment of laboratory methods to improve surveillance and diagnostics procedures.

4. Biorisk management

*Drug susceptibility testing of *Mycobacterium tuberculosis**

Supervisors: Juan Carlos Toro, Jim Werngren

The fellow undertook an activity in the BSL3 laboratory dedicated to Mycobacteria. The aim of this activity was to become acquainted with laboratory practices and protocols associated with work undertaken in a level 3 containment facility. The fellow was introduced to the laboratory workflow for the growth and characterization of mycobacteria and the different methods of antimicrobial susceptibility testing (MGIT, microtiter plates).

Characterisation of STEC isolates

Supervisor: Ingela Hedenström

The fellow undertook an activity in the BSL3 laboratory as part of the two STEC projects (see "Surveillance" section). The aim of this activity was to become acquainted with laboratory practices and protocols associated with bacteria work undertaken in a level 3 containment facility. The fellow was introduced to the laboratory workflow for the growth and identification of STEC. She grew STEC isolates, extracted DNA from bacterial cultures, run qPCR and performed library preparation in order to sequence the whole genome of STEC and identify virulence genes present.

Training modules

During the 'Biorisk and Quality Management Module', fellows were introduced to quality management practices and trained in performing risk assessment and proposing mitigation measures. Fellows used an assessment tool to assess process management, quality control and documentation available. Fellows were also introduced to procedures for laboratory accreditation and certification. During this module, fellows also received training in international regulations and good practices for biological specimen shipment and obtained the WHO certificate for International Transport of Infectious Substances. The module included a visit to the Biosafety Level 4 Laboratory of the Public Health Agency of Sweden. During this visit, fellows were able to observe the rooms, equipment and discuss practices of the level 4 laboratory.

Educational outcome: Understanding and gaining experience with the processes associated with biosafety in the laboratory at different levels (BSL2/BSL3/BSL4), biorisk management, and international biosafety regulations. Understanding of the aspects to consider for improving laboratory preparedness against emerging and re-emerging pathogens.

5. Quality management

External quality assessment (EQA) for the molecular diagnostic of Influenza viruses

Supervisor: Mia Brytting, Elin Arvesen

Every year, an external quality assessment (EQA) for the molecular detection and characterization of currently circulating influenza viruses is performed for the diagnostic laboratories in Sweden. Participating laboratories receive a panel of temporally representative influenza specimens, which they identify and subtype using methods of their choice. The fellow reviewed the selection process of influenza specimens included in the EQA panel together with her supervisor, performed the respective laboratory work and was part of the evaluation and reporting of results obtained from the 2017 influenza panel. A total of 19 diagnostic laboratories participated to this EQA. 68 % of the laboratories performed to high standard and the laboratories who had a different outcome had all missed the same weak sample positive for influenza A. All laboratories performing subtyping of influenza viruses determined the subtypes of the panel samples correctly. No participating laboratory submitted false positive results. In conclusion, the results of this panel indicate that laboratories in Sweden are prepared for the coming flu season.

External quality assessment (EQA) for the molecular diagnostic of Hepatitis A virus

Supervisor: Josefine Lundberg Ederth, Tatjana Tallo

An external quality assessment for the molecular detection and characterization of hepatitis A virus is performed annually in Sweden. The aim is to evaluate the ability of laboratories in the molecular detection of Hepatitis A Virus (HAV) in terms of sensitivity and specificity. Participating laboratories receive a panel of ten circulating hepatitis A virus strains which they identify and subtype using methods of their choice. The fellow performed the respective laboratory work (sample preparation and typing) and was part of the evaluation and reporting of results obtained from the 2018 hepatitis A virus panel. The results of the EQA demonstrated that the Public Health Agency of Sweden typed all samples correctly and is able to detect even low viral loads of HAV in human serum.

Internal audit/revision of Enterovirus genotyping

The fellow joined an internal audit/revision of the Enterovirus genotyping at the Public Health Agency of Sweden. The audit/revision was focused on processes management and quality control in the laboratory, as well as the documentation available to describe procedures and show practices (eg. equipment management). A feedback meeting with staff from the laboratory was organised to discuss the findings from this audit.

Training modules

During the 'Biorisk and Quality Management Module', fellows were introduced to quality management practices and trained in performing risk assessment and proposing mitigation measures. Fellows used an assessment tool to assess process management, quality control and documentation available. Fellows were also introduced to procedures for laboratory accreditation and certification. During this module, fellows also received training in international regulations and good practices for biological specimen shipment.

Educational outcome: Understanding and applying the principles and practices of quality assurance, administering, analysing and reporting the results of an external quality assurance scheme, understanding accreditation procedures, understand the role and missions of a WHO reference laboratory.

6. Teaching and pedagogy

Introduction to Infectious Diseases Epidemiology and Surveillance

Supervisor: Moa Rehn, Viktor Dahl

This was a 2-day course organised for "Infectious disease epidemiology" students from Södertörn Högskola. The course was co-organised by the Public Health Agency of Sweden (PHAS) with the support of facilitators from the Epidemiology department of Södertörn Högskola. Lectures and case studies were prepared and delivered by fellows. In particular, the fellow modified and facilitated a case study on outbreak investigation together with the EPIET fellow Fanny Chereau. Furthermore, the fellow delivered a lecture on Microbiology and Surveillance including a short exercise about the analysis of next generation sequencing (NGS) data. Following the lecture, the fellow guided a tour through the laboratories at PHAS and the NGS facility. The fellows were also responsible for evaluating the course.

Facilitation of a case study for students at the Swedish University of Agricultural Sciences, Uppsala

Supervisors: Nils Fall, Uppsala

The fellow was responsible for facilitating a case study for students at the Faculty of Veterinary Medicine and Animal Science, Swedish University of Agricultural Sciences, Uppsala as part of the course "Veterinary public health with applied epidemiology and epizootiology". The case study aimed at training the students in conducting an outbreak investigation and performing analytical steps. Therefore, the fellow led the students through the ten steps of an outbreak investigation. The case study was based on an investigation of an outbreak of Trichinosis in France.

Lecture on the immunological basis of vaccines and immunisation

Supervisors: Chris Williams

The fellow was responsible for giving a lecture on the Immunological basis of vaccines and immunisation during the Vaccinology module for EPIET fellows. The fellow adapted the lecture slides prepared by former fellows and added an additional exercise on interpreting laboratory results of hepatitis B virus infections and vaccination. The fellow was assisted by the former EPIET facilitator Chris Williams.

Educational outcome: Planning and organising a course for public health/epidemiology students, re-structuring and adapting a case study, defining learning objectives, preparing lecture and case study material and exercises, delivering lectures and facilitating group work around case studies, assessing a course.

7. Public health microbiology management

Primary diphtheria immunisation for adults using a low dose vaccine: a literature review

Supervisor: Adam Roth, Tiia Lepp, Ann Lindstrand

In Sweden, high-dose diphtheria and tetanus vaccine (DT) is used for primary vaccination of children and until recently also for adults. Due to recent vaccine shortages and increasing adverse reactions against DT with age, a low dose (LD) diphtheria and tetanus vaccine (dT) was used for individuals ≥ 7 years for primary vaccination. A systematic review of scientific literature was undertaken to identify studies providing evidence on whether three doses of reduced diphtheria toxoid induce sufficient immunity in unvaccinated adults previously not exposed to diphtheria.

PubMed, Cinahl and Scopus online articles published between 1921-10/2017 using key words of "adult" or "elderly" and "diphtheria" or "diphtheria toxoid", combined with "immunisation" or "vaccination" or "vaccine" were evaluated. Additionally, references of identified articles were screened. Main inclusion criteria were immunity status (seronegative: unvaccinated and no previous diphtheria exposure), age (≥ 7 years) and vaccine dose (≤ 7.5 Lf, minimum of two doses). Identified articles were graded based on evidence and included in a qualitative synthesis.

3289 records were identified and screened based on titles, resulting in the exclusion of 3064 articles. 147 more articles were excluded after abstract reading. Full-text of 78 articles was evaluated and 15 relevant records included

in a qualitative synthesis. Seven studies met the inclusion criteria (total population n=517) demonstrated seroprotection rates between 62.5-100% after three doses of 1.5-7.5 Lf each. The limited record number was mainly due to the difficulty of identifying studies including unvaccinated seronegative individuals. Studies about the immunogenicity of reduced diphtheria toxoid for primary vaccination of adults were scarce and with heterogeneity in design. Although findings should be interpreted with caution, they may help guide policy making in Sweden.

Fellowship's projects and activities

As part of the projects conducted during the fellowship the fellow performed public health microbiology management by having to communicate with different public health actors (Swedish National Food Agency, Karolinska hospital, ECDC, etc.). The fellow also participated in different management and communication exercises, applying principles of scientific communication to peers, stakeholders, media/public and engaging in and experience a debate with the higher authorities. Furthermore, the fellow had to communicate public health relevant findings from her work at different conferences and different working groups within the Swedish Public Health Agency (PHAS). The fellow participated in several outbreak investigation meetings and in order to manage the outbreaks she was involved in, she had to re-structure and adapt her working schedule to re-set priorities. In addition, she joined the round table meetings at PHAS where the Swedish surveillance data were discussed on a weekly basis. The fellow was also involved in several co-projects with other EUPHEM or EPIET fellows at PHAS.

Training modules

During the 'Management, Leadership and Communication in Public Health Module', fellows practiced communication (e.g. giving and receiving feedback) and discussed management styles, time management and leadership through multiple individual and group activities and exercises.

Educational outcome: Gaining experience in team and project management, planning and managing research and surveillance projects, respecting ethical principles regarding data protection and confidentiality, communication with different public health actors and the scientific community.

8. Communication

Publications

1. **T. Enkirch**, E. Severi, H. Vennema, L. Thornton, J. Dean, ML Borg, AR Ciccaglione, R. Bruni, I. Christova, SL Ngui, K. Balogun, V. Němeček, M. Kontio, M. Takács, A. Hettmann, R. Korotinska, A. Löve, A. Avellón, M. Muñoz-Chimeno, R. de Sousa, D. Janta, J. Epštein, S. Klamer, S.W. Aberle, H. Holzmann, K. Mellou, J. Lundberg Ederth, L. Sundqvist, A.M. Roque-Afonso, S. Kurečić Filipović, M. Poljak, L. Vold, K. Stene-Johansen, S. Midgley, T. Kølsten Fischer, M. Faber, J.J. Wenzel, J. Takkinen, K. Leitmeyer. Improving preparedness to respond to cross-border hepatitis A outbreaks in the European Union/European Economic Area: towards comparable sequencing of hepatitis A virus. (*submitted to Eurosurveillance, July 2018*)
2. **T. Enkirch**, T. Lepp, AL. Johansson, K. Zakikhany, A. Lindstrand, A. Roth. Primary diphtheria immunisation for adults using a low dose vaccine: a literature review (*manuscript in preparation*)
3. N. Lagerqvist, E. Löf, **T. Enkirch**, A. Roth, C. Jernberg. Outbreak of EIEC gastroenteritis at a hotel and conference venue in Halland, Sweden, 2017 (*manuscript in preparation*)
4. **T. Enkirch**, E. Löf, L. Sundqvist, J. Lundberg Ederth. An ongoing hepatitis A outbreak linked to frozen strawberries identified through sequencing, Sweden, June 2016 (*manuscript in preparation*)
5. **T. Enkirch**, I. Hedenström, C. Flink, C. Jernberg. Characterization of shiga toxin-producing Escherichia coli isolates found in human samples leading to haemolytic uremic syndrome in Sweden, 2010-2017 (*manuscript in preparation*)
6. **T. Enkirch**, I. Hedenström, C. Jernberg, C. Flink. Serogroups and virulence factors in STEC isolates found in food items and human samples in Sweden, 2010-2017 (*manuscript in preparation*)

Reports

1. **T. Enkirch**, M. Brytting. External quality assessment (EQA) for the molecular diagnostic of Influenza viruses (in Swedish). December 2017
2. N. Lagerqvist, E. Löf, **T. Enkirch**. Outbreak of EIEC gastroenteritis at a hotel and conference venue in Halland, Sweden, 2017. November 2017

Conference presentations

1. **T. Enkirch**, T. Lepp, AL. Johansson, K. Zakikhany, A. Lindstrand, A. Roth. Primary diphtheria immunisation for adults using a low dose vaccine: a literature review. Nordic Vaccine Meeting 2018, Helsinki, Finland. Poster presentation.
2. **T. Enkirch**, I. Hedenström, C. Jernberg, C. Flink. Serogroups and virulence factors in STEC isolates found in food items and human samples in Sweden, 2010-2017. ESCAIDE 2018, Malta. Accepted for poster presentation.
3. **T. Enkirch**, T. Lepp, AL. Johansson, K. Zakikhany, A. Lindstrand, A. Roth. Primary diphtheria immunisation for adults using a low dose vaccine: a literature review. ESCAIDE 2018, Malta. Poster presentation.
4. **T. Enkirch**, E. Severi, H. Vennema, L. Thornton, J. Dean, ML Borg, AR Ciccaglione, R. Bruni, I. Christova, SL Ngui, K. Balogun, V. Němeček, M. Kontio, M. Takács, A. Hettmann, R. Korotinska, A. Löve, A. Avellón, M. Muñoz-Chimeno, R. de Sousa, D. Janta, J. Epštein, S. Klamer, S.W. Aberle, H. Holzmann, K. Mellou, J. Lundberg Ederth, L. Sundqvist, A.M. Roque-Afonso, S. Kurečić Filipović, M. Poljak, L. Vold, K. Stene-Johansen, S. Midgley, T. Kølser Fischer, M. Faber, J.J. Wenzel, J. Takkinen, K. Leitmeyer. Improving preparedness to respond to cross-border hepatitis A outbreaks in the European Union/European Economic Area: towards comparable sequencing of hepatitis A virus. ESCAIDE 2018, Malta. Accepted for poster presentation.

Other presentations

1. 10 min presentation on Whole Genome Sequencing of Hepatitis B Virus to Support Molecular Epidemiology. EPIET-EUPHEM meeting (Public Health Agency of Sweden, 30.03.2017)
2. 1.5 h presentation and discussion on Whole Genome Sequencing of Hepatitis B Virus to Support Molecular Epidemiology. Nordic mini project review module (Helsinki, 04.04.2017)
3. 45 min presentation on the EPIET/EUPHEM program including an overview of the fellows' projects. Microbiology forum (Public Health Agency of Sweden, 15.09.2017)
4. 2 h presentation and discussion on Characterization of shiga toxin-producing Escherichia coli isolates found in human samples leading to haemolytic uremic syndrome in Sweden, 2010-2017. Joint meeting with collaborators from the Swedish Food Agency (Public Health Agency of Sweden, 07.12.2017)
5. Short presentation on "Feedback from ESCAIDE". Joint Meeting for Vaccine Groups (Public Health Agency of Sweden, 19.01.2018)
6. Short presentation on Whole Genome Sequencing in Surveillance and Outbreak Investigations, Sweden. Panel: Head of ECDC, chief microbiologist and chief scientist. Followed by 10 min questions. Presentation delivered jointly with EUPHEM fellow Nina Lagerqvist and EPIET fellows Fanny Chereau and Emma Löf. (ECDC, 16.02.2018)
7. 10 min presentation on Primary diphtheria immunisation for adults using a low dose vaccine. Joint Meeting for Vaccine Groups (Public Health Agency of Sweden, 20.04.2018)
8. 2 h presentation and discussion on serogroups and virulence factors in STEC isolates found in food items and human samples in Sweden, 2010-2017. Joint meeting with collaborators from the Swedish Food Agency (Public Health Agency of Sweden, 24.04.2018)
9. 1 h presentation and discussion on Primary diphtheria immunisation for adults using a low dose vaccine. Joint meeting of the diphtheria vaccine group. (Public Health Agency of Sweden, 30.05.2018)

Other

1. Situation simulation exercise conducted during Management, Leadership and Communication in Public Health module– preparation of a situation report and team management (scenario Plague outbreak in Madagascar) (15.02.2018)
2. Simulation exercise during Management, Leadership and Communication in Public Health module – 5 min presentation on crisis management communication. (15.02.2018)
3. Feedback on Internal audit/revision of Enterovirus genotyping, (April 2018)

Training modules

1. 3 min presentation to EUPHEM fellows and facilitators on public health importance of Influenza infections (Spetses, 07.10.2016)
2. 3 min presentation to EUPHEM fellows and facilitators on Gene Transfer in Bacteria (Spetses, 13.10.2016)
3. Modification of an existing case study with inclusion of new materials: Outbreak of gastrointestinal illness in Sweden. (Public Health Agency of Sweden, Dec. 2016)
4. 60 min lecture on Microbiology and Surveillance for "Infectious disease epidemiology" students from Södertörn Högskola (Stockholm, 20.12.2016)
5. 60 min lecture and exercise on the 'Immunological basis of vaccines and immunization'. Vaccinology module (Stockholm, 12.08.2017). Attendees: EPIET fellows.

9. EPIET/EUPHEM modules attended

1. Introductory Course, Spetses, Greece, 26th September-14th October 2016
2. Outbreak Investigation module, Berlin, Germany, 5th-9th December 2016
3. Multivariable Analyses module, Zagreb, Croatia, 13th - 17th March 2017
4. Rapid Assessment module, Athens, Greece, 08th - 13th May 2017
5. Vaccinology module, Stockholm, Sweden, 12th-16th August 2017
6. Project Review Module, Lisbon, Portugal, 28th August - 1st September 2017
7. Biorisk and Quality Management module, Stockholm, Sweden, 5th-9th February 2018
8. Management, Leadership and Communication in Public Health, Stockholm, Sweden, 12th - 16th February 2018
9. Project Review module, Lisbon, Portugal, 27th – 31st August 2018

10. Other training

1. Vaccinology Fun Massive Open Online Course (MOOC), Pasteur Institute, Dec 2016-Jan 2017.
2. Workshop on hepatitis & cancer vaccines and adjuvants, Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, 26th April 2017
3. Weekly EPIET-EUPHEM meetings. Weekly meetings organised by fellows and supervisors. These meetings offered the opportunity to fellows to discuss their progress, current projects and outbreak investigations and receive feedback and advice in an informal setting on both epidemiological and microbiological aspects of their projects.
4. EAN-MediPIET joint module on Refugee and Migrant Health, Athens, 14th-16th October 2017
5. Visit to the ECDC Epidemic Intelligence Unit, Stockholm, April 23rd-27th 2018. Insight into the office's activities.

Rapid assessment survey of health needs and living conditions in a refugee camp, Greece

Supervisors: Iro Evlampidou, Javiera Rebolledo (EAN members and module organizers)

As part of the EAN-MediPIET joint module on Refugee and Migrant Health in Athens, the fellow was able to contribute to a rapid assessment survey to assess health needs and living conditions in a refugee camp. The fellow was visiting the camp and was involved in filling the survey together with healthcare workers of the refugee camp. The results were discussed afterwards and the survey indicated an improvement in living conditions like access to basic hygiene materials in the camp compared to the previous year.

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 report summarises all activities and projects conducted by Theresa Enkirch during her two-year EUPHEM fellowship (cohort 2016) at the Swedish Public Health Agency, Stockholm, Sweden. Theresa is the second appointed EU track EUPHEM fellow in Stockholm. The portfolio includes laboratory and epidemiological projects covering viral, bacterial and parasitic pathogens across a variety of disease programmes, such as sexually-transmitted diseases, food and waterborne diseases, respiratory tract infections, vaccine-preventable disease and antimicrobial resistance. The projects here described are in line with the 'learning by doing' approach of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and beyond. 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 to detect *C. difficile* or STEC genotypes or antiviral resistant markers in *Mycobacterium tuberculosis*. Moreover, Theresa developed a new WGS protocol for hepB that will be used from now on in the national laboratory as a support for outbreak investigation. The fellow has had an active role in outbreak investigations at regional and national level (EIEC or hepA) and carried out surveillance investigations at national and international level (Rubella or hepA). The projects have been nicely selected to cover not only important international and national public health topics such as hepA, hepB, rubella, diphtheria, *C. difficile*, tuberculosis, STEC among others but also a very broad panel of microorganisms and 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 and to adapt to different environments and contexts. Theresa has been active in contributing to training of others during her fellowship with the development of new training materials as well as direct training and facilitation activities which highlights the contribution that fellows can make to capacity

building beyond the programme. All projects had a clear outcome, with results communicated in scientific journals and at conferences and the activities were complimented by nine training modules providing theoretical knowledge. The contributions made by Theresa indicate the importance of developing and maintaining a critical mass of highly skilled field public health microbiologists within Member States to contribute towards national preparedness as well as being available for responses in the interest of the EU. The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all her tasks to a very high standard and has conducted herself in a highly professional and effective manner throughout. We wish the fellow every success in her future career.

Supervisor's conclusions

The EUPHEM programme was a great opportunity for Theresa and has provided her with many tools to find her way in the field of public health microbiology and epidemiology. It has been a pleasure to mentor and supervise Theresa for the past two years and it has been interesting to see her develop and grow within the programme and the change from an academic focus to a public health perspective.

Theresa's work contributed in many ways to the agencies mission to strengthen and develop public health: e.g. sequencing of a unique Hepatitis A outbreak strains from strawberries and thereby contributing to public health actions regarding the handling of frozen berries; or performing a review on '*Primary diphtheria immunization for adults using a low dose vaccine*', a systematic literature review, which will contribute to policy making in Sweden; just to name a few. The projects she was involved in covered all areas within the scope of EUPHEM programme and showed that she was able to work on all these different projects independently; but also knowing when to ask for help if needed. Theresa works well as a member in a multidisciplinary team as well as the team-lead, which she has proven through being involved in different outbreak investigations from both the epidemiological and microbiological side. She has been collaborating with other agencies and hospitals which has broaden her public health management skills. Her scientific knowledge, technical and organizational skills have been appreciated by all supervisors and colleagues.

It was a great pleasure to have Theresa as a EUPHEM fellow within PHAS and we highly appreciate her contribution and achievements within the fellowship programme and the host institute. We wish Theresa every success for the future and her future career.

Personal conclusions of fellow

The EUPHEM programme provides an excellent opportunity to get insights into the different public health disciplines including the fields of epidemiology, virology, bacteriology and parasitology. Joining the programme had a strong impact on my professional life and gave it a new direction. It provided me with valuable skills for a future career in the public health field and I'm grateful that I had this opportunity. I highly enjoyed the experience to work in a multidisciplinary and international environment. One of the things I appreciated most was the learning by doing approach and the great variety of projects and opportunities across different fields of public health. I was fortunate to broaden my knowledge by working on excellent projects and to develop respective technical expertise. I enjoyed working with different agencies like the Swedish Food Agency and to collaborate with them not only during outbreak investigations. For me personally, I'm looking forward to apply what I learned towards the prevention and control of infectious diseases. Additionally, I am glad to have gained many friends and colleagues in the European region and wish to continue to contribute to this unique network of specialists to strengthen public health.

Acknowledgements of fellow

I would like to thank my EUPHEM supervisors Katherina Zakikhany and Mia Brytting from the Public Health Agency of Sweden for their excellent supervision, support and encouragement during the last two years. I highly appreciated their inputs, their open and constructive feedback and their way to make feel as part of the team from the very beginning. Special thanks go to all my project supervisors on site who gave me the opportunity to work on a variety of interesting and exciting projects, for their great supervision and confidence. Thanks to my project supervisors from the Swedish Food Agency, Karolinska Hospital, Jönköpings regional hospital (Länssjukhuset Ryhov) and ECDC for the valuable insights in their respective institutions and for great collaborations.

I would like to thank the whole team of coordinators and facilitators, for their excellent training activities, enthusiasm and patience and for a great learning atmosphere during the modules. In particular, my acknowledgements go to my frontline coordinators Aftab Jasir and Silvia Herrera-León for their guidance and support and for always challenging me in my role.

A big thank you to the amazing C2016 fellows, for the great company and fun times during the modules and beyond and who made these two years a fantastic experience. Last but not least, a big thank you to the other fellows on site, Fanny Chereau (EPIET C2016), and Nina Lagerqvist (EUPHEM) and Emma Löv (EPIET) from C2017, for their team spirit during joint projects and their friendship.