



Summary of work activities

Andreas Peter Hoefler

European Public Health Microbiology Training Programme (EUPHEM), 2019 cohort

Background

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 in 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 provides experts in all relevant communicable diseases at the regional, national and international level with the tools they need to mount rapid responses to emerging health threats. This enables them to plan appropriate prevention strategies, assess existing prevention disciplines, develop microbiological guidelines, evaluate/produce new diagnostic tools, assess 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' which is why 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 Andreas Hoefler, cohort 2019 of the European Public Health Microbiology Training Programme (EUPHEM) at the Centro Nacional de Microbiología, Instituto Carlos III in Madrid.

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The fellow, Andreas Peter Hofer, holds a bachelor's degree in Medical Microbiology and Virology as well as a master's degree in research in Medical Sciences from the University of Warwick Medical School. Following his master's, he relocated to Madrid, Spain where he completed his EU-funded Marie Curie PhD on antimicrobial resistance, specifically on elucidating the regulatory mechanisms underlying the expression of aminoglycoside resistance-conferring methylases. In addition to the training received as part of the Initial Training Network (ITN) TRAIN-ASAP, the fellow participated in several international capacity-building projects and collaborations, including an onsite training course in Ghana. His post-doctoral research was performed in the small island nation of St Kitts and Nevis, at the School of Veterinary Medicine, Ross University. His research topics there included the characterisation of the microbiomes of local animals as well as a molecular characterisation of MRSA isolated from local monkey populations.

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.

Methods

This report accompanies a portfolio demonstrating 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; bio-risk management; quality management; teaching and public health microbiology management and the summary and communication of 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, with the exception of those prohibited for reasons of confidentiality.

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

1.1.1 2020 SARS-CoV-2 Outbreak in a Hotel in Tenerife, Spain

Supervisors: Domingo Núñez Gallo, Silvia Herrera León, Laura Herrera León and Aftab Jasir

On 24 February 2020, a person travelling from an at-risk region in Italy presented to a hospital in Tenerife with symptoms of an acute respiratory infection that had started on 16 February, the day before arriving in Spain. This individual was then tested and confirmed to have contracted SARS-COV-2. Due to the prolonged exposure of this symptomatic index case to their travel group and other hotel guests, public health authorities quickly realised the potential threat and immediately placed the hotel under quarantine.

On 26 February, the organisational body responsible for coordinating public health emergency responses (Centro de Coordinación de Alertas y Emergencias Sanitarias, CCAES) in Spain received a request for help from the autonomous province of the Canary Islands to assist with the ongoing COVID-19 outbreak. This request was then forwarded to the fellow's host institution, the National Centre for Microbiology (CNM) of the Instituto Carlos III. On 28 February, the EUPHEM fellow and an EPIET fellow were urgently deployed to support the local public health authorities in Tenerife. The fellows worked directly under the supervision of the director of the local epidemiology and preventative medicine department, with the objective of supporting the mitigation and control of the ongoing outbreak by participating in contact tracing, data entry, and case interviews to help local staff deal with the increasing number of cases. In total, eight confirmed cases were associated with this outbreak. Due to the international nature of the guests, the timely precautions implemented are likely to have avoided a multinational cluster.

As part of this deployment, the fellows prepared a manuscript that was published in the International Journal of Infectious Diseases, in addition to an abstract presented at ESCAIDE 2020.

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>

Role: Participation in the epidemiological support of an outbreak; application of microbiological and epidemiological knowledge to investigate an outbreak; work alongside interdisciplinary local public health officials; field deployment; case interviews; publication of relevant findings in peer-reviewed journal; participation in the mitigation of a potential multi-national cluster; communication at ESCAIDE 2020.

1.1.2 COVID-19 Emergency diagnostic support

Supervisors: Silvia Herrera León and Laura Herrera León

On 7 January 2020, a novel coronavirus (Severe Acute Respiratory Syndrome coronavirus 2, SARS-CoV-2) was identified as the causative agent of coronavirus disease 2019 (COVID-19) causing severe and potentially fatal respiratory symptoms. Since the beginning of this outbreak the number of cases has been steadily increasing, affecting more than 80 countries as of early March 2020. On 5 March 2020, ECDC reported a total of 95 315 cases globally, including 3 282 fatalities, of which 200 cases were confirmed in Spain. As little was known about the prevalence of asymptomatic infections at the time, there was a detection bias towards severe cases in Europe, and it was believed that the actual number could be higher.

Early during the pandemic, the capacity for COVID-19 diagnostics was not wide-spread in Spain and the National Centre for Microbiology (CNM) was responsible for confirming all cases of COVID-19 and supporting centres of the National Health System with COVID-19 diagnostics. The purpose of the CNM providing emergency diagnostic support was to facilitate testing to all regions of Spain until the capacity of each centre could be established to perform their own diagnostics. Upon the request of the director of the CNM, the fellow was asked to participate in all stages of the diagnostic pathway, from receiving, unpacking, and registering samples to viral inactivation, RNA extraction, and RT-PCR processing. Over the course of the next two months a significant proportion of the tests performed in Spain were managed by the CNM. By May/June of 2020, hospital and regional public health laboratories were performing most of the COVID-19 diagnostic tests, which gradually reduced the necessity for COVID-19 diagnostics at the CNM.

Role: Participation in the laboratory support of an outbreak; application of microbiological knowledge to perform laboratory diagnostics; high-pressure and high-throughput laboratory diagnostic work; participation in pandemic mitigation.

1.1.3 2020 Spanish West Nile Virus outbreak

Supervisors: Ana Vázquez González

The index case of this West Nile Virus (WNV) outbreak, discovered via retrospective case finding, presented with symptoms on 12 June 2020. In total, 77 cases were identified in three different provinces of Spain: Sevilla (57 cases), Cadiz (14 cases), and Badajoz (six cases). The age of the cases ranged between four and 88 years, with an average age of 65 years. Of these cases, 93.5% presented neurological symptoms, of which 94.8% required hospitalisation. There were eight fatalities (six males and two females) aged between 59 and 87 years. Initially, the province of Sevilla reported five cases along with 15 suspected cases on 11 August 2020.

The EUPHEM fellow worked alongside the department of Arboviruses in the CNM, the Spanish reference laboratory, and the ECDC focal point. It was the fellow's responsibility to urgently screen pools of mosquitoes captured in the affected region around the time of the initial infection. Using in-house protocols, the pools of mosquitoes were homogenised, and the viral RNA was extracted after inactivation. The RNA extracts were then assessed for the presence of WNV via reverse-transcriptase real-time PCR (RT-RT-PCR) and conventional Rt-Nested-PCR. The results of this screening were then communicated to local authorities to coordinate vector-control strategies to mitigate the public health burden. The sequences obtained from the mosquito pools analysed in this work, showed that the virus detected was WNV lineage 1. The results of this investigation were presented at a national conference by the project supervisor with the fellow listed as an author. The results of this study have been accepted for a communication at a national conference. A peer-reviewed article outlining this outbreak will be published in the future.

Role: Participation in the laboratory support of an outbreak; application of microbiological and epidemiological knowledge to investigate an outbreak; communicate relevant findings to local public health authorities to mitigate public health burden of outbreak; understanding of high-pressure laboratory work within a team and alongside various local and national stakeholders.

1.1.4 Diphtheria outbreak diagnostic support

Supervisors: Laura Herrera León and Silvia Herrera León

Over the course of the fellowship, the fellow participated in the laboratory response of suspected diphtheria cases. This involved receiving the clinical samples, plating them on selective media, and identifying them using conventional PCRs and API strips. As the fellow was simultaneously working on the implementation of an RT-PCR capable of detecting and characterising relevant *Corynebacterium spp.* directly from clinical samples, this RT-PCR was also used in the laboratory support. Over the course of the fellowship, several suspected cases of diphtheria

were reported. If found to be toxigenic, contact tracing was performed and samples were taken from all close contacts. All contacts were negative for toxigenic diphtheria. Based on the condition of the patients and the requirements of the hospitals, these were frequently urgent lab responses conducted late in the evenings and weekends. All genotypically toxigenic strains were sent to the *Streptococcus* and Diphtheria Reference Unit for phenotypic toxigenicity testing in the UK.

Role: Participation in the laboratory support of an outbreak; application of microbiological and epidemiological knowledge to investigate an outbreak; communication of relevant findings to clinicians and National Epidemiological services; urgent laboratory diagnostics work within a team.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course – The basics of outbreak and epidemiological investigations were vital to the fellow's successful participation in the outbreaks listed above. In particular, the case studies and public health communication portions of the introduction course provided valuable insights on actively participating as part of the outbreak team.

Outbreak Investigation Module – The outbreak investigation module provided the technical skills required during high-pressure outbreak investigations with regards to high quality data collection, management, and analysis. The material learned during this module allowed the fellow to become a versatile member of the team who could confidently perform any task assigned.

Educational outcome

Over the course of the pandemic and the 2020 West Nile Virus outbreak, the fellow participated in a wide range of outbreak related competencies. Working alongside diverse stakeholders and local public health authorities from the initial characterisation to the dissemination of findings and recommendations, both from the epidemiological and laboratory side. The competencies acquired during these outbreak investigations covered all stages of an outbreak investigation and have provided the fellow the necessary skills to confidently participate in future outbreaks, both in the field and from the laboratory. Having participated in outbreak investigation during the COVID-19 pandemic provided additional experiences with regards to highpressure work on the containment of a little-known pathogen.

1.2. Surveillance

1.2.1 Phlebovirus and Flavivirus surveillance in Spain from 2016-2019 and molecular characterisation of the detected viruses

Supervisors: Ana Vázquez González

The WHO suggests that more than 60% of infectious diseases that affect humans have a zoonotic origin. In recent years it has been well documented that the distribution of these critical vectors is very strongly affected by climate change. Increased temperatures alongside mild winters have increased the dissemination of these vectors throughout the world. This, among other factors (e.g., globalisation, migration, and evolution of the microorganisms), poses a significant threat to public health. As such, it is of the utmost importance to public health to implement surveillance programs to carefully monitor and characterise the vectors captured within a country as well as the pathogens these vectors transmit.

Spain has a National Preparedness and Response Plan for Vector Transmitted Diseases, specifically for the *Aedes* vector in place for the monitoring of flaviviruses (dengue, chikungunya, and zika viruses) that are mostly mediated by the individual autonomous regions. The Arboviruses laboratory from the CNM, ISCIII, is working on a surveillance project to monitor and to study the flaviviruses and phleboviruses circulating in several areas of Spain via various research projects and participation in several networks. The fellow's responsibility as part of this surveillance project was to analyse and interpret the data obtained to determine the incidence of phlebo- and flaviviruses in the most affected regions of Spain. The surveillance system data acquired did not indicate a significant increase in arboviruses identified but the presence of arboviruses were detected in areas not detected previously. Based on the size of the 2020 WNV outbreak and international trends, a recommendation was made to consider a more active surveillance within at least the affected regions. In addition, the fellow and his supervisor have identified a need for an improved diagnostic RT-PCR to distinguish between phleboviruses that share portions of the genome that are the conventional targets for diagnostics. This RT-PCR shows a promising capacity to distinguish between previously indistinguishable viruses and will likely form a part of the future laboratory surveillance process.

Role: Participation in the laboratory support of a surveillance program; application of microbiological and epidemiological knowledge to analyse surveillance data; large-scale laboratory sample and data management design of improved laboratory surveillance techniques; presented full outbreak report; participated in future peer-reviewed publication.

Training modules related to the assignment/projects

EPIET/EUPHEM introductory course – The competencies taught during the introductory course were vital to the successful completion of this surveillance project. Lectures on the design, implementation and evaluation of different surveillance strategies were crucial when using the data analysed to formulate recommendations.

Rapid Assessment and Survey Methods module – The skills learned over the course of this module were instrumental in evaluating the quality of the current surveillance mechanism. Additionally, material regarding the risk assessments were applied to determine the future risk associated with arboviruses in Spain, leading to the recommendation of a more active surveillance.

Educational outcome

Over the course of this surveillance project, the fellow participated in a wide range of surveillance-related competencies, such as evaluating the previously established laboratory techniques for surveillance, performing large scale sample management and data analysis as well as using the data collected to formulate action-oriented recommendations. The combined experience provided by the training modules and the project experience have left the fellow with the skills required to confidently establish, interpret, and evaluate surveillance systems and the data they provide in a wide array of future applications.

2. Applied public health research

2.1 Extended spectrum β -lactamases in human *Salmonella* isolates in Spain from 2002 to 2018

Supervisors: Silvia Herrera León and Laura Herrera León

Along with the concerning spread of multidrug-resistant bacteria, outbreaks of extended-spectrum β -Lactamases (ESBLs) and carbapenemase-producing bacteria lead to first choice antibiotic treatment failures. To monitor the clinically relevant AMR determinants circulating in *Salmonella enterica*, we described the prevalence of ESBLs among the isolates collected from 2002 to 2018. β -Lactams (ampicillin or third-generation cephalosporins) are the first line antibiotics, alongside fluoroquinolones, to treat complicated cases of salmonellosis. Third-generation cephalosporin resistance is generally due to the production of extended-spectrum β -lactamases (ESBLs) or AmpC-type enzymes. In this study we outlined the prevalence of these resistance determinants in *Salmonella* isolates in correlation to the mobile genetic environments underlying their dissemination. Of the 22 503 human samples submitted to the Spanish National Centre for Microbiology (CNM), antimicrobial susceptibility testing was performed on 33% and on 50% of the *Salmonella* isolates received between 2002 and 2011 and between 2012 and 2018, respectively. WGS and cgMLST was performed on all *Salmonella* isolates that displayed resistance or reduced susceptibility to β -lactams (cefotaxime or/and ceftazidime).

Among the 256 isolates the fellow and the project supervisors identified 17 ESBLs belonging to the families CMY, SHV, and CTX-M as well as an ampC-type β -lactamase. The most commonly identified ESBLs were bla_{CTX-M-9} (50%) followed by bla_{SHV-12} (12%) and bla_{CMY-2} (11%). The fellow identified 32 different serotypes harbouring ESBLs of which the most common were ST-34 monophasic Typhimurium (31%), ST-16 Virchow (18%) and ST-15, -19, -36, -110 and -323 Typhimurium (12 %). The ESBLs identified were most commonly associated with the plasmid replicon types IncH12a (49%) of which 95% harbour bla_{CTX-M-9}, followed by incl1 (17%) and IncFIIS (7%). 187 (72%) of the isolates in this study grouped into 21 clusters. The largest cluster was composed of 45 *Salmonella* Virchow (ST16) all of which harboured bla_{CTX-M-9}. We identified isolates of the serotypes Corvallis, Rissen and Enteritidis harbouring bla_{OXA-48}. This is the first description of bla_{OXA-48} in clinical samples of human origin.

While bla_{OXA-48} is described in *Salmonella enterica* of animal origins, its recent appearance in human *Salmonella* strains poses a grave threat to first choice treatment options. National surveillance efforts should consider declaring these resistance determinants when identified in human isolates.

Role: Laboratory sample and data management; application of microbiological and epidemiological knowledge to investigate public health threat; sample size calculation and WGS analysis of representative population; analysis of antimicrobial resistance genes and their mobile genetic environment; identification of future public health threats; submitted ESCAIDE abstract; peer-reviewed manuscript in preparation.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course- The introductory course touched upon many different techniques and methods used over the course of this study. Lectures on WGS analysis and management of large-scale data bases proved invaluable when organising the work.

Time Series Analysis module – This module was very pertinent to this project as it introduced the fellow to several techniques that were directly applicable to this study. Upon the completion of the module the fellow had a much better understanding of the potential within the data that had been collected for a large time period.

Management, Leadership and Communication in Public Health Module – As the project was conducted among different departments of the CNM this module introduced valuable interpersonal skills to facilitate the completion of the project.

Educational outcome

Having *Salmonella* isolates submitted to the CNM for almost 20 years is an invaluable resource for applied microbiology research. Large-scale sample and data management were a new experience for the fellow but the combination of teaching modules and institute support allowed the fellow to successfully complete this project. Working alongside the institute bioinformatics department to extract the necessary WGS data to accurately characterise the resistance determinants harboured by this important human pathogen was a valuable experience working alongside multidisciplinary stakeholders. Having discovered a carbapenemase of high clinical significance in samples of human origin highlight the continued importance of such projects in applied public health.

3. Applied public health microbiology and laboratory investigations

3.1 Molecular and Epidemiological Characterisation of Toxigenic and non-toxigenic *Corynebacterium diphtheriae*, *Corynebacterium belfantii*, *Corynebacterium rouxii*, and *Corynebacterium ulcerans* isolates identified in Spain from 2014 to 2019

Supervisors: Laura Herrera Leon, Silvia Herrera Leon, Noemí López-Perea, and Josefa Masa-Calles

This study examines the microbiological and epidemiological characteristics of toxigenic and nontoxigenic *Corynebacterium* isolates submitted to the national reference laboratory in Spain, between 2014 and 2019, in order to describe the current situation and improve our knowledge regarding these emerging pathogens. Epidemiological information was extracted from the Spanish Surveillance System. Microbiological and molecular characterisation was carried out using phenotypic methods, multilocus sequence typing (MLST), whole-genome sequencing (WGS), and core genome MLST (cgMLST).

Thirty-nine isolates were analysed. Twenty-one isolates were identified as *Corynebacterium diphtheriae* (six toxigenic), 14 as *C. belfantii*, four as *C. ulcerans* (three toxigenic), and one as *C. rouxii*. One *C. diphtheriae* isolate was identified as nontoxigenic tox gene bearing (NTTB). Ages of patients ranged from one to 89 years, with 10% (3/30) of nontoxigenic and 22% (2/9) of toxigenic isolates collected from children younger than 15 years. Twenty-five of the patients were males (17/30 in nontoxigenic; 8/9 in toxigenic). MLST identified 28 sequence types (STs), of which seven were described for the first time in Spain. WGS analysis showed that 10 isolates, including three toxigenic isolates, harboured a variety of antibiotic resistance genes in addition to the high prevalence of penicillin resistance phenotypically demonstrated. Phylogenetic analysis revealed one cluster of isolates from family members. Risk information was available for toxigenic isolates (9/39); three patients reported recent travels to countries of endemicity and three had contact with cats/dogs. One unvaccinated child with respiratory diphtheria had a fatal outcome. Including nontoxigenic *Corynebacterium* infections in disease surveillance and using WGS could further improve current surveillance.

Peer-reviewed manuscript published in the Journal of Clinical Microbiology.

Role: Laboratory sample and data management; application of microbiological and epidemiological knowledge to investigate public health threat; WGS analysis; analysis of antimicrobial resistance and virulence genes; identification of future public health threats; communication at ESCAIDE 2020; peer-reviewed manuscript published.

3.2 COVID-19 Emergency diagnostic support

Supervisors: Silvia Herrera León and Laura Herrera León

On 7 January 2020 a novel coronavirus (Severe Acute Respiratory Syndrome coronavirus 2, SARS-CoV-2) was identified as the causative agent of coronavirus disease 2019 (COVID-19) causing severe and potentially fatal respiratory symptoms. Since the beginning of this outbreak the number of cases has been steadily augmenting, affecting more than 80 countries in multiple WHO regions as of early March 2020. On the 5 March 2020, ECDC reported a total of 95 315 cases globally, including 3 282 fatalities, of which 200 cases were confirmed in Spain. As little was known about the prevalence of asymptomatic infections at the time, there was a detection bias towards severe cases in Europe, and it was believed that the actual number may be higher.

Early in the pandemic, the capacity for COVID-19 diagnostic was not widespread in Spain, and the National Centre for Microbiology (CNM) was responsible for confirming all cases of COVID-19 and supporting centres of the

National Health System with COVID-19 diagnostics. The purpose of the CNM providing emergency diagnostic support was to facilitate testing to all regions of Spain until the capacity of each centre could be established to perform their own diagnostics. Upon the request of the director of the CNM, the fellow was asked to participate in all stages of the diagnostic pathway, from receiving, unpacking, and registering samples to viral inactivation, RNA extraction, and RT-PCR processing. Over the course of the next two months, a significant proportion of the tests performed in Spain were managed by the CNM. By May/June of 2020, hospital and regional public health laboratories were performing most of the COVID-19 diagnostic tests, which gradually reduced the necessity for COVID-19 diagnostics at the CNM.

Role: Participation in the laboratory support of an outbreak; application of microbiological knowledge to perform laboratory diagnostics; high-pressure and high-throughput laboratory diagnostic work; participation in pandemic mitigation.

3.3 Study of the epidemiological and virologic characteristics of rapidly expanding HIV-1 transmission clusters in Spain

Supervisors: Horacio Gil, Elena Delgado, Miguel Thomson

The human immunodeficiency viruses (HIV) infect cells of the human immune system (e.g. CD4⁺ T cells, macrophages and dendritic cells) and over time lead to the lethal acquired immunodeficiency syndrome (AIDS). HIV is transmitted by contact with infected body fluids during sexual intercourse, by transfusion of contaminated blood, or sharing of needles, syringes, or other sharp instruments, and vertically from mother to child. In Spain, the HIV-1 incidence in 2019 was 7.5 per 100 000 inhabitants (around 3 500 new diagnosed cases per year), with men who have sex with men being the most frequent transmission route. HIV-1 infection remains a major public health problem, which requires the implementation of new strategies to control the epidemic. Viral sequences from patients whose transmission is epidemiologically linked group phylogenetically in clades which are called transmission clusters (TCs). The analysis of TCs allows knowing the HIV-1 epidemic structure in a region and select the most appropriate control measures for reducing the HIV-1 infections. Currently, in Spain there is no molecular epidemiology HIV-1 surveillance system at a national level.

TCs presenting short genetic distances suggest short viral evolution times due to rapid transmission events and are classified as rapidly expanding TCs. The timely detection of HIV TCs with rapid expansion is critical for focusing efforts on particular populations where the opportunity for impact in avoiding future transmission is greatest. The aim of this study was to determine the epidemiological and virologic characteristics of rapidly expanding HIV-1 TCs in Spain, in order to define early indicators for the investigation of potential HIV-1 outbreaks and the implementation of preventative public health interventions.

The HIV Biology and Variability Unit (UBVVIH) of the National Centre for Microbiology (CNM) has partial *pol* sequences from more than 13,000 HIV-1 patients diagnosed in Spain obtained from routine antiretroviral drug resistance tests and molecular epidemiological studies. In addition, clinical and epidemiology data from these patients are available in the UBVVIH database. This database currently contains information on more than 400 TCs. However, a systematic software analysis has not yet been implemented to automatically identify rapidly expanding HIV-1 TCs.

It was the roll of the fellow to participate in the cleaning of the database to obtain a set of unique sequences per patient and the subsequent identification of rapidly expanding TCs using the HIV-Trace (TRANSMISSION CLUSTER ENGINE) pipeline and various genetic distance thresholds, starting at 0.5%. The clusters identified by the HIV-Trace analysis were then compared to previously identified TCs to determine the most adequate threshold. Based on our previous phylogenetic analyses we identified a total of 26 TCs with at least five cases diagnosed between 2018-2020. Among them, the HIV-Trace platform identified eight rapidly expanding TCs at a threshold of 0.5% and a total of 11 using the threshold of 0.6%. Both thresholds identified three TCs with at least five patients diagnosed during 2019-2020, which are potential candidates to launch an HIV outbreak investigation. Data collection and management will be adapted for a continued use of the HIV-Trace platform.

Role: Laboratory data management; application of microbiological and epidemiological knowledge to investigate public health threat; large-scale data management; phylogenetic analysis; identification of future public health threats; future peer-reviewed manuscript.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course- The introductory course touched upon many different techniques and methods used over the course of this study. Lectures on WGS analysis and management of large-scale data bases proved invaluable when organising the work.

Outbreak Investigation Module – The outbreak investigation module provided the technical skills required during high-pressure outbreak investigations with regards to high quality data collection, management and analysis. The material learned during this module allowed the fellow to become a versatile member of the team, that could confidently perform any task assigned.

Multivariable Analysis Module – This module was particularly useful for the HIV project performed. The skills acquired allowed the fellow to actively contribute in every stage of this project.

Management, Leadership and Communication in Public Health Module – The skills acquired during this module especially with regards to communication styles and personality types was extremely useful during the high-pressure lab diagnostic support during the COVID-19 pandemic. It allowed the fellow to remain positive and productive even in the most trying times.

Educational outcome

The fellow's involvement in this study exposed the fellow to several public health competencies, such as large-scale data cleaning, management and analysis to formulate action oriented public health recommendations. Combining phylogenetic data acquired with the epidemiological data underlying rapidly spreading TCs was a valuable lesson in using microbiological data collected for subsequent action. While the majority of this project was spent preparing the databases and obtaining initial HIVTrave analysis this project has definitely highlighted the importance of such studies and their potential to mitigate the future public health burden of this significant human pathogen.

4. Biorisk management

4.1 *Mycobacterium spp.* management, identification and molecular characterisation as part of the diagnostic services of the CNM

Supervisors: Laura Herrera León

Tuberculosis (TB) causes major public health concerns, especially in low- and middle- income countries. TB is an infectious disease caused by *Mycobacterium tuberculosis*, that typically affects the lungs, but has been shown to affect other parts of the body. Although most cases show no symptoms, known as latent TB, about 10% of these infections progress into the active disease, which if left untreated, is fatal in about 50% of those affected. The prevention of TB involves screening those at high risk, early detection, treatment of cases and vaccination with the bacillus Calmette-Guerin (BCG) vaccine. Those at high risk include individuals that have come into contact with people with active TB at home, work or socially. Case management typically involves extended periods of antibiotic treatment, although AMR is a growing problem with *Mycobacterium tuberculosis* infections. The rate of TB cases involving multi-drug and extensively drug resistant strains has been increasing over the past decade.

As part of the routine services of the CNM, and as the ECDC focal point, the fellow spent several weeks observing the BSL-3 diagnostic activities of *Mycobacteria tuberculosis*. The fellow was introduced to the weekly routine of this highly fastidious pathogen including receiving and registering clinical samples, culturing methods and antimicrobial resistance studies followed by molecular characterisation and notification of the results.

Role: BSL-3 diagnostic activity, biorisk management, laboratory sample management; application of microbiological and epidemiological knowledge to investigate public health threat; molecular characterisation; analysis of antimicrobial resistance and virulence genes.

4.2 Highly pathogenic pathogens EQAE

Supervisors: Isabel Jado Garcia

The External Quality Assurance Exercise (EQAE) targets at the identification of Risk Group 3 bacteria and is embedded in the Joint Action SHARP. Three different samples sets are offered comprising living (infectious) samples, inactivated (non-infectious) samples and serological (potentially infectious) samples. Depending on the selected sample set, specific parts of the instructions are relevant whereas others can be ignored.

All participants are asked to freely choose the analytical methods for the sample analysis applying an appropriate workflow to address the tasks of this EQAE based on individual capabilities and capacities.

The EQAE will be performed in compliance with international standards specified in DIN EN ISO 17043. The 'clinical', 'environmental' and 'food' samples are part of the accreditation scope of the EQAE provider.

The exercise included several tasks: i) to report arrival of the parcel and shipment conditions;

ii) to identify or to rule out the target inside of all coded samples; iii) to specify for *Bacillus anthracis* and *Yersinia pestis* the possible plasmids content, if identified; iv) to specify the *Brucella* species and the *Francisella tularensis* subspecies, if identified and v) to report the methods chosen for analysis. The target bacterial species include:

Bacillus anthracis, *Yersinia pestis*, *Francisella tularensis* subspecies (included are: *F.t. tularensis*, *F.t. holarctica*, *F.t. mediasiatica*, *F.t. novicida*) *Burkholderia pseudomallei*, *Burkholderia mallei*, *Brucella species* and *Coxiella burnetii*.

The fellow observed all previously mentioned stages of this EQAE, most of which was performed in the BSL-3 laboratory.

Role: BSL-3 diagnostic activity, biorisk management, laboratory sample management; application of microbiological and epidemiological knowledge to complete EQAE; molecular characterisation.

Training modules related to the assignment/projects

Biorisk and Quality Management Module – This module was cancelled due to the COVID-19 pandemic.

Educational outcome

This was the fellow's first experience working in a BSL-3 laboratory, and based on the diverse activities the fellow was able to witness a variety of techniques. These activities have provided the fellow with a foundation for future independent work in the BSL-3 laboratory and insights into the management of such a laboratory environment.

5. Quality management

5.1 Validation of a quadruplex real-time PCR assay and the modified ELEK test for the rapid identification of potentially toxic *Corynebacterium spp.* in Spain

Supervisors: Laura Herrera León and Silvia Herrera León

Diphtheria is an acute infectious disease that affects the upper respiratory tract and occasionally the skin caused by the production of the diphtheria toxin (Dtx) of certain species of *Corynebacterium*, usually, *C. diphtheriae* and *C. ulcerans*. While the incidence in Spain resembles that of the rest of EU, diphtheria has been increasing in relevance due to surges in mass relocation events of travelers, refugees, asylum-seekers and immigrants from diphtheria endemic countries. This mobilisation in combination with a growing vaccine hesitancy in non-endemic countries, gives diphtheria a high potential for reemergence.

With an increased amount of suspected diphtheria cases being submitted to the national reference centre, the objective of this project was to reduce the time to diagnosis in order to assist in the patient management, thus reducing the public health burden of diphtheria in Spain. In 2014, a group in the UK developed, validated, and implemented a quadruplex real-time PCR assay to achieve just this. While the standard time for the identification and toxin expression of isolates can range between 24-48 hours this qPCR is capable of identifying *C. ulcerans* and *C. diphtheriae* within only 3-4 hours after receipt of the clinical sample. This qPCR was validated according to established guidelines and demonstrated a very high diagnostic sensitivity (100%) and high specificity (98-100%). After optimisation and extensive testing we achieved the same sensitivity and specificity as previously published. To further improve the diagnostic capacity of the CNM to identify the presence of toxigenic *Corynebacterium spp.* we also implemented the modified ELEK test to phenotypically confirm the expression of the *tox* gene. A process that was previously performed in England which took between three and five days including shipping. Performing this assay at the CNM further reduces the time to diagnoses by 2-3 days, as toxigenicity can be confirmed within 24 hours of obtaining a pure culture. The public health impact of implementing both the novel RT-PCR and the modified ELEK test are a drastic reduction in the time to diagnosis – furthermore, it provides the opportunity to assist neighbouring countries with their ELEK tests, as currently only Spain and England perform this assay.

Role: Laboratory sample and data management; application of microbiological and epidemiological knowledge to improve diagnostic capacity; implementation, optimisation and validation of diagnostic techniques; formulating technique specific SOPs for the CNM.

5.2 EQA for the establishment of international standards for *Mycobacterium tuberculosis* diagnostics using lyophilised DNA

Supervisors: Laura Herrera León

Tuberculosis (TB) causes an infectious disease caused by *Mycobacterium tuberculosis*, that typically affects the lungs, but has been shown to affect other parts of the body. Although most cases show no symptoms, known as latent TB, about 10% of these infections progress into the active disease, which if left untreated, is fatal in about 50% of those affected. The prevention of TB involves screening those at high risk, early detection, treatment of cases and vaccination with the bacillus Calmette-Guerin (BCG) vaccine. Case management typically involves extended periods of antibiotic treatment, although AMR is a growing problem with *Mycobacterium tuberculosis* infections.

In order to achieve the ambitious goal of ending TB worldwide, the diagnostic capacity to detect TB is of utmost importance. Traditional techniques involving sputum-smear microscopy or culture-based techniques are effective for the diagnosis of highly infectious TB but less effective in the diagnosis of individuals with less severe symptoms. Additionally, these traditional methods are very time consuming. Recently, more sensitive and rapid diagnostic tests (RDTs) based on molecular detection (nucleic acid amplification techniques, NATs) are becoming the new norm for *Mycobacterium tuberculosis* diagnostics. With several new RDTs coming to the market the WHO identified a need for international standards for *Mycobacterium tuberculosis* DNA testing with designated international units. Doing so would facilitate the harmonisation between molecular detection assays to ultimately allow for improved comparative potential of international diagnostic features (e.g. limits of detection).

The WHO has commissioned an international collaborative study for *Mycobacterium tuberculosis* diagnostics using lyophilised DNA. As the ECDC contact point for *Mycobacterium tuberculosis* in the ISCIII, the Laboratory of Mycobacteria was asked to participate in this EQA to determine how viable lyophilised DNA is for *Mycobacterium tuberculosis* identification for future EQAs. To support the WHO in this objective, the fellow and his supervisor performed the EQA within the timeframe stipulated by the WHO and all results were submitted accordingly. The WHO is currently still evaluating the results of all groups participating in this EQA.

Role: Laboratory sample and data management; application of microbiological and epidemiological knowledge to improve diagnostic capacity for the detection of TB; implementation, optimisation and validation of diagnostic techniques; participation in international EQA.

Training modules related to the assignment/projects

Biorisk and Quality Management Module – This module was cancelled due to the COVID-19 pandemic.

Educational outcome

The fellow's participation in these quality management projects has not only provided the fellow with necessary skills to independently conduct such projects in the future, but it has also improved the diagnostic capacity of the CNM with regards to diphtheria diagnostics and it has reduced the time to diagnosis substantially, improving patient outcome. The implementation, optimisation and validation of diagnostic techniques has provided the fellow with the necessary skills to identify gaps in the current diagnostic capacity and to implement the most recent techniques in the field from scratch. In the case of the modified ELEK test, this included the complicated process of organising the shipment of the scarce antitoxin from India.

6. Teaching and pedagogy

6.1 Laboratory introduction for collaborating EPIET fellow

The audience of this project was an EPIET fellow from the National Centre for Epidemiology (CNE) in Madrid that was collaborating with the EUPHEM for a project on diphtheria (3.1). To facilitate this collaboration, the EUPHEM fellow, gave a complete laboratory introduction of all relevant techniques used for our project, allowing the EPIET fellow to perform many of the techniques herself.

6.2 Case study for students of the 'Microbiology Applied to Public Health and Infectious Diseases Research' degree at the University of Alcalá

The ECDC case study (Gastroenteritis in Kalundborg, Denmark) was performed for Masters students of the University of Alcalá, once in person (2019) and once virtually (2020) due to the pandemic. Both case studies required 2 hours of preparation and ran for about 4 hours each. Verbally feedback from the students was very positive and throughout the case study a productive and dynamic conversation was maintained.

6.3 Seminar for Masters course in Crisis Management at the University of Camillo Jose Cela

After discussing the current curriculum of the Master's degree on Crisis management, the fellow and the course directors agreed for the fellow to teach a seminar on Emerging diseases in Europe. The fellow then designed and recorded a one-hour lecture on Emerging diseases and their management in Europe to a very mixed audience of civil servants (including doctors, police officers, firefighters, etc). The course evaluation performed by the Master's program came back very positive.

6.4 Adapted case-study of gastroenteritis in Kalundborg, Denmark for second^s semester Biotechnology Masters students at the Katholieke Universiteit Leuven, Belgium

In collaboration with two EUPHEM fellows and an EPIET fellow, along with one of their supervisors, Andreas participated in the adaptation of the ECDC case study (Gastroenteritis in Kalundborg) for a group of biotechnology students with a limited microbiology background. Presenting this case study to this particular audience served well to introduce them to applied public health work. Although it was also taught virtually, with 12 students per group, the participant feedback performed was very positive.

6.5 Co-supervision of final year dissertation project

Alongside their host-site supervisor, the fellow, co-supervised a laboratory based final year dissertation of a Medical Biology undergraduate student from the University of Alcalá. This included the daily supervision of the student's laboratory activities, to support the student in the implementation and optimisation of a novel RT-PCR

capable of distinguishing between different *E. coli* pathotypes. While this is currently still ongoing, the project is moving along nicely and the student will have plenty of data for his report.

6.6 *Salmonella kentucky* case study for cohort 2020 introductory course

The fellow participated in the preparatory session as well as the facilitation of the ECDC case study on multidrug resistance *Salmonella Kentucky*. The fellow facilitated this case study alongside a ex-EUPHEM fellow from Austria, and initial feedback on the course was very positive. Throughout the exercise the conversation was very dynamic and productive. We finished all of the learning objectives thoroughly and in the allotted time.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course – The pedagogic techniques introduced during the introductory course, and the experience with the case studies were very valuable in creating and harbouring and open discussion where the participants of the course do most of the talking. In combination with the technical skills taught during the course, public health management and time management principles were invaluable to the successful completion of the learning objectives for each teaching activity.

Educational outcome:

These activities provided valuable experience in modern pedagogical techniques to the fellow. Facilitation rather than lecturing is a very effective way to achieve diverse learning objectives, even as most teaching activities moved to a virtual environment. Teaching in an online format during a pandemic does require some innovative strategies to make sure students participate and are following actively, but using Google forms and other online tools one can ensure that students are achieving the set learning objectives. The foundation provided by the various other projects and outbreaks the fellow has participated in have provided the fellow with the confidence to teach several different public health capacities.

7. Public health microbiology management

7.1 Urgent diagnostic support for suspected diphtheria cases

Over the course of the fellowship several clinical samples of suspected diphtheria cases were submitted for confirmation to the CNM. As the fellow was currently implementing improved diagnostic techniques for diphtheria (5.1), he participated in several 'urgent' after-hour diagnostic processes to provide accurate and rapid results to treating physicians. As patients are kept in isolation until the cases are confirmed or discarded, applying the novel RT-PCR alongside the conventional methods helped support the findings of the previously established methods. Furthermore, this process helped us optimise the RT-PCR technique for further diagnostic applications.

7.2 2020 SARS-CoV-2 Outbreak in a Hotel in Tenerife, Spain

The field deployment to support the epidemiological response to one of the first COVID-19 clusters in Spain was a valuable public health management experience for the fellow. His participation in the management the quarantined hotel, the cases and their potential contacts as well as the incoming microbiological and epidemiological data required the application of a large variety of public health competencies. Despite the prolonged exposure of a symptomatic case to the hotel population, the swift and strict measures implemented by public health authorities are believed to have effectively prevented an international cluster from forming.

7.3 COVID-19 Emergency diagnostic support

The fellow's participation in the pandemic diagnostic support has provided the fellow with a vast array of experiences in public health management. With regards to working with a little known-human pathogen, in a high-pressure, high-through-put laboratory setting while maintaining a positive and productive attitude in the face of thousands of incoming samples daily, the fellow was a productive member of the diagnostic team during its most active phase of the pandemic response. The public health management skills acquired during this period range from interpersonal skills to large scale sample management and processing.

7.4 COVID-19 risk evaluation at a reception centre for immigrants, refugees and asylum-seekers in Melilla, Spain

The Ministry of Health, alongside the organisational body responsible for coordinating public health emergency responses (Centro de Coordinación de Alertas y Emergencias Sanitarias or CCAES), requested the assistance of both the EPIET and EUPHEM fellow from Madrid in the formulation of a risk assessment in a temporary immigrant reception centre. The fellow's tasks included extensive interviews with staff and residents, receiving, collating, and

analysing all case and resident information available to the camp and then formulated a detail risk assessment with targeted and feasible recommendations. The recommended actions submitted to the corresponding authorities to reduce the COVID-19 associated burden among these vulnerable populations were: (i) decongestion, (ii) facilitated testing, (iii) screening for symptoms, and (iv) targeted public health and risk communication.

Training modules related to the assignment/projects

Management, Leadership and Communication in Public Health Module – The skills acquired during this module were crucial in the successful completion of the aforementioned projects. In particular, time management and communication strategies learned were incredibly useful during the highly intense COVID-19 related activities. Despite being very tired and stressed, effective communication and organisational skills were instrumental in maintaining a positive and productive attitude.

RAS Module – The skills acquired during this module were crucial for the successful completion of both of my COVID-19 deployments. Especially, when tasked to perform a risk assessment of an ongoing outbreak in the refugee center. The ECDC risk assessment algorithms presented as part of the module during a practical exercise were very applicable.

Vaccinology – The skills acquired during the vaccinology module were very useful to the successful completion of the diphtheria laboratory support, especially concepts of secondary vaccine failure with regards to toxigenic diphtheria cases discovered in elderly individuals.

Educational outcome

Public health management skills were heavily tested during the COVID-19 pandemic. In particular, projects conducted in the early phases of the pandemic required a wealth of experience in public health communication, management, and dissemination. The combination of skills acquired during the modules and throughout the projects completed have provided the fellow with the necessary skills to work independently or as part of a multidisciplinary group during high-pressure public health activities, including field work. Particularly the communications strategies and interpersonal relations strategies learned during the modules were particularly useful in managing stressful situations in the laboratory.

8. Communication

Publications related to the EUPHEM fellowship

1. Management of a COVID-19 outbreak in a hotel in Tenerife, Spain (Submitted)
2. Molecular and Epidemiological Characterisation of Toxigenic and Non-toxigenic *Corynebacterium diphtheriae*, *Corynebacterium belfantii*, *Corynebacterium rouxii*, and *Corynebacterium ulcerans* isolates identified in Spain from 2014 to 2019
3. Priorities for COVID-19 management in reception centres for asylum-seekers and refugees in Melilla, Spain (Submitted)
4. Domestic animals as a reservoir for toxigenic *Corynebacterium ulcerans*. Core-genome MLST (cgMLST) confirms first zoonotic transmission of diphtheria in Spain. (To be submitted)

Reports

1. Arbovirus Surveillance report
2. Diphtheria RT-PCR SOP
3. Modified ELEK test SOP
4. EQA *M tuberculosis* report
5. COVID-19 outbreak in a refugee centre report
6. JIACRA National AMR Surveillance report

Conference presentations

1. Management of a COVID-19 outbreak in a hotel in Tenerife, Spain
2. Molecular and Epidemiological Characterisation of Toxigenic and Nontoxigenic *Corynebacterium diphtheriae*, *Corynebacterium belfantii*, *Corynebacterium rouxii*, and *Corynebacterium ulcerans* isolates identified in Spain from 2014 to 2019
3. 2020 West Nile Virus Outbreak in Spain, National Society of Epidemiology

Other presentations

1. COVID-19 Interview for JISEM - Spain

Other activities

Throughout the fellowship, Andreas was elected as one of the EUPHEM representatives. This involved his participation in the training sites forums, various ECDC fellowship workgroups, meetings with the fellowship office and a variety of other tasks to best represent Cohort 2019. As a liaison between the fellows and the fellowship office, it was particularly important to facilitate communication during the COVID-19 pandemic. In addition to many meetings with the cohort representatives from Cohort 2018 and 2021 satisfaction surveys were also key to support the continuous improvement of the EPIET/EUPHEM fellowship.

Other training modules

Bioinformatics module – ISCIII

9. EPIET/EUPHEM modules attended

1. *C2019 Introductory course, 23/09-12/10 2019, Spetses, Greece*
2. *Outbreak Investigation module, 9-13/12/2019, Nicosia, Cyprus*
3. *Management, Leadership and Communication in Public Health, 10-14/12/2020, Stockholm, Sweden*
4. *Multivariate analysis, 15-19/06 + 26/06 2020, Virtual Module*
5. *Project review module, 24-27/08/2020, Virtual Module*
6. *Time series analysis, 25-29/01/2021, Virtual Module*
7. *Risk assessment and survey methods, 27/04 + 4-6/05 2021, Virtual module*
8. *Vaccinology, 14-18/06 2021, Virtual module*

10. Other training

1. *WHO Infodemic management (2nd cohort), 01-23/06/2021, Virtual course*

Discussion

Coordinator's conclusions

One of the main goals of the EUPHEM programme is to expose fellows to diverse and multidisciplinary public health experiences and activities, thus enabling them to work across different disciplines. This report summarises all activities and projects conducted by Andreas during his two-year EUPHEM fellowship (cohort 2019) as an EU-track fellow at the Instituto Carlos III in Madrid, Spain.

The work depicted in this portfolio attests for the dedication and talent of Andreas Peter Hoefer. He was already a very accomplished microbiologist with expertise in the area of antimicrobial resistance, in particular elucidating the regulatory mechanisms underlying the expression of aminoglycoside resistance conferring methylases. At the start of the programme and when he undertook the EUPHEM fellowship from the beginning showed a high level of competency in management and leadership. The laboratory and epidemiologically based projects covered all diverse range of disease programmes involving multidisciplinary working and teamwork on all levels such as physicians, laboratory technicians, epidemiologists, statisticians, government officials and public health officers, showing strength of the fellow and ability to work within such an extended environment(s). Andreas has shown a high capacity of public health management by working with an active role in interdisciplinary groups and bringing different professionals together. During the two years he has not only achieved his primary objectives but was very productive in producing valuable public-health-related outputs, contributed to the response to the COVID-19 pandemic in Spain at regional and national level and in different areas such as COVID-19 emergency diagnostic support risk evaluation at a reception centre for immigrants, refugees and asylum-seekers in Melilla, Spain and the field deployment to support the epidemiological response to one of the first COVID-19 clusters in Spain.

His dedication to the objective of programme and public health goes above and beyond expectations. Andreas is a very good teacher and his willingness to cascade his competencies are important to be mentioned. A good example is his contribution to the phylogeny session at introductory course for cohort of 2020 being facilitator of a very technical case study. He has not only shown his abilities to handle challenges at the professional level but also at the personal level by being strong, humble in receiving feedback and putting the feedback into action for improvement. In addition to COVID-19 response he has taken a very important role in surveillance of Phlebovirus and Flavivirus in Spain from 2016-2019 and molecular characterisation of the detected viruses. Activities were in line with the 'learning by doing' of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and above. Activities were complimented by training modules providing theoretical and practical knowledge and skills. Projects had a clear outcome, with results communicated in scientific

journals and at conferences. The contributions made by Andreas to his work at the training site indicates the importance of developing a future critical mass of highly skilled field public health microbiologists within the 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 performed all his tasks to a very high standard and with a professional attitude. We wish the fellow every success in his future career and congratulate the training site for a successful training of the fellow.

Supervisor's conclusions

Andreas has been outstanding, accomplishing an extremely successful fellowship during a very difficult period. He started his fellowship with a project on *Salmonella* spp and was soon invited to participate in the early COVID-19 response of the National Centre for Microbiology. He was involved in every single step of the response working long days while always being positive and collaborative. He was deployed on two missions related to the COVID-19 outbreak, representing our centre and doing exceptional work. Apart from COVID-19 Andreas has allowed our centre to improve our public health capacities by developing tools to implement in our reference services. We have to highlight that he is always willing to help and has been involved in a large number of projects in which all supervisors have highlighted his commitment and responsibility as well as appreciating his hard work. He has stood up as a very professional fellow, a very hard worker and collaborative. He is an excellent team player and has very good social skills that have helped him developed very good personal and professional relationships with many people in and out of the CNM. In addition, he has been extremely productive publishing his findings. We could not be prouder of him and are sure that he will have an excellent future as a Public Health Microbiologist.

Personal conclusions of fellow

Throughout this fellowship my host site and supervisory team have gone above and beyond to fulfil not only the requirements of the course but also my personal learning objectives. The relevance and diversity of the projects and public health competencies I have been able to work on have fully met my original expectations of the fellowship.

During the COVID-19 pandemic my host-institute has made it possible for me to gain a wealth of experience supporting the pandemic response from both the field epidemiology and the laboratory diagnostics side. This has provided me with invaluable experiences that I am eager to apply in my next position as a WHO Laboratory technical officer at the WHO Vietnam country office, where I will be supporting the COVID-19 laboratory response.

In summary, I highly recommend this fellowship for microbiologists and public health professionals looking to gain experience at the national level and broaden their foundation within several pathogen-groups and public health competencies. The fellowship has significantly improved my career prospects and has provided me with an invaluable network of public health professionals across Europe and the world.

Acknowledgements of fellow

First and foremost, I would like to very much thank my supervisors at my host-site, Silvia, Laura and Ana, who went above and beyond in securing training opportunities for me. Whether it be my participation in field assignments, outbreaks or personal learning objectives, they consistently supported any and all endeavours I pursued. Scientifically, professionally and personally, their dedication and motivation are admirable, and I very much look forward to working with them in the future. I would also, of course like to thank all of my project supervisors and their tireless efforts and support towards completing our collaborations.

I would also like to thank Aftab Jasir who was an excellent front-line coordinator and professional mentor throughout my fellowship. As with my host-site supervisory team, Aftab always supported and accommodated my personal learning objectives and was a pleasure to work with.

I am also very grateful to the entire cohort 2019 for their support during the COVID-19 pandemic. Their support, both technically and personally, during all stages of the pandemic were a constant source of encouragement. Within my institute, the past EUPHEM fellows Horacio and Lola also provided excellent support in projects and personally regarding the fellowship and my upcoming role within the WHO. It was a pleasure working with all other cohort representatives from Cohorts 2018 to 2021. I'd also like to thank Adam Roth for his scientific inputs and time spent with the cohort representatives.