



# Summary of work activities

## Ragnhild Tønnessen

### The ECDC Fellowship Programme

#### Public Health Microbiology path (EUPHEM), 2020 cohort

## Background

The ECDC Fellowship Programme is a two-year competency-based training with two paths: the field epidemiology path (EPIET) and the public health microbiology path (EUPHEM). After the two-year training, EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control.

Both curriculum paths provide training and practical experience using the 'learning by doing' approach in acknowledged training sites across European Union (EU) and European Economic Area (EEA) Member States.

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 Ragnhild Tønnessen, cohort 2020 of the European Public Health Microbiology Training Programme (EUPHEM) at the Norwegian Institute of Public Health (NIPH).

## Pre-fellowship short biography

Ragnhild Tønnessen received her education as a veterinarian (2008) and obtained a Ph.D. in virology on avian influenza (2013) from the Norwegian School of Veterinary Science, Oslo. Ragnhild has work experience as a research scientist at the Norwegian Veterinary Institute, Oslo, (2013–2014) in laboratory diagnostics of viral diseases in animals. In 2014, she started her career as senior advisor and epidemiologist at the NIPH, focusing on establishing surveillance of severe influenza. She was responsible for setting up and running the national surveillance systems for influenza hospitalisations, influenza intensive care unit (ICU) admissions and all-cause mortality in Norway (NorMOMO). She was also heavily involved in the early outbreak response to the COVID-19 pandemic in Norway where she led the first outbreak group in early January 2020.

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She then focused on setting up surveillance systems for the first COVID-19 cases in Norway and for severe COVID-19 cases (ICU admissions and hospitalisations). In parallel, she worked to enhance the influenza surveillance.

## Methods

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

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

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

## Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the ECDC Fellowship Manual <sup>1</sup>.

### 1. Epidemiological investigations

#### 1.1 Outbreak investigations

**Supervisors:** Heidi Lange, Trine Hessevik Paulsen, Solveig Jore, Olav Hungnes, and Karoline Bragstad, NIPH

##### *1.1.a Outbreak of hepatitis A virus, genotype IA, April–October 2021, Norway*

**Supervisor:** Heidi Lange (Senior Advisor, Department of Infection Control and Preparedness), NIPH

Hepatitis A virus (HAV) can cause food-borne outbreaks. In September 2021, an unusual increase in the number of reported HAV cases was detected in Norway. All cases belonged to the same genotype IA cluster (NOR-2021-V1). An outbreak investigation was conducted by NIPH and the Norwegian Food Safety Authority (NFSA) in collaboration with the municipality doctors to find the source and stop the transmission. The patients were interviewed, sales receipts from grocery stores were collected, and suspected food items were traced. A case control study including 10 cases, and 30 controls was also performed.

A total of 20 cases (18 confirmed and 2 probable) of hepatitis A met the case definition and were included in the outbreak. The cases were from six counties mainly located in southern Norway. Among the cases, 65% (13) were male, the median age was 49 (range 10 to 81 years), and 80% (16) were hospitalised. The results indicated that 50% of the cases had been exposed to frozen raspberries originating from Bulgaria and Poland and that these berries were the probable source of the outbreak. The imported berries had been used without heat-treatment in different cakes and berry sauce eaten by the 10 cases either at a specific bakery chain, local bakery or restaurant. Frozen raspberries could not be identified in the case control study. The batches of berries were no longer on the market, no new cases were detected, and the outbreak was considered over. The public was reminded to heat-treat imported frozen berries before they are eaten or used in cakes or smoothies. NFSA issued an alert in the Rapid Alert System for Food and Feed (RASFF).

**Role of the fellow:** The fellow was involved in framing the case definition, collected information and performed descriptive and analytical epidemiological analysis. The fellow drafted the outbreak report [4], participated in contributing to news items [29, 30] and answered questions from the media [31]. She also presented the project at the weekly EPIET/EUPHEM meeting at NIPH [13] and at the Nordic Project Review Mini Module 2022, at NIPH, Oslo [14].

<sup>1</sup> European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2020. Available from: <https://www.ecdc.europa.eu/en/publications-data/ecdc-fellowship-programme-manual-cohort-2021>

### ***1.1.b First outbreak of highly pathogenic avian influenza (HPAI) in wild birds in Norway, November 2020, risk assessment on human infection with A(H5N8)***

**Supervisors:** Trine Hessevik Paulsen (Medical Officer, Department of Infection Control and Vaccines), Solveig Jore (Senior Scientist, Department of Infection Control and Preparedness), Olav Hungnes (Senior Scientist, Department of Virology), NIPH.

A large outbreak of highly pathogenic avian influenza virus (HPAIV) A(H5N8) clade 2.3.4.4b started in Europe in late summer 2020. The virus was likely introduced from western Russia and Kazakhstan to Europe by migratory birds and caused a high number of outbreaks in wild birds, captive birds and poultry. No cases in humans had been detected. In Norway, the virus was detected for the first time in a wild bird in November 2020. HPAIV had never previously been detected in Norway. The NIPH assessed the risk of human infection with HPAIV A(H5N8) in Norway. Information was collected from the veterinary authorities and scientific literature. Since whole-genome virus sequences from birds in Norway were not available at this stage, sequences from birds in northern Europe available in the Global Initiative on Sharing Avian Influenza Data (GISAID) EpiFlu were analysed phylogenetically and screened for substitutions in key amino acids previously associated with mammalian adaptation. The analysed viruses belonged to clade 2.3.4.4b and had an avian profile. The risk of human infection with HPAIV A(H5N8) in Norway was assessed as very low. Since avian influenza viruses (AIVs) are constantly changing genetically, it was recommended that the viruses in birds should be closely monitored to detect changes leading to human transmission. As a precautionary measure, the public was recommended not to touch sick or dead birds. For occupationally exposed people handling infected birds, use of personal protective equipment (PPE) was recommended. Healthcare workers and laboratory personnel were encouraged to be vigilant to enable rapid detection of potential human cases.

**Role of the fellow:** The fellow collected epidemiological information, searched the literature, participated in making public health recommendations and drafted the risk assessment report [5]. She also drafted a news item [32] and a web article [35] and updated the information on the NIPH's webpages [34]. Moreover, the fellow revised the risk assessment on 03.03.21 [6] after the first human cases were reported from Russia in February 2021 and drafted a news item [33]. The fellow arranged a One Health meeting between NIPH, the Norwegian Veterinary Institute (NVI) and NFSA, where she gave a presentation about zoonotic influenza [15].

### ***1.1.c First outbreak of highly pathogenic avian influenza (HPAI) in poultry in Norway, November 2021, risk assessment on human infection with A(H5N1)***

**Supervisors:** Trine Hessevik Paulsen (Medical Officer, Department of Infection Control and Vaccines), Karoline Bragstad (Head of Section, Department of Virology), and Olav Hungnes (Senior Scientist, Department of Virology), NIPH

During autumn 2021, HPAIV H5N1 caused numerous outbreaks in wild birds and poultry in several European countries. In November 2021, Norway experienced the first ever outbreak of HPAI in commercial poultry when HPAIV H5N1 was detected in a flock of 7500 layers (hens) in Klepp municipality, Rogaland, in southwestern Norway. The virus was also detected in another equally large layer flock nearby, as well as in wild ducks hunted from the same area. The NIPH assessed the risk of human infection. Information was obtained from the NVI and literature searches. The NIPH performed whole-genome sequencing on virus from the layers. The hemagglutinin (HA) gene of HPAI H5N1 belonged to clade 2.3.4.4b. The genetic constellation of the virus differed from the constellation of HPAI H5N8 detected in Europe in 2020–2021. The HA gene of H5N1 was closely related to the HA gene in the H5N8 clade 2.3.4.4b viruses, a group of viruses that has zoonotic potential and has caused a few asymptomatic or mild infections in humans, and severe disease in some mammals. The HA gene from H5N1 was also related to the HA gene of A(H5N6) that have recently caused severe disease in humans in China, but the other genes were different. H5N1 in Norway also differed from the zoonotic H5N1 virus found in Asia and Africa. Only a few substitutions in viral proteins previously known to be associated with mammalian adaptation were found in the H5N1 from hens in Norway, and the virus had an avian profile. For the HPAI H5N1 virus circulating in birds in Europe and Norway there had been no human cases reported so far despite numerous outbreaks in commercial poultry flocks. The risk of human infection with HPAIV A(H5N1) in Norway was assessed as very low. For poultry workers and others exposed to large amounts of virus, the risk was assessed as low, but this could be reduced to very low by the correct use of PPE. The public was recommended not to touch sick or dead birds. People handling infected birds were recommended to wear PPEs. Moreover, HPAI H5N1 and related viruses should be closely monitored to detect changes that may lead to increased human transmission.

**Role of the fellow:** The fellow collected information, searched the literature and drafted the risk assessment report [7]. Besides, she drafted news items [36, 38], updated the NIPH webpages on avian influenza [37], and held a presentation about the HPAI H5N1 outbreak in poultry at NIPH [16]. The fellow also participated in meetings with the NFSA, NVI and other stakeholders.

### ***Training modules related to the assignment/projects***

The EPIET/EUPHEM Introductory Course provided an introduction to public health microbiology and intervention epidemiology. The course introduced the 10 steps of an outbreak investigation, risk assessment methodology and the statistical tool STATA. The Outbreak Investigation Module gave in-depth information on outbreak investigations through lectures and case studies.

Design and use of questionnaires, descriptive analyses in STATA, communication, implementation of control measures and One Health were among the topics covered. An introduction on how to use whole-genome sequencing data was also provided. The Multivariable Analysis Module gave a comprehensive overview of statistical analyses, and practical training on how to build regression models. The RAS module gave practice in risk communication using case studies.

### ***Educational outcome***

The fellow gained experience from two types of outbreak investigations covering a food-borne outbreak (hepatitis A), and two outbreaks in animals (avian influenza) requiring a One-health approach. As a member of multidisciplinary outbreak investigation teams, she gained experience in all the 10 steps of an outbreak investigation and further developed her microbiological and epidemiological skills. The activities performed by the fellow included collecting and compiling epidemiological and microbiological information, making case definitions, descriptive and analytical statistical analysis in STATA, risk assessment, making public health recommendations and communication with the NFSA, the NVI, municipality doctors, the media and the public. She also participated in outbreak meetings, wrote outbreak and risk assessment reports and updated webpages.

## **1.2 Surveillance**

**Supervisors:** Trine Hessevik Paulsen, Robert Neil Whittaker, Hilde Kløvstad, and Astrid Løvlie, NIPH

### ***1.2.a Establishing a register-based surveillance system for influenza hospitalisations in Norway during the COVID-19 pandemic***

**Supervisors:** Trine Hessevik Paulsen (Medical Officer), and Robert Neil Whittaker (Research Scientist), Department of Infection Control and Vaccines, NIPH

Since the upsurge of the COVID-19 pandemic in 2020, a concern for an influenza and COVID-19 'twindemic' that could overburden hospital capacity was raised. To enhance influenza surveillance in Norway during the 2020–2021 season, a national register-based surveillance system for influenza hospitalisations was established, in order to monitor the severity of the season. Individual-level hospital surveillance data was provided from the Norwegian Patient Registry (NPR). Influenza hospitalisations were defined as in-patient hospital admissions combined with codes from the International Classification of Diseases, tenth revision (ICD-10) for influenza (J09–J11). The data for each season (week 40 to week 20) were stratified per sex and age. Only the first admission with influenza per season was included. To be able to assess severity, historical data from NPR was also obtained. Data from the newly established national laboratory database was collected as well to be able to verify the cases if needed by linking the data. The national preparedness register for COVID-19 in Norway (Beredt C19) was used as infrastructure for the surveillance. Register-based surveillance with an infrastructure that enables linkage of different data sources should be considered in the surveillance of respiratory viral infections, in the future.

**Role of the fellow:** The fellow was responsible for planning and designing the surveillance system and collaborated with data scientists at NIPH to solve the technical aspects and coding that was required for the implementation. She drafted a report [8], operated the system in the 2020–2021 influenza season, and communicated the results to the public, media and healthcare sector through the weekly influenza reports published by the NIPH. The fellow also wrote abstracts – one for the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), and one for The European Scientific Working group on Influenza and other Respiratory Viruses (ESWI), and presented a poster [12] at the eighth ESWI influenza conference, online, in December 2021. Moreover, she made and held several other presentations [17, 18, 19].

### ***1.2.b Biobehavioural survey, people who inject drugs (PWID), Oslo, 2018***

**Supervisors:** Robert Neil Whittaker (Research Scientist), Hilde Kløvstad (Head of Section), Department of Infection Control and Vaccines, NIPH

People who inject drugs (PWID) are at increased risk of blood-borne infections. Cross-sectional prevalence studies have been performed since 1999 in Oslo to monitor the transmission of such infections among PWID. The aim of this study was to describe the prevalence of hepatitis A, B, C and HIV infections, as well as drug use, among PWID in Oslo, 2018. In addition, we examined if there is an association between hepatitis B or C infection and the number of years injecting drugs. A point prevalence study was conducted among PWID over 18 years of age attending low-threshold health and social services in Oslo, 2018. Blood samples from the participants were screened for hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV. They also answered a questionnaire about drug use. Descriptive analysis was performed. Univariable and multivariable logistic regression were used to examine the association between HBV or HCV infection and the number of years injecting drugs. The study included 299 PWID aged from 21–69 years (median 41), of whom 75% were male. The median number of injection years was 13.5 and ranged from <1–54 years. The prevalence of HIV, HBV and HCV infection was 1.4% (4/284), 0.7% (2/283) and 26% (74/284), respectively. The prevalence of HAV-antibodies was 65% (186/284). Detection of antibodies against HBV core antigen (odds ratio (OR)=1.07, 95% confidence interval (CI) 1.03–1.11), HCV (OR=1.14, 95% CI 1.10–1.18), and HCV RNA (OR=1.04, 95% CI 1.02–1.06), were all associated with increasing years of injection.



The prevalence of acute or chronic HCV infection among PWID in Oslo declined compared to previous years, indicating that the control measures implemented for this risk group have been effective. However, the odds of HCV infection increase with increasing number of years of drug injection. Thus, it is important to reach this risk group with measures as early as possible. The prevalence of HIV and HBV infections among PWID in Oslo, 2018 were comparable with previous years and remained low. For hepatitis A, the prevalence reflected both previous infection and vaccination and was comparable to earlier years. The results from the study indicate that long term and targeted infection prevention and control measures towards PWID have been efficient. We recommend that this targeted work as well as the regular point prevalence studies among PWID in Oslo continues to enhance surveillance of blood-borne viral infections in this risk group.

**Role of the fellow:** The fellow contributed equally to this work along with the EUPHEM fellow Lin Thorstensen Brandal (Cohort 2019). Ragnhild was involved in analysing and interpreting the data using analytical epidemiological methods, writing the report [9], and suggesting public health recommendations.

### ***1.2.c Description and evaluation of the variable, 'underlying disease' for COVID-19 in The Norwegian Surveillance System for Communicable Diseases (MSIS)***

**Supervisor:** Astrid Løvlie (Senior Advisor, Department of Infectious Disease Registries), NIPH

When SARS-CoV-2 was first detected in 2020, it was essential to obtain as much information as possible from the first COVID-19 cases to learn about the new disease. ECDC and WHO developed a standardised COVID-19 case-reporting form for reporting the cases to The European Surveillance System (TESSy). This was implemented at The Norwegian Surveillance System for Communicable Diseases (MSIS), NIPH. The variable, 'underlying disease' included a list of 17 different conditions. As the number of COVID-19 cases increased, the detailed reporting on underlying disease per case became challenging for the clinicians, and some experienced technical problems in the reporting to MSIS. There were also concerns about the quality and usefulness of the collected data. An evaluation of the variable, 'underlying disease' in MSIS was performed. The aim was to describe the surveillance of underlying disease for COVID-19 in MSIS and to evaluate the data quality, sensitivity, simplicity, flexibility, acceptability and usefulness, in order to give recommendations about the future use of this variable. A retrospective descriptive study was performed. All COVID-19 cases in Norway reported to MSIS between 17.02.20 – 30.05.21 were included (N=125 261). Overall, the reporting completeness for underlying disease was low (33.3%), but higher among cases reported as deceased (64.7%). The implementation of technical solutions likely improved the percentage of reporting completeness over time. The objective for reporting underlying disease was partially fulfilled since the data were used in European surveillance. For some underlying diseases, the trend in the data seemed relatively representative despite the low reporting completeness. Several limitations in the data were identified and the data on underlying disease in MSIS should therefore be used with caution. The accessibility and usability of MSIS to report underlying disease were rated as low. It was recommended to stop the data collection on underlying disease in MSIS and report underlying disease as 'unknown' to TESSy until a more feasible solution can be found. It was also suggested that new technical solutions be explored to improve future reporting.

**Role of the fellow:** The fellow coordinated the work, participated in data analyses and was responsible for drafting the report [10]. She collaborated with EUPHEM fellow, Andreas Rohringer (cohort 2020), and Elina Seppälä (EPIET fellow cohort 2019). The fellow was also a co-author of a manuscript using data on underlying disease in COVID-19 cases from Norway reported to TESSy [3]. She participated in quality checks of the Norwegian data and gave feedback on the manuscript.

### ***Training modules related to the assignment/projects***

The EPIET/EUPHEM Introductory Course provided information on how to analyse and interpret surveillance data. A brief introduction to STATA was provided. The Outbreak Investigation Module also provided information on methods used to evaluate surveillance systems, and the RAS Module provided practice through case studies. The Multivariable Analysis Module provided a comprehensive overview of statistical analyses, and practical training in univariable and multivariable regression. The TSA Module provided information on time series data in surveillance.

### ***Educational outcome***

The fellow gained experience in three different projects which covered establishing and evaluating surveillance systems as well as summarising data from a survey. Both microbiological and epidemiological knowledge was applied, and the fellow increased her skills in data analysis using STATA, including univariable and multivariable logistic regression. She also obtained experience in how to interpret different types of surveillance data, writing reports, communicating the results, and formulating recommendations. She further learnt the importance of using surveillance data for public health action and the value of giving feedback to those who report the data.

## 2. Applied public health research

**Supervisors:** Astrid Louise Wester and Ignacio García, NIPH

### *Molecular epidemiology and antibiotic resistance in invasive *Haemophilus influenzae* in Norway 2017–2021*

**Supervisors:** Astrid Louise Wester (Senior Consultant), Ignacio García (Scientific Researcher), Department of Bacteriology, NIPH

Invasive *Haemophilus influenzae* (Hi) disease has decreased in countries that included Hi type b (Hib) vaccination in their childhood immunisation programmes in the 1990s. Non-typeable (NT) and non-b strains are now the predominating causes of invasive Hi disease in Europe, with the highest number of cases reported in young children and the elderly. There are no vaccines available against these strains and beta-lactam resistance is increasing.

In this project, the epidemiology of invasive Hi disease reported to The Norwegian Surveillance System for Communicable Diseases (MSIS) (2017–2021, n=407) was described. The molecular epidemiology (core genome phylogeny) and the presence of antibiotic resistance markers (including chromosomal mutations associated with beta-lactam or quinolone resistance) were examined among 245 previously whole-genome sequenced (WGS) isolates. For the 113 isolates characterised with both WGS and phenotypic antibiotic susceptibility testing (AST) correlation between resistance markers and susceptibility categorisation was assessed by calculation of sensitivity, specificity, and predictive values. Incidence rates of invasive Hi disease in Norway ranged from 0.7 to 2.3 cases per 100 000 inhabitants/year and declined during the COVID-19 pandemic. The Hi isolates clustered in two major phylogenetic groups with subclustering by serotype and multi-locus sequence type (ST). NTHi accounted for 71.8% (176) of the isolates. The distribution of STs was in line with previous European reports. In total, 13 clusters were identified, including four encapsulated and three previously described international NTHi clones with *bla*<sub>TEM-1</sub> (ST103) or altered PBP3 (rPBP3) (ST14/IIA and ST367/IIA). Resistance markers were detected in 25.3% (62/245) of the isolates, with *bla*<sub>TEM-1</sub> (31, 50.0%) and rPBP3 (28, 45.2%) being the most frequent. All isolates categorised as resistant to aminopenicillins, tetracycline or chloramphenicol had relevant resistance markers, and the absence of relevant substitutions in PBP3 and GyrA/ParC predicted susceptibility to cefotaxime, ceftriaxone, meropenem and quinolones. Among the 132 WGS-only isolates, one isolate had PBP3 substitutions associated with resistance to third-generation cephalosporins, and one isolate had GyrA/ParC alterations associated with quinolone resistance. The detection of international virulent and resistant NTHi clones underlines the need for a global molecular surveillance system. WGS is a useful supplement to AST and should be performed on all invasive isolates as part of routine surveillance.

**Role of the fellow:** The fellow drafted the study protocol and participated in project management activities, including drafting the application on ethical approval and Data Protection Impact Assessment. She also organised monthly project meetings and held presentations about the project [20, 21, 22]. She performed data cleaning, analysed the epidemiological and microbiological data in collaboration with the project group, as well as drafted and submitted a manuscript to a peer-reviewed journal [1].

### *Training modules related to the assignment/projects*

The EPIET/EUPHEM Introductory Course gave an introduction to statistical tools, public health microbiology, whole genome sequencing, phylogeny, sensitivity and specificity, and a brief introduction to operational research. The Operational Research Training provided training on how to write an operational research protocol. The Outbreak Investigation Module provided information on data collection, data cleaning and data analysis and communication. An introduction to antibiotic resistance and Quantum Geographic Information System (QGIS) mapping was also provided. The Management, Leadership and Communication in Public Health Module gave training in project management. The Vaccinology Module provided information on vaccine-preventable disease epidemiology.

### *Educational outcome*

The fellow expanded her knowledge in public health epidemiology, bacteriology, antibiotic resistance, and bioinformatics. She got experience in analysing WGS data together with epidemiological data using the Microreact tool. She also gained experience in project management and team management.

## 3. Applied public health microbiology and laboratory investigations

**Supervisor:** Ettore Amato, NIPH

### *3.1 Validation of the *Vibrio cholerae* whole genome sequencing (WGS) pipeline in Finland using an in-house pipeline developed by the Norwegian Institute of Public Health (NIPH)*

**Supervisor:** Ettore Amato (Senior Advisor, Department of Infection Control and Preparedness), NIPH.

The Finnish Public Health Institute (THL) developed a whole genome sequencing (WGS) pipeline for *Vibrio cholerae* that they needed to validate. The NIPH was asked to contribute to the validation by analysing a set of sequences previously analysed at THL in order to compare the outputs from the two pipelines.

At NIPH, 392 sequences were analysed, using the in-house WGS bioinformatic pipeline for detection of *Vibrio*, adapted with Python modules for selected toxigenic *V. cholerae* markers (*toxR*, *ctxA*, *wbeO1*, *wbfO139*, *tcpA* classical and *tcpA* El Tor). All isolates were classified into nine groups based on different combinations of the tested markers. A total of 23 (5.9%) of the isolates were grouped under a non-plausible combination of markers. Sample contamination or phage interaction were identified in six isolates, and several examples of poor sequence quality were found. The results from the species identification using Kraken and the *toxR* marker did not always match. Further, there seemed to be inaccuracies in the biotype marker genes, especially for El Tor. The output from NIPH was compared to the output from the THL pipeline at the defined threshold coverage of 80%. Comparison of the results from the two pipelines showed that the overall concordance of the validation was 96.7% – out of 392 analysed sequences, 379 had an identical typing result. Only 13 sequences had a discordant typing result. The validation indicated that the selected method for WGS-based typing of *V. cholerae* is suitable to be used in THL's reference laboratory for national *V. cholerae* surveillance. Further studies evaluating the use of WGS data compared to traditional laboratory testing could be valuable to estimate the predictive values for the six *V. cholerae* marker genes.

**Role of the fellow:** The fellow analysed the bioinformatic data, gave a presentation [23], wrote a report [11] and submitted a manuscript [2] to a peer-reviewed journal.

### **Training modules related to the assignment/projects**

The EPIET/EUPHEM Introductory Course gave a brief introduction to WGS. The Outbreak Investigation Module provided training in the use of WGS data through case studies. The Biorisk and Quality Management Module provided information about laboratory quality management.

### **Educational outcome**

The fellow obtained new knowledge in bacteriology, bioinformatics and analysis of WGS data and how such data can be used in molecular diagnostics and surveillance. She also got experience in project management, scientific writing and cross-country collaboration.

## **4. Biorisk management**

**Supervisors:** Tone Bjordal Johansen, NIPH, and Aftab Jasir, ECDC

### **4.1 The BSL-3 Laboratory Basic Training Course at The National Biopreparedness Laboratory, NIPH**

**Supervisor:** Tone Bjordal Johansen, Senior Scientist, Department of Infection Control and Preparedness, NIPH

The NIPH organised a biosafety level (BSL)-3 laboratory basic training course at The National Biopreparedness Laboratory for the EUPHEM fellows at the training site. The training was provided by Tone B. Johansen, Irene Rauk and Veronica K. Jensen, and contained information about biosafety and biosecurity. Both theoretical and practical training were given. The course gave an overview of selected highly pathogenic agents and diagnostic methods used. Information about laboratory biosafety levels, microbial risk group classification, shipment of dangerous goods, donning and doffing of PPE, physical barriers, and safe working practices was also provided. The training covered biorisk assessment in an incident-and-accident workshop that simulated potential real-life scenarios. This included handling suspicious letters potentially contaminated with Crimean-Congo haemorrhagic fever virus in the BSL-3 laboratory glove box and viral RNA extraction. FilmArray and real-time PCR were demonstrated. Cultivation of risk group 3 bacterial agents in Class 2 cabinet and DNA isolation were performed.

**Role of the fellow:** The fellow obtained knowledge about biosafety and biosecurity in public health and received practical training in a BSL-3 laboratory. The fellow received a certificate issued by NIPH.

### **4.2 Biorisk and Quality Management (BQM) Module**

**Supervisor:** Aftab Jasir, ECDC

The objective of the module was to provide training on quality management in biomedical and public health laboratories according to the International Organization for Standardization (ISO) 15189 norm and biorisk management in biomedical laboratories. The module provided the fellows with theoretical background in biorisk assessment, quality management and working in a high-containment laboratory. The module contained lectures and case studies to practise biorisk assessment and laboratory audit at the training sites. A two-day BQM module was organised by ECDC in collaboration with scientific coordinators as well as current and previous EUPHEM fellows. The team, consisting of Aftab Jasir, Loredana Ingresso, Silvia Herrera-Leon, Aura Andreasen, Ketija Danovska, Natalie Girin and Rahul Kanjilimadom, organised the module together with EUPHEM fellows Ragnhild Tønnessen, Andreas Rohringer (both cohort 2020), Camille Jacqueline (cohort 2021) and Tone B. Johansen (cohort 2018) from the NIPH.

**Role of the fellow:** In this project, the fellow and Andreas Rohringer from cohort 2020 were involved in organising the module. She participated in the planning and implementation processes. She also revised, amended the content and gave presentations [24, 25, 26, 27] in biosafety management (biorisk assessment, mitigation and performance). Moreover, she helped amend and review the presentation given by Andreas Rohringer on 'Introduction to Biosafety levels, Mitigation and Performance'. The fellow was responsible for making questions in Slido to make the online lectures interactive. The fellow further participated in the module as a facilitator for the case study leading a group through an exercise. She attended the other lectures as well, as an attendee and completed both homework assignments, the biorisk assessment and the laboratory audit.

### **Training modules related to the assignment/projects**

The BQM Module provided the participants with a training in biorisk management in biomedical laboratories, and quality management in biomedical and public health laboratories according to the ISO 15189 norm, in order to build capacity in the EU/EEA Member States for quality and biorisk management.

### **Educational outcome**

The fellow increased her knowledge about biosafety management and biosecurity in public health, which supplemented her previous experience from the animal health sector. She also increased her teaching skills.

## **5. Quality management**

**Supervisors:** Ettore Amato, Didrik F. Vestrheim and Lene Haakensen Kolstad, NIPH

### **5.1. Validation of the *Vibrio cholerae* whole genome sequencing (WGS) pipeline in Finland using an in-house pipeline developed by the NIPH**

**Supervisor:** Ettore Amato (Senior Advisor, Department of Infection Control and Preparedness), NIPH

The THL developed a WGS pipeline for *Vibrio cholerae* diagnostics that needed validation. The NIPH was asked to analyse the sequences previously analysed at THL in order to compare the outputs and contribute to the validation. At NIPH, 392 sequences were analysed, using the in-house WGS bioinformatic pipeline for detection of *Vibrio*, adapted with Phyton modules for selected toxigenic *V. cholerae* markers (*toxR*, *ctxA*, *wbeO1*, *wbfO139*, *tcpA* classical and *tcpA* El Tor). All isolates were classified into nine groups based on different combinations of the tested markers. A total of 23 (5.9%) of the isolates were grouped under a non-plausible combination of markers. Sample contamination or phage interaction were identified in six isolates, and several examples of poor sequence quality were found. The results from the species identification using Kraken and the *toxR* marker did not always match. Further, there seemed to be inaccuracies in the biotype marker genes, especially for El Tor. The output from NIPH was compared to the output from the THL pipeline at the defined threshold coverage of 80%. Comparison of the results from the two pipelines showed that the overall concordance of the validation was 96.7% – out of 392 tested sequences, 379 had an identical typing result. Only 13 sequences had a discordant typing result. The validation indicated that the selected method for WGS-based typing of *V. cholerae* is suitable to be used in THL's reference laboratory for national *V. cholerae* surveillance. Further studies evaluating the use of WGS data compared to traditional laboratory testing could be valuable to estimate the predictive values for the six *V. cholerae* marker genes.

**Role of the fellow:** The fellow analysed the data, gave a presentation [23], wrote a report [11] and submitted a manuscript [2] to a peer-reviewed journal.

### **5.2. EQA *Streptococcus pneumoniae* serotyping**

**Supervisors:** Lene Haakensen Kolstad (Senior Engineer, Department of Bacteriology) and Didrik F. Vestrheim (Senior Medical Officer, Department of Infection Control and Vaccines), NIPH

*Streptococcus pneumoniae* can cause respiratory infections and invasive bacterial disease. The polysaccharide capsule of the bacterium is an important virulence factor. About 100 serotypes of *S. pneumoniae* exist based on differences in the capsular antigens. In Norway, two vaccines protecting against invasive pneumococcal disease are available – a 23-valent polysaccharide vaccine that is mainly recommended for risk groups and a 13-valent conjugate vaccine that is included in the childhood vaccination programme. The National Reference Laboratory for *S. pneumoniae* at the NIPH regularly participates in an external quality assessment (EQA) for serotyping. In May 2021, an interlaboratory EQA (2021A) was arranged by Statens Serum Institut (SSI) in Denmark. Laboratories from seven countries participated. The aim of the EQA was to assess the ability to serotype *S. pneumoniae*, using currently implemented laboratory methods. NIPH received seven samples on transport medium. On arrival, the samples were inoculated on Colombia blood agar and incubated overnight at 35°C with 5% CO<sub>2</sub>. Two different methods were used at NIPH to determine the serotype of the bacteria. The Quellung reaction is considered the gold-standard method and uses antisera against different serogroups and serotypes for the identification. When a specific antiserum binds to a specific capsular antigen, a swelling reaction of the bacterial cells can be observed under the light microscope.



The other method used was MiSeq WGS with SeroBA pipeline for prediction of serotype based on the capsule biosynthesis locus (*cps*) locus. The sequence type was also determined by multi-locus sequencing typing (MLST). For six of the samples, concordant results between NIPH and SSI were found. Serotype 38, 17F, 24F, 15, 6C and 10A were correctly identified. A discrepancy was identified for one sample. In this sample, SSI identified 15B, whereas NIPH identified 15C. The result from NIPH for this sample was solely based on serotyping by WGS and SeroBA. The Quellung reaction could not be performed at NIPH due to lack of bacterial growth after freezing of the sample. It is well known from previous laboratory experience and from the literature that a switch between 15B and 15C may occur. Due to this, the discrepancy was not considered to be an error. However, upon future identification of the 15B or 15C serotypes, it is recommended that the reference laboratory at NIPH report such findings as 15B/C.

**Role of the fellow:** The fellow participated in the laboratory work (Quellung reaction), reviewed the WGS results and drafted the report to SSI and the final report [12].

### ***Training modules related to the assignment/projects***

The BQM Module provided training in quality management in biomedical and public health laboratories, according to the ISO 15189 norm. The module gave an overview of internal and external quality assessment and provided experience in simulating a laboratory audit.

### ***Educational outcome***

The fellow increased her knowledge and practical skills in laboratory quality management. Through the *Vibrio cholerae* project, she obtained experience in validation of a diagnostic pipeline using WGS data. She also wrote a report [11] and submitted a manuscript [2] to a peer-reviewed journal. She also gained experience in EQA and laboratory audits.

## **6. Teaching and pedagogy**

### ***6.1 Management of food-borne and waterborne diseases: 10 steps of an outbreak investigation***

The fellow gave a 45-minute online lecture in Management of Food-borne and Waterborne Diseases [28] at the University of Oslo on 18 May 2021. The lecture focused on the 10 steps of an outbreak investigation. The target audience was master students attending the course, 'INTE4121 Water and Food in a Global Health Perspective'. The fellow revised a presentation previously developed by Emily MacDonald, NIPH, prepared questions for the evaluation, and wrote a reflection note.

### ***6.2 ECDC fellowship Biorisk and Quality Management (BQM) module***

The fellow taught online during the ECDC fellowship BQM module on 17 January 2022. The target audience was EUPHEM fellows (cohorts 2020–2021) and EPIET/PAE fellows (cohort 2020). She was involved in planning, implementation, revision and alignment of presentations, and using Slido to enhance interactivity. She revised, amended and gave presentations in biosafety management [24, 25, 26, 27], and was a facilitator during the group exercise ('HIV' scenario), using the BioRAM tool. The fellow participated in the evaluation of the module and wrote a reflection note.

### ***6.3 The Nordic Mini Project Review Module 2022***

The fellow was a member of the organising team for the Nordic Mini Project Review Module (NMPRM) 2022, NIPH, Oslo, together with Jeanette Stålcrantz, Lèa Franconeri, Andreas Rohringer and Ettore Amato. A two-day hybrid meeting was arranged from 7–8 March 2022. The aim was to network, have informal discussions, and offer guidance on projects that the EPIET and EUPHEM fellows (cohort 2020–2021) from the Nordic countries were working on. The fellow was involved in the planning, implementation and evaluation, gave a presentation [14] and wrote a reflection note.

### ***6.4 Introduction to virology in public health, microbiology lecture series for EPIET, PAE and EUPHEM fellows***

The fellow gave a one-hour online lecture on 'Introduction to Virology in Public Health' on 12 May 2022, as part of the public health microbiology course organised by Andreas Rohringer. The aim was to provide all fellows in cohorts 2020 and 2021 with a basic understanding in public health virology. The fellow made the presentation [29] together with Andreas Rohringer and Daniela Michlmayr (EUPHEMs cohort 2020), prepared questions in Slido and wrote a reflection note.

### ***Training modules related to the assignment/projects***

The EPIET/EUPHEM Outbreak Investigation Module provided the fellows with information on learning styles and techniques, and how to adapt information to a target audience. The Project Review Module provided experience in communication including feedback.

### ***Educational outcome***

The fellow gained experience in teaching by making learning objectives, developing and revising lectures, presenting, making surveys and evaluations. She got experience on how to make online teaching interactive.

## **7. Public health microbiology management**

### ***7.1 ECDC fellowship Biorisk and Quality Management (BQM) module***

The fellow gained experience in management during the planning of the ECDC fellowship BQM module 17-18 January 2022. This included planning of the lectures and schedule, implementation and evaluation of the module, participating in meetings and team collaboration.

### ***7.2 The Nordic Mini Project Review Module 2022***

The fellow was a member of the organising team for the Nordic Mini Project Review Module (NMPRM) 2022, NIPH, Oslo. A two-day hybrid meeting was arranged for EPIET and EUPHEM fellows (c2020-2021) from 7-8 March 2022. The aim was to network and offer guidance and informal discussion on projects that the EPIET and EUPHEM fellows (c2020-2021) from the Nordic countries were working on. The fellow was involved in the planning, implementation, and evaluation of the module. The organising team at NIPH made and sent out information about the module, made pre-module surveys, identified internal and external supervisors, planned the schedule, solved logistics around meeting rooms, security check, ordering of food and social events, performed technical checks, designed and sent out the evaluation, and shared the experiences from the module with the next organisers.

### ***7.3 Management during outbreak investigations***

During the outbreaks of avian influenza, the fellow was actively involved in management and communication on the public health side. She coordinated and drafted the risk assessments [5,6,7] and communicated the results to the public, health-care sector, animal health sector, and the media, and she was involved in writing several news items [32, 33, 36, 38]. The fellow also gained experience in communication during the hepatitis A outbreak and contributed to the writing of news items [29, 39], communicated with the media [31] and drafted the outbreak report [4].

### ***7.4 Management during other EUPHEM projects***

In the operational research project on *Haemophilus influenzae*, the fellow drafted the study protocol and was highly involved in project management collaborating with the project leader on administrative tasks such as drafting the Data Protection Impact Assessment (DPIA) and the application to the Regional committees for medical and health research ethics (REK). The fellow arranged monthly project meetings to discuss the project and assess the progress. The project on *Vibrio cholerae* pipeline validation, also provided valuable experience in project management and coordination.

### ***7.5 Management during other activities***

The fellow also got management and communication experience from participating as a member of the steering group of the Norwegian Preparedness Register for COVID-19 (Beredt C19), and the NIPH's representative in the professional council of the Norwegian Intensive Care and Pandemic Register (NIPaR).

### ***Training modules related to the assignment/projects***

The Outbreak Investigation Module provided information and exercises in risk assessment and communication. The Management, Leadership and Communication in Public Health Module gave information about project management and team management.

### ***Educational outcome***

The fellow developed her competencies and skills in project management during the fellowship through managing several projects in parallel. She got experience in administrative work, logistics, time management and communication. She also developed her skills in team management through collaborating with different people not just from the NIPH, but also with external collaborators.

## 8. Communication

### Publications related to the EUPHEM fellowship

1. **Tønnessen R**, García I, Debech N, Lindstrøm JC, Wester AL, Skaare D. Molecular epidemiology and antibiotic resistance profiles of invasive *Haemophilus influenzae* from Norway 2017-2021. *Frontiers in Microbiology, section Antimicrobials, Resistance and Chemotherapy* doi: 10.3389/fmicb.2022.973257 (published)
2. **Tønnessen R**, Antony-Samy JK, Halkilahti J, Nyholm O, Amato E, Salmenlinna S. Accessible and validated processing of a Whole-Genome Sequencing pipeline for toxigenic *Vibrio cholerae*: a Bioinformatics Workflow. (submitted)
3. Funk T, Innocenti F, Gomes JD, Nerler L, Melillo T, Gauci C, Melillo JM, Lenz P, Sebestova H, Slezak P, Vlckova I, Berild JD, Mauroy C, Seppälä E, **Tønnessen R** Mossong J, Masi SMD, Huart L, Cullen G, Murphy N, O'Connor L, O'Donnell J, Mook PAN, Pebody R, Bundle N. Age Specific Associations Between Underlying Conditions Hospitalisation, Death In-Hospital Death Among Confirmed COVID-19 Cases: A Multi-Country Study Based on Surveillance Data. *Eurosurveillance* <https://doi.org/10.2807/1560-7917.ES.2022.27.35.2100883> (published)

### Reports

4. **Tønnessen R**, Ødeskaug LE, Jensvoll L, Berglund T, Veneti L, Franconeri L, Stene-Johansen K, Rykkvin R, Elshaug H, Lange H. Outbreak of hepatitis A virus, genotype IA, April to October 2021 in Norway [internal report]
5. **Tønnessen R**, Paulsen TH, Jore S, Sorknes N, Bentele H, Hungnes O. Risk assessment on human infection with highly pathogenic avian influenza A(H5N8) in Norway 25.01.21 (<https://www.fhi.no/publ/2021/vurdering-av-risiko-for-smitte-til-mennesker-med-hoypatogen-fugleinfluensa-/>)
6. **Tønnessen R**, Paulsen TH, Jore S, Sorknes N, Bentele H, Hungnes O. Risk assessment on human infection with highly pathogenic avian influenza A(H5N8) in Norway revised 03.03.21 (<https://www.fhi.no/publ/2021/vurdering-av-risiko-for-smitte-til-mennesker-med-hoypatogen-fugleinfluensa-/>)
7. **Tønnessen R**, Bragstad K, Paulsen TH, Taxt A, Grenersen MP, Svarstad E, Iversen B, Hungnes O. Risk assessment on human infection with highly pathogenic avian influenza A(H5N1) in Norway 03.12.21 (<https://www.fhi.no/publ/2021/vurdering-av-risiko-for-smitte-til-mennesker-med-hoypatogen-fugleinfluensa-/>)
8. **Tønnessen R**, Grøslund M, Paulsen TH, Whittaker RN, Dahl J, Klüwer B, Rydland KM, Berg AS, Telle K. Establishing a register-based surveillance system for influenza hospitalisations in Norway during the COVID-19 pandemic [internal report]
9. Brandal L\*, **Tønnessen R\***, Whittaker RN, Rykkvin R, Ulstein K, Wüsthoff L, Steen T, Kløvstad H. Biobehavioral survey, people who inject drugs (PWID), Oslo, 2018 [internal report] (\*Lin Brandal and Ragnhild Tønnessen contributed equally and are shared first authors).
10. **Tønnessen R**, Rohringer A, Seppälä E, Løvlie A. Description and evaluation of the variable 'underlying disease' for COVID-19 in The Norwegian Surveillance System for Communicable Diseases (MSIS) [internal report]
11. **Tønnessen R**, Antony-Samy JK, Halkilahti J, Nyholm O, Amato E, Salmenlinna S. Validation of the *Vibrio cholerae* whole genome sequencing (WGS) pipeline in Finland using an in-house pipeline developed by the Norwegian Institute of Public Health (NIPH) [internal report]
12. **Tønnessen R**, Haakonsen LK, Vestrheim, DF. EQA *Streptococcus pneumoniae* serotyping [internal report]

### Conference presentations

12. **Tønnessen R**, Grøslund M, Telle K, Dahl J, Aune T, Whittaker RN, Paulsen TH. Low number of influenza hospitalisations in Norway 2020–2021. ESWI 2021. [Poster presentation].

### Other presentations

13. Outbreak of hepatitis A in Norway April–October 2021, EPIET/EUPHEM meeting, 25 November 2021, NIPH
14. Outbreak of hepatitis A in Norway April–October 2021, Nordic Project Review Mini Module, 7 March 2022, NIPH
15. Zoonotic influenza. Annual One Health meeting NIPH/NVI/NFSA, 14 December 2020, online
16. Outbreak of HPAI H5N1 in poultry in Norway, NIPH, 24 November 2021, online
17. Influenza during COVID-19, Knowledge program for COVID-19, NIPH, 23 November 2020, online
18. Team Influenza, Beredt C19, Christmas seminar, NIPH, 17 December 2020, online

19. Almost no laboratory-confirmed influenza hospitalisations detected during season 2020–2021 in Norway Results from register-based surveillance. Project Review Module, ECDC, 24 August 2021, online
20. *Haemophilus influenzae* project. Nordic Project Review Module, FHM, 24 March 2021, online
21. Invasive *Haemophilus influenzae* in Norway 2017–2021, Department of Bacteriology, 3 June 2022, online
22. Invasive *Haemophilus influenzae* in Norway 2017–2021: Molecular epidemiology and antibiotic resistance. Project Review Module, Lisbon, Portugal, 1 September 2022.
23. Validation of the *Vibrio cholerae* whole genome sequencing (WGS) pipeline in Finland using an in-house pipeline developed by the NIPH, project meeting FHI/THL, 12 May 2021, online
24. Biorisk management. BQM module. 17 January 2022, online
25. Biorisk assessment. BQM module. 17 January 2022, online
26. Mitigation. BQM module. 17 January 2022, online
27. Performance. BQM module. 17 January 2022, online
28. Management of food-borne and waterborne diseases. University of Oslo, 18 May 2021, online
29. Introduction to virology in public health, Public health microbiology lecture series, 12 May 2022, online

## Other activities

29. [News item](#) Hepatitis A outbreak, published 16 October 2021, NIPH webpages
30. [News item](#) Hepatitis A outbreak, published 3 December 2021, NIPH webpages
31. [Media item](#) Hepatitis A outbreak published 7 December 2021, Food Safety News
32. [News item](#) avian influenza A(H5N8), published 27 November 2020, NIPH webpages
33. [News item](#) HPAI A(H5N8), published 1 March 2021, NIPH webpages
34. [NIPH webpages on avian influenza](#), update, published 1 March 2021
35. [Web article](#) about infection control measures against avian influenza, published 26 March 2021, NIPH
36. [News item](#) HPAI A(H5N1), published 11 November 2021, NIPH webpages
37. [NIPH webpages on avian influenza](#), update, 12 November 2021
38. [News item](#) about risk assessment HPAI A(H5N1), published 3 December 2021

## Other training modules

39. Nordic project review mini module 23.03.2021 – 24.03.2021, Folkhälsomyndigheten, Sweden, online
40. Nordic project review mini module, 07.03.2022 – 08.03.2022, Oslo, Norway, hybrid

## 9. Other activities

None.

## 10. EPIET/EUPHEM modules attended

1. Outbreak investigation, 07.12.2020 – 11.12.2020, online
2. Introductory course, 28.09.2020 – 16.10.2020, online
3. Operational research training, 09.11.2020 – 10.11.2020, online
4. Multivariable analysis, 15.02.2021 – 19.02.2021, online
5. Multivariable analysis Cox regression inject day, 18.03.2021, online
6. Intro course part 3, week 1, 24.04.2021 – 30.04.2021, online
7. Intro course part 3, week 2, 04.05.2021 – 07.05.2021, online
8. Rapid Assessment and Survey Methods, 05.05.2021 – 06.05.2021, online
9. Project review module 2021, 23.08.2021 – 26.08.2021, online
10. Biorisk management and quality, 17.01.2022 – 18.01.2022, online
11. Vaccinology, 14.02.2022 – 18.02.2022, online
12. Time series analysis, 04.04.2022 – 08.04.2022, Rome, Italy
13. Management, Leadership and Communication in Public Health, 13.06.2022 – 17.06.2022, Stockholm, Sweden
14. Project review module 2022, 29.08.2022 – 02.09.2022, Lisbon, Portugal

## 10. Other training

1. ESCAIDE, 24.11.2020 – 27.11.2020, online
2. ESCAIDE, 16.11.2021 – 19.11.2021, online
3. ESCAIDE, 23.11.2022 – 25.11.2022, Stockholm, Sweden



# Discussion

## Coordinator's conclusions

One of the main goals of the EUPHEM programme is to expose fellows to diverse multidisciplinary public health experiences, thus enabling them to work across different disciplines. This report summarises all the activities and projects conducted by Ragnhild Tønnessen during her two-year EUPHEM fellowship (cohort 2020) as an MS-track fellow at the Norwegian Institute of Public Health in Oslo, Norway.

The portfolio includes laboratory and epidemiological projects covering a variety of disease programmes, such as emerging diseases, sexually transmitted diseases, food and waterborne diseases, respiratory tract infections, vaccine-preventable disease and antimicrobial resistance. The projects described here 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 demonstrated the capability of addressing communicable disease threats in a structured joint approach between public health microbiology, epidemiology and link with zoonotic diseases which could be a future threat for humans (for example, the first outbreak of highly pathogenic avian influenza (HPAI) in wild birds in Norway, and the first outbreak of highly pathogenic avian influenza (HPAI) in poultry in Norway). By performing risk assessment the fellow has demonstrated the importance of timely assessment of risks and providing evidence for future preparedness. In addition, she has learnt and applied the use of whole-genome sequencing to detect genotypes and link it with epidemiological data to increase the accuracy of the transmission of the diseases. Furthermore, she has been able to identify resistance markers and take part in key steps of outbreak investigations at the national level, set up or evaluated surveillance systems to optimise correct control measures. The projects have been methodically selected to cover not only important international and national public health topics such as, influenza, infections or drug-resistant bacteria among others, but also a very broad panel of microorganisms. Also involved were different professional groups, such as physicians, laboratory technicians, epidemiologists, statisticians, government officials, public health officers and logisticians, which strengthened the fellow's ability to work in a multidisciplinary team and to adapt to different environments and contexts. Ragnhild has been active in contributing to the training of others during her fellowship, with her 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, or provided to the public health authorities to promote decision making in the context of public health. All the activities were complimented by the training modules providing theoretical knowledge and a baseline for learning by doing. The contributions made by Ragnhild indicate the importance of developing and maintaining a critical mass of highly skilled field public health microbiologists within Member States and 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

Ragnhild started the EUPHEM fellowship after being heavily involved in the initial assessment and management of COVID-19 in Norway, with a strong motivation to broaden her knowledge and experience. She quickly outlined how to complete the fellowship. Ragnhild took on a research project on *Haemophilus influenzae* molecular epidemiology, a field far from her previous experience. In this project, as in other activities, she has engaged her co-workers and established good, strong relationships with project supervisors and co-workers. She has worked independently, and managed a high workload with several tasks in parallel.

Ragnhild has pulled through different projects during a challenging time due to the pandemic response. She has demonstrated a very good understanding for the need and aim of the different tasks she has performed, resulting in outputs that have added to national and international public health activities. In her work, she has balanced very well between pragmatic problem-solving and scientific work according to the need of the situation.

## Personal conclusions of fellow

The EUPHEM programme has been an excellent experience that has expanded my knowledge in public health microbiology and epidemiology. The two-year training has through different modules, projects and activities, provided me with a very useful toolbox that I will always carry with me and use in the face of new challenges. I have particularly enjoyed increasing my knowledge within vaccinology, bacteriology, antibiotic resistance, One Health and use of whole-genome sequencing data.

Going through this training during a pandemic has been challenging in many ways. However, it has given me a unique experience, and provided another dimension into the fellowship on how to deal with pandemics, and how to learn and improve for the future. The programme has also provided important skills in management, leadership and communication, which I have personally found very useful and inspiring. Through this journey, I have expanded my professional network in Norway and Europe, and I really appreciate having met so many wonderful people. The training has provided me with several new competencies and skills that I will use in my future career.

## Acknowledgements of fellow

First, I would like to thank my frontline coordinator at ECDC, Aftab Jasir, who has always been there for me during these two years, sharing her expertise and experience and mentoring me in an excellent way. I would also like to thank Didrik F. Vestrheim, my training site supervisor at the NIPH, for his wisdom, availability and constructive feedback. I am very grateful to NIPH for giving me the opportunity to join the fellowship in the middle of a pandemic. I thank my fantastic colleagues at NIPH, including the EPIET and EUPHEM alumni, who have supported and encouraged me through the training and given me time to focus on the fellowship. I especially thank Trine Hessevik Paulsen and Elina Seppälä. I am very grateful to all the supervisors as well as internal and external collaborators who have shared their knowledge and experience with me during these two years. I thank Pawel Stefanoff and Ettore Amato for their coordination of the EPIET/EUPHEM activities at NIPH during these years. I would like to thank all the EUPHEM and EPIET fellows in cohort 2020 for their kindness, support and collaboration. A special thanks goes to my co-fellows at NIPH, Andreas Rohringer, Jeanette Stålcraantz and Lèa Franconeri. Finally, I thank my family for their patience, love and support.