



Summary of work activities

Teodora Vremeră

European Public Health Microbiology Training Programme (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 Teodora Vremeră, cohort 2020 of the European Public Health Microbiology Training Programme (EUPHEM) at the National Institute for Public Health (Institutul Național de Sănătate Publică, INSP), Bucharest, Romania.

Pre-fellowship short biography

Teodora Vremeră is a medical doctor, with residency in Laboratory Medicine. She graduated from the Grigore T. Popa University of Medicine and Pharmacy, Iași, Romania, where she also completed her PhD (her thesis was entitled, 'Evaluation by molecular biology techniques of antibiotic resistance and of certain virulence factors of *Staphylococcus aureus* (2012)'). Before starting the Fellowship, Teodora was a lecturer at the Microbiology department of the Grigore T. Popa University of Medicine and Pharmacy, Iași (2008–2019). She was also in charge of the Mycology department at St. Spiridon Emergency Clinical County Hospital (2013–2019). Teodora was employed at the Molecular Biology department, Regional Centre of Public Health (RCPH), Iași (2014–2019).

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From 2019, Teodora has been working at the National Centre for Communicable Diseases Surveillance and Control (NCCDSC) which is a part of the National Institute for Public Health (NIPH), Bucharest.

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 ¹.

1. Epidemiological investigations

1.1 Outbreak investigations

1.1.a A possible food-borne illness outbreak at the Socola Institute of Psychiatry Iași, Iași County, Romania, 2021

Supervisors: Prof. Dr. Adriana Pistol (NIPH), Prof. Dr. Luminita Smaranda Iancu (NIPH)

On 9 February 2021, 43 cases of gastroenteritis among patients and staff at the Socola Institute of Psychiatry, Iași, Romania were reported by the District Public Health Authority (DPHA), Iași. Case definition included any person hospitalised or working at the Institute of Psychiatry who presented symptoms (such as nausea, vomiting, abdominal pain, or diarrhoea) since 5 February 2021, after consuming food at the hospital canteen from 4 February. The DPHA Iași identified 286 food consumers (overall attack rate: 15%). Of those that met the case definition, 37 were hospitalised patients and six were medical staff. The food was prepared daily at the food block. The patients who got ill were hospitalised in 10 wards, with total number of patients at 136 (attack rate: 27%). The first patient developed illness on 5 February 2021, the outbreak peaked between 5–6 February, and the last case was reported on 9 February. The shape of the epidemic curve suggested the point source of the outbreak. There were no deaths. All illness cases were mild and resolved within 24 hours without antibiotic treatment. Throat, nasal swabs and stool samples from patients and the food block staff were sent to the DPHA Iași for laboratory testing. No microbial pathogen was detected in the stool samples of the sick patients. The presence of other *Enterobacteriaceae* and/or coagulase-positive *Staphylococcus* on the hands of the food block staff and on the various surfaces of the food block suggested poor hygiene practices. Sending trawling questionnaires to the patients and analytical epidemiology was not possible, due to the nature of the disease of patients hospitalised at the Socola Institute. The epidemiological investigation lead by the DPHA Iași concluded that the acute gastroenteritis illness was a result of non-compliance of staff with hygiene measures. The recommendations aimed at enforcing compliance to hygiene measures in the food block by the working staff.

Role: The EUPHEM fellow was co-investigator, assisting DPHA Iași and Regional Center for Public Health (RCPH), Iași during the investigation, participating in descriptive epidemiology and data analysis, making the epidemic curve, sending to the DPHA Iași a list of questions to be included in their questionnaires for the staff at the Socola Institute, analysing the reports from the DPHA and RCPH, Iași and reporting back to the NIPH–NCCDSC.

¹ 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 Acute gastroenteritis outbreak of possible norovirus origin in Râșnov city, Brașov County, Romania, 2021

Supervisors: Prof. Dr. Adriana Pistol (NIPH), Prof. Dr. Luminita Smaranda Iancu (NIPH)

On 21 July 2021, family doctors from Râșnov city, Brașov County, notified DPHA, Brașov regarding a significant increase in the number of patients with digestive symptoms: nausea, vomiting, watery diarrhoea, asthenia, loss of appetite, or fever. The team from DPHA Brașov, including representatives from the Public Health Control Service, the Department for the Assessment of Risk Factors in Living and Working Environment, and the Communicable Disease Surveillance and Control Department (CDSCD), Brașov launched an investigation into the possibility of an outbreak by water transmission. A case was defined as a sudden onset of at least one symptom (vomiting, diarrhoea, abdominal pain, and/or fatigue) with the start date on 19 July 2021, in residents of Râșnov city between 17–25 July 2021. Additional symptoms and signs included fever, chills, headache, and muscle aches. DPHA Brașov sent water specimens and stool samples for laboratory testing. Case finding involved family doctors, Râșnov Permanent Center and the hospital units which were requested to send the nominal evidence of acute diarrhoeal disease cases. DPHA Brașov described the outbreak by time, place and person. They identified 352 cases (with no deaths) among the 18 481 population of Râșnov city (Attack rate: 1.9%) between 18–30 July 2021. Five of the seven stool samples sent for RT-PCR testing were positive for Norovirus genotype GII.P17-GII.17 with grouping of strains in the same cluster (100% identity for ORF1-ORF2 junction sequence). The attack rate was highest among 1–4-year olds (7%). Cases first occurred on 18 July 2021, peaked in 20 July and decreased rapidly after 24 July. Following the outbreak investigation, DPHA Brașov concluded that norovirus is a probable etiology for the outbreak, but was not able to establish with certainty the route of transmission. Recommendations to the city population: to consume bottled drinking water or boiled and cooled water, and to respect personal and collective hygiene rules.

Role: The fellow was not the main investigator, but assisted the District Public Health Authority Brașov during the descriptive epidemiology. She drew the epidemic curve, and was involved in writing the questionnaire that was sent to the population.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course: At the Introductory Course, the fellow learnt principles of outbreak investigation, data collection through questionnaires, choosing and conducting epidemiological studies, and how to formulate appropriate public health recommendations.

Outbreak Investigation Module: The fellow learnt the ten steps of an outbreak investigation, development of case definitions, making and interpreting epidemic curves, writing questionnaires, and writing an outbreak report.

Educational outcome

The fellow collaborated with epidemiologists in all the steps of their investigation and applied the microbiological and epidemiological knowledge that was acquired during the Introductory Course and the Outbreak Investigation module. The fellow contributed to making the questionnaires, descriptive epidemiology, and data analysis.

1.2 Surveillance

1.2.a Seroprevalence study of SARS-CoV-2 infection in Romania, 2020

Supervisors: Prof. Dr. Adriana Pistol (NIPH), Prof. Dr. Luminita Smaranda Iancu (NIPH)

Many COVID-19 cases remain undiagnosed by RT-PCR, due in part to uneven distribution of PCR testing capacity across the country. In this context, the aim of the seroprevalence study was to estimate the burden of SARS-CoV-2 infection, based on the detection of anti-SARS-CoV-2 antibodies, in order to substantiate preventive measures, such as immunisation strategy. This represented the largest national seroprevalence study of SARS-CoV-2 infection in Romania. The project took place between June and November 2020 and involved the collection of residual sera from a representative sample of the Romanian population, in each county of the eight regions (South, South-East, South-West, West, North-West, North-East, Center and Bucharest-Ilfov). The project was coordinated by the National Institute for Public Health and all samples were tested at the NIPH laboratory for detection of IgG antibodies, using chemiluminescent immunoassay. There was a total of 19 597 samples from persons aged 0–97 years (median 48 years), and of those, 6.2% (N=1 213) showed anti-SARS-CoV-2 IgG antibodies. No significant differences between females and males ($p=0.95$) were observed. Taking into account the official population of over 19 million inhabitants, the seropositivity rate suggested that almost 1.2 million people had COVID-19 by the end of the study, 4.5 times more than those officially confirmed. The project revealed that the seropositivity rate varied by age group, and was higher in middle-age population, 40–59 years (8.4%). Observed variations between age groups might be due to differences in work life and social interaction, this supports early vaccination policies targeting certain population groups. The prevalence of the immune response varied across the eight regions of Romania, being higher in the North-East and South (8%) than in the North-West (3%) and Center (4.1%) ($p<0.00001$). This may reflect differences in public health responses and behavior, and highlight the importance of maintaining non-pharmaceutical preventive measures. Although there were limitations, the study showed that COVID-19 seroprevalence was low in the general population with a level insufficient to ensure herd immunity. Based on that, the recommendation was to repeat the study in the context of vaccination, to reflect population immunity more accurately.

Role: The fellow was involved in drafting the laboratory criteria for the study methodology, selection of reagent characteristics, procurement of consumables, and data analysis. She presented the poster 'Seroprevalence study of SARS-CoV-2 infection in Romania, 2020' – at the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) in November 2021.

1.2.b COVID-19 pandemic support for surveillance of SARS-CoV-2

Supervisors: Prof Dr Adriana Pistol (NIPH)

The NIPH coordinates the activities in the field of disease prevention, surveillance, control and health policies. The 'COVID-19 Surveillance Methodology' is the document elaborated by the NIPH-NCCDSC that guides the surveillance and the testing activities for this disease in Romania. The document includes: epidemiological case definitions, criteria for prioritisation of testing, case reporting, and laboratory recommendations (sample collection, testing, interpretation, quality control, results reporting and biosafety measures). According to the national legislation, the laboratories that carry out RT-PCR testing for SARS-CoV-2, from either the public or private sector, have the responsibility to report case-by-case results to the Ministry of Health on the national online platform, Corona Forms, and aggregated data on the national online platform, Alerte.ms, or to the NIPH via e-mail, with respect to: the total number of samples tested, the number of tested samples in the previous 24 hours (on demand or according to COVID-19 methodology), the number of persons tested, the reagent stocks for amplification, and for extraction. The database layout for the centralisation of the reports from all the laboratories was created. Before the start of reporting, laboratories received instructions regarding the reporting requirements. Aggregated data reported by laboratories, either on the online platform, Alerte.ms, or via e-mail, were centralised and verified for errors at the level of NIPH-NCCDSC. In case of errors, laboratories were contacted and explained the correct way of data reporting. The corrected version of the database was then confronted with the database held by the Ministry of Health and sent to the main decisionmakers. This was a daily process, from the start of laboratory reporting of SARS-CoV-2 testing in Romania during the pandemic. Also, the NIPH proposed the project, 'Seroprevalence study of SARS-CoV-2 infection in Romania, 2021', to the Ministry of Health, with the aim to estimate the proportion of the immune population after the introduction of anti-COVID-19 vaccination in 2021. The project objectives were: to estimate the prevalence of SARS-CoV-2 infection at national and regional levels and by age groups, through detection of anti-N antibodies, to estimate the proportion of people with post-vaccination immunity by detecting the presence of anti-S antibodies, to estimate of the fraction of subclinical / asymptomatic infections. The cross-sectional study was planned to take place from June to August 2021, and would involve the selection of a sample of 10 000 people, with regional representation and by age groups, with collection of residual sera from 3–5 laboratories selected at the level of each county, excluding laboratories belonging to COVID-19 or pulmonology hospitals. Testing of specimens was planned to be done by the NIPH laboratories using chemiluminescent technology for qualitative detection of anti-Nucleocapsid IgG antibodies and quantitative detection of IgG anti-Spike/RBD. Data collection from consenting participants would aim at gathering information on sex, age, as well as chronic underlying diseases such as: diabetes, obesity, and other metabolic diseases, including congenital, cardiovascular, kidney, oncological, and pulmonary diseases. Since funding from the Ministry of Health was not approved for 2021, the project was postponed, initially estimated for 2022, and remains to be finalised by a fellow employed at the site in the future.

Role: The fellow was responsible for writing and updating the 'COVID-19 Surveillance Methodology' recommendations for laboratories regarding biosafety and testing procedures. She also participated in creating the database layout for the centralisation of lab reports, and was involved in data centralisation, verification of lab reports, contacting laboratories and communicating with the Ministry of Health representatives to report errors. The fellow was responsible for the training and supervision of medical residents who assisted in this task. Also, the fellow wrote the project proposal that was sent for approval to the Ministry of Health, regarding 'Seroprevalence study of SARS-CoV-2 infection in Romania, 2021'.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course: During the Introductory Course, the fellows were familiarised with surveillance systems (development, evaluation and data analysis), as well as writing a project.

Project Review Module: During this module, the fellows were trained on basic presentation and communication skills; the poster presentation for ESCAIDE 2021 was reviewed by peers.

Multivariable Analyses module: During this module, the fellows learnt how to apply statistics for epidemiological analysis.

Educational outcome

The fellow gained knowledge on the COVID-19 surveillance system and reporting methodology, communicating with peers and stakeholders, writing the study protocol and surveillance methodology, data cleaning and analysis, writing abstract proposals and presenting results to international conferences.

2. Applied public health research

2.1 Assessment of immune response in elderly persons from residential facilities following COVID-19 vaccination

Supervisors: Prof Dr Luminita Smaranda Iancu, Prof Dr Adriana Pistol

Given that severe COVID-19 affects with predilection the elderly, this category was among the first included in the Romanian national vaccination campaign. In order to support the decision making for COVID-19 management in this vulnerable population group, the project aimed to assess the immunisation status and antibody dynamics in elderly people from residential facilities following vaccination. The prospective longitudinal cohort study was conducted between April–October 2021 and involved the detection of anti-SARS-CoV-2/RBD IgG antibodies from volunteers in residential care facilities, aged 65 years and above. Repeated serum samples at minimum two weeks and then at three months and six months after vaccination, were obtained from consenting participants. The project was coordinated by the National Institute for Public Health and all samples were tested at the NIPH laboratory for detection of IgG antibodies, using chemiluminescent immunoassay (SARS-CoV-2 IgGII Quantitative, Abbott), and the results were expressed in binding antibody units ($1 \text{ BAU/mL} = 0.142 \times \text{AU/mL}$). A total of 650 samples were analysed from participants in 23 residential facilities from seven counties. Participants were aged 65–110 years (median 79 years), and 408 (62.8%) were women. With one exception, all volunteers had received the same type of mRNA vaccine (BNT162b2). The project showed that, of the total number of volunteers, 59.4% ($N=386$) have had COVID-19 disease before vaccination. Analysis at the first sample collection ($N=635$) showed the presence of antibodies in 98.7% of participants (median 1287.2 BAU/mL, range: 7.1–5680 BAU/mL). The study revealed that the antibody levels were significantly higher among those previously infected, than in those without previous infection ($p < 0.00001$). In the case of 533 volunteers, for which all three serum samples were available for the duration of the study (at two weeks, three months and six months), the dynamics of antibody response was also evaluated, and loss of detectable antibodies was observed in 0.4% of cases at three months and 2.8% of cases at six months after vaccination. A significant decline in median antibody levels was observed at each new sample collection (first serum sample=1273.4 BAU/mL, at three months=887.6 BAU/mL, at six months =339.3 BAU/mL, $p < 0.001$). The study findings supported vaccination even in those previously infected and who benefited from naturally acquired immunity.

Role: The fellow wrote the study protocol, the final reports for the Ministry of Health, developed questionnaires, developed data entry mask, performed data analysis, presented results through a poster presentation at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2022) and submitted a manuscript to a peer-reviewed journal (*Eurosurveillance*-D-22-00154, and *Frontiers in Epidemiology*, ID 944820).

2.2 Assessment of immune response in healthcare workers following COVID-19 vaccination

Supervisors: Prof Dr Luminita Smaranda Iancu, Prof Dr Adriana Pistol

The aim of this project was to evaluate antibody dynamics in healthcare workers one year after the completion of COVID-19 vaccination (two doses of BNT162b2 vaccine), with or without booster shots. The rationale for this was the knowledge that SARS-CoV-2 continuous variability and the waning immune response against the virus may represent a threat to the efficacy of COVID-19 vaccines. The project was coordinated by the National Institute for Public Health. Laboratory testing was carried out at NIPH laboratories, in collaboration with the Ștefan S. Nicolau Institute of Virology (IVN). The project was a prospective longitudinal cohort study. The study group was followed up between March 2021 and January 2022. The project involved the detection of anti-SARS-CoV-2/RBD IgG antibodies from volunteer healthcare workers in four major hospitals in Bucharest. Repeated serum samples at minimum two weeks, and then at three months, six months, nine months and 12 months after vaccination, were analysed at NIPH using chemiluminescent immunoassay (SARS-CoV-2 IgGII Quantitative, Abbott), and the results were expressed in binding antibody units ($1 \text{ BAU/mL} = 0.142 \times \text{AU/mL}$). In addition, neutralising antibody activity was determined using a commercial SARS-CoV-2 surrogate virus neutralisation test (sVNT) (GenScript cPass™ SARS-CoV-2 Neutralization Antibody Detection Kit, GenScript, USA), and was carried out at IVN. The study revealed a marked decrease in anti-S/RBD antibody levels during the first eight months post-vaccination, followed by a temporary increase after the booster shot. An increase in antibody level was also noticed at three months post-booster administration, but only in volunteers with prior infection. The project concluded that the protection against the ancestral variant and Omicron variant is maintained at least three months after booster in healthcare workers, possibly reflecting a continuous antigenic stimulation in the healthcare professional setting.

Role: The fellow wrote the study protocol, the final reports for the Ministry of Health, developed questionnaires, developed data entry mask, participated in data analysis as well as writing and submitting a manuscript to a peer-reviewed journal.

2.2 Determining the epidemiology of drug-resistant invasive candidiasis

Supervisors: Prof Dr Luminita Smaranda Iancu, Dr Adriana Pistol

Fungal infections have emerged as important public health problems, especially among hospitalised individuals with serious underlying diseases. In these patients, invasive candidiasis is the most common fungal disease. The main aim of the project was to describe the epidemiology of invasive drug-resistant *Candida* spp isolates causing infections in hospitalised patients in Romania, in order to evaluate the impact on public health and the appropriate infection management for the design of a national programme strategy surveillance for the future. The project aimed to describe the incidence, mortality, and resistance patterns of invasive *Candida* spp infections in Romania.

The retrospective study was meant to be carried out for a period of one year. The objectives were: to identify patients with invasive drug-resistant *Candida* spp infections in selected Romanian acute care public hospitals from the eight country regions; to assess the mortality rate among patients with invasive drug-resistant *Candida* spp infections; to determine the duration of hospital stay in those patients as opposed to patients with invasive drug-susceptible *Candida* spp infections; and to characterise demographics and co-morbidities in the two categories of patients. The three aspects to be monitored were: the monthly number of positive blood cultures with non-albicans species since an increase could indicate a possible outbreak of *C. auris* bloodstream infection, the antifungal susceptibility of non-albicans *Candida* spp isolated from invasive infections and resistance to fluconazole as it may indicate that further confirmatory identification was needed. Isolates from bloodstream, catheter, or cerebrospinal fluid with particular antimicrobial-resistance profile would be collected from hospital laboratories, in order to be retested for identification and antimicrobial resistance profile. The study was designed as a pilot starting from a laboratory network of minimum six laboratories with the idea of having a baseline to design a surveillance system at the national level.

Although the project was planned to take place between January 2021 and December 2021, the COVID-19 pandemic and the lack of funding, caused the study to be postponed. It will be finalised by another fellow in the future.

Role: Teodora wrote the project proposal form for this project and set up communication with the laboratories participating in the pilot study.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course: During the EPIET/EUPHEM Introductory Course, the fellow learnt to develop a research question, design a study and write the protocol, as well as to present the results and draft a manuscript. Notions such as prevalence, incidence and analytical epidemiological analysis were presented.

Management, Leadership and Communication in Public Health Module: The module trained the fellow on successful project management and communication with public health authorities.

Educational outcome

The fellow gained experience in writing study protocols and managing projects, data analysis and communicating with peers and public health authorities. She participated in writing scientific papers and had several presentations at national and international level.

3. Applied public health microbiology and laboratory investigations

3.1 Identification of antimicrobial-resistant *Neisseria gonorrhoeae* during training at Instituto de Salud Carlos III (Carlos III Health Institute), Madrid, Spain

Supervisors: Dr Julio Vázquez Moreno, Dr Raquel Abad Torreblanca

Currently, a very small number of gonorrhoea cases are captured by the STD surveillance system in Romania and the disease remains under reported. Given the difficulties related to the culturing of this fastidious microorganism and the costs for molecular diagnosis, the microscopic exam remains the most available method for diagnosis in males. It is possible that the disease remains frequently undetected in females, especially considering its clinical evolution and diagnostic particularities. This is why data on antimicrobial resistance is limited to a few reports from individual studies in literature. Introduction of NGS-based analysis at the national level will help identify resistance determinants and their spread in the gonococcal population, and ultimately improve the reporting of country data and develop better responses to the goals set by ECDC and WHO for disease surveillance. The objective was to apply whole-genome sequencing methodologies and tools for molecular epidemiology and surveillance of gonococcal antimicrobial resistance, during fellow training at Instituto de Salud Carlos III, Madrid, Spain (16 May – 3 June 2022). The minimum inhibitory concentrations (MICs) of penicillin, ceftriaxone, cefixime, azithromycin, ciprofloxacin, tetracycline, gentamicin and spectinomycin were determined on subcultures of gonococcal strains of interest using E-test (bioMérieux) and the results were interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) standard. Whole genome sequencing was also carried out. After DNA extraction and quantification, multiplexed libraries were created with Nextera® XT DNA Library Preparation kits (Illumina, San Diego, California) and WGS was performed using NextSeq Illumina platform. The assembled genomes were analysed using the platforms – PubMLST (<https://pubmlst.org/neisseria/>) and Pathogenwatch (<https://pathogen.watch/>).

Role: The fellow participated in antimicrobial susceptibility testing, DNA extraction, whole genome sequencing and sequence analysis. She presented the results in the Instituto de Salud Carlos III (ISCIII) Training Report.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course: During the Introductory Course, the fellow was presented a summary on microbiological techniques, including antimicrobial resistance and sequencing, as well as the basics of analysis of whole genome sequencing data and interpretation of phylogenetic trees for public health purposes.

Educational outcome

The fellow gained understanding of the Spanish surveillance system for gonorrhoea, in sequencing technique and sequence analysis. She applied concepts of bacteriology, improved her knowledge about genetic determinants of resistance, learnt about preparation of clinical isolates for sequencing, and gained more expertise in analysing WGS data.

4. Biorisk management

4.1 Mycobacterium tuberculosis diagnostics workflow in BSL-3 laboratory during training at Instituto de Salud Carlos III (Carlos III Health Institute), Madrid, Spain

Supervisor: Laura Herrera Leon

The objective of this project was to train the fellow on the working protocol and biosafety requirements for a BSL-3 laboratory. During the training period at Instituto de Salud Carlos III, the fellow learnt about the workflow for *M. tuberculosis* diagnosis at the BSL-3 laboratory. She became familiar with the facilities, the use of personal protective equipment, protocol for entry and exit of personnel to the laboratory and decontamination, planning of a safe experiment in the BSL-3 lab, sample reception at *Orientación diagnóstica* Department and the control of regulations for the shipment of dangerous goods, sample preparation and storage, handling of cultures, antimicrobial susceptibility testing and interpretation, DNA extraction for molecular tests, result data sharing.

Role: The fellow carried out subculture of *M. tuberculosis* strains of interest from stock culture onto Lowenstein-Jensen medium, preparation of spin-column DNA extraction from *M. tuberculosis* cultures and quantification with QuantiFluor® ONE dsDNA System kit (Promega, Wisconsin, US), and participated in the training on *M. tuberculosis* genome assembly using SeqSphere and Enterbase. She presented the results in the ISCIII Training Report.

Training modules related to the assignment/projects

Biorisk and Quality Management Module: During the module, the fellow learnt about methods for biorisk identification and mitigation, sample packaging, international shipment and guidelines on biosafety management in laboratories.

Educational outcome

The fellow gained knowledge on the different biosafety levels, their uses and characteristics. She learnt about the organisation of the TB laboratory and the basic principles when working at a BSL-3 facility.

5. Quality management

5.1 Laboratory visit and internal audit at the Regional Centre for Public Health Iași, Romania

Supervisors: Prof Dr Adriana Pistol

The National Institute of Public Health, Romania has four molecular biology laboratories at the level of Regional Centre for Public Health – Bucharest, Cluj, Iași and Timișoara – which were involved in RT-PCR testing for COVID-19 during the pandemic. The fellow participated in a lab visit on 5–6 August 2021 at the Regional Centre for Public Health, Iași on behalf of the National Centre for Communicable Diseases Surveillance and Control. Another expert was invited to participate on behalf of the Institutul Național de Cercetare-Dezvoltare Medico-Militară (INCDMM) Cantacuzino and the Albanian Foundation Southeast European Centre for Surveillance and Control of Infectious Diseases (SECID). The visiting team met with the head of the Epidemiology Department and the Department for Environmental Hygiene, the PCR laboratory being common for the two departments. The following laboratory personnel were interviewed: one medical resident responsible for the PCR amplification and the results interpretation, one medical specialist responsible for the extraction, one technician responsible for the sample reception, and one medical assistant responsible for reporting results on the online national platform. The team evaluated the existing laboratory space and rooms, equipment, working protocols and procedures. A summary of the main findings of the visit was produced to include: lab organisation, staff, activity, and quality management system. The presence of a unidirectional workflow for molecular amplification procedures comprised of a separate PCR master mix room, a reception room, a nucleic acid extraction room, and an amplification room; the existence of SOPs; equipment maintenance, metrology and calibration managed by specialised suppliers contracted for specific equipment, and recordings of intervention reports; compliance with biosafety requirements for COVID-19 testing with RT-PCR; the procedures for disinfection; management of contaminated and non-contaminated waste; procedures for reception and recording of biological samples: existence of logbooks and patient records; storage conditions of samples and reagents: separation of specimens and reagents, labelling of boxes and storage vials in freezers and refrigerators; the protocol for viral RNA extraction; conditions for preparation of PCR master mix; the protocol for RT-PCR amplification; result interpretation; test reports of molecular genetic testing to include: patient identifier, test method, nucleic acid targets, test performance specifications and limitations; participation in available proficiency testing and the results for molecular EQA. Laboratory staff involved in COVID-19 testing were evaluated for their level of experience, need for training, collaboration with the surveillance system and the National Reference Laboratory, management and supervision.

Recommendations for the optimisation of lab activity and implementation of best laboratory practices and organisation for COVID-19 testing using RT-PCR were made with emphasis on the need for the implementation of a Lab Information Management System, the need to increase testing capacity by increasing technical staff, and the need for periodic on-site training in specialised laboratories.

Role: The fellow, together with the expert from INCDMM Cantacuzino, evaluated the laboratory of the Regional Centre for Public Health, Iași during a two-day period. The results of the evaluation were presented in the Lab audit RCPH Report.

5.2 Quality management module homework: laboratory audit for RCPH Bucharest

Supervisors: Prof Dr Adriana Pistol

On 23 March 2022, the fellow and the Laboratory coordinator carried out an audit on the processes of management, quality control and the documentation available at the NIPH Bucharest laboratory. The audit focused on issues such as, accommodation and environmental conditions, quality management, quality assurance, pre-analytical process and specimen management, analytical process, post analytical process, quality improvement, quality document and document control, technical record, control of non-conformities, equipment logbooks, documentation of biosafety, documentation of personnel and stock, standardised operating procedures, standardised report format, surveillance and outbreak response documentation, and transport documentation. Overall, it was concluded that the laboratory activity was satisfactory, with a general indicator of 91%. Process Management and Quality Control were well registered. However, the audit showed that the laboratory could improve in areas regarding documentation in preparation for ISO 15189 accreditation, and there was a need for quality manual and documentation logbook.

Role: The fellow conducted the audit and produced the RCPH, Bucharest Lab audit report.

Training modules related to the assignment/projects

Biorisk and Quality Management Module: The fellow learnt to conduct an internal audit. The module emphasised the role of quality management system in the laboratory, technique validation, existence of SOPs and quality manual, as well as the importance of external quality assessments.

Educational outcome

Teodora has extended previous experience of being involved in the accreditation procedure and participating in EQAs, and is thus familiar with concepts of quality assurance. However, this training allowed her to become more knowledgeable in the role of performing a lab audit and writing an audit report.

6. Teaching and pedagogy

6.1 Laboratory investigations for COVID-19, integrated with those for influenza, in 2020–2021 season

This lecture was held for two days (19–20 November 2020) during a national online workshop for general practitioners, epidemiologists and clinicians involved in ARI, ILI/SARI surveillance. The theme of the presentation was predetermined in the context of introducing a new methodology for surveillance of respiratory diseases. Learning objectives focused on the advantages and disadvantages of PCR and rapid antigenic testing for COVID-19 and the interpretation of the results for laboratory testing for COVID-19. Participants could interact and ask questions regarding the content of the presentation.

6.2 Teaching medical residents on data centralisation and database cleaning from reports send by laboratories on SARS-CoV-2 RT-PCR

The aim was to train medical residents in epidemiology with regards to the daily process of centralisation of SARS-CoV-2 aggregated data received from RT-PCR laboratories on the national platform, Alerte.ms, in order to assist the fellow in the task of data validation and reporting the data to the Ministry of Health. The training was held face to face, at the NIPH - NCCDSC for two days (19–20 October 2020). Upon completion, the medical residents were able carry out data centralisation based on laboratory reports, verify the data, and communicate with laboratory representatives for correction or additional instructions. The participants were able to interact, ask questions and work in parallel with the fellow.

Training modules related to the assignment/projects

EPIET/EUPHEM Introductory Course: During the Introductory Course, the fellow learnt about different teaching techniques, assessing needs of the audience when delivering a lecture, identifying knowledge gaps, as well as how to set objectives and carry out the final evaluation.

Educational outcome

The fellow learnt how to adapt the content of the lecture according to training needs and purpose, as well as the type of training (online versus face to face) as well as how to deliver the message in a clear format to persons from diverse backgrounds.

7. Public health microbiology management

7.1 Setting up a molecular biology laboratory at the NIPH - RCPH, Bucharest

Through its laboratories in Bucharest, Cluj, Iași, and Timișoara and the National Center for Surveillance and Control of Communicable Diseases, the NIPH plays an essential role in the surveillance of infectious diseases. In order to implement the most effective measures to limit the phenomenon of cross-border outbreaks of infectious diseases and pandemics it is necessary to ensure rapid diagnosis at the level of public health laboratories, phylogenetic analysis and analysis of viral variability. Developing sequencing and Real Time PCR testing capacity allows public health laboratories to play a valuable role in monitoring SARS-CoV-2 variants and to be prepared for future outbreaks. The process of establishing a molecular biology laboratory at the NIPH, Bucharest began in 2019, and the COVID-19 pandemic highlighted the need to expand the laboratory and increase diagnostic capacity. The project involved obtaining funding for procurement of PCR and sequencing equipment and reagents, as well as renovation of the existing infrastructure to accommodate the growing molecular biology laboratory. New workflows for PCR and sequencing were established, new staff members were employed and trained in molecular biology techniques and bioinformatics, followed by method validation for SARS-CoV-2 variant detection and interlaboratory comparison.

Role: The fellow was involved in this effort, alongside the lab coordinator, since the start of the project. She contributed in preparing the documents needed for the procurement of equipment and consumables, obtaining funding, organisation of infrastructure and workflows for PCR and sequencing, method validation, results interpretation, and staff training in PCR technique.

7.2 Strengthening the institutional capacity for the control of hospital infections and managing the consumption of antibiotics in Romania

In Romania, antimicrobial resistance represents an important public health problem. The Ministry of Health set in place the National Program for surveillance and limitation of healthcare-associated infections (HAIs) and antimicrobial resistance (AMR), coordinated by the NIPH - National Center for Surveillance and Control of Communicable Diseases, that aims to increase the quality of medical services and patient safety by reducing the risk of healthcare-associated infections. However, the problem of microbial resistance to antibiotics and excessive use of antibiotics remains high. The project began in March 2020 in partnership with the Norwegian Institute of Public Health, with a team of experts from different key areas, such as microbiology, epidemiology as well as infectious diseases experts from the National Institute of Infectious Diseases "Prof. Dr. Matei Bals" (INBIMB) and the National Institute of Public Health Romania. The proposed actions were aimed at: identifying key areas needed to control AMR and HAIs, developing a national strategy and a national action plan, developing guidelines for microbiology, epidemiology and infectious diseases specialists, organising workshops for professionals and information campaign for general public. The development of the National Strategic Framework had the following directions: improving the legal framework on how to limit AMR, improving the knowledge and attitude of the medical staff regarding HAI and the rational use of antibiotics, timely reporting of HAI and AMR data, communicating information to the public in a transparent manner, development of adequate human and technical resources policies for AMR monitoring at national level, optimising the use of antibiotics and vaccination in human and veterinary medicine, agriculture and the environment, and control of HAI.

Role: The fellow participated in the working group/network meetings and was involved in the following activities: identifying key areas needed to control antimicrobial resistance and healthcare-associated infections, national legislation review and submission of an assessment report on existing legislation, analysis of WHO and ECDC global strategies, WHO checklist analysis and comparison with Romania's needs, evaluation of the existing documents on the Global Action Plan to combat the phenomenon of antibiotic resistance and healthcare-associated infections, and contribution to the development of the National Strategic Framework.

7.3 COVID-19 pandemic support: communication to the Ministry of Health, and the District Public Health Authorities

The Romanian public health system involves National and Regional Public Health Centers, belonging to the National Institute of Public Health, as well as 42 District Public Health Authorities (DPHA), all governed by the Ministry of Health. The NIPH ensures the implementation of the national public health programs for which it is designated by the Ministry of Health. District Public Health Authorities are also involved in this effort. The main objectives of the NIPH activity are prevention, surveillance and control of communicable diseases, elaboration of regulations in the field of public health and ensuring public health management.

The fellow's activity at the NIPH - NCCDSC involved frequent communication with the Ministry of Health, Public Health District Authorities, and laboratories participating in public health programs, via formal letters. During the

COVID-19 pandemic the fellow was involved in communicating the point of view and recommendations of the NIPH to the Ministry of Health, through formal letters, with respect to the National COVID-19 testing strategy – existing PCR-testing capacity and the need to extend it, the opportunity for COVID-19 pooling testing, the use of rapid antigenic tests, as well as testing in saliva samples; the procedures for detection of new variants of SARS-CoV-2 and the opportunities for SARS-CoV-2 sequencing; proposal for changes that need to be made with regards to the Order of the Minister of Health No 1.829 / October 2020 for the approval of the information flow used in reporting SARS-CoV-2 infection data and the Order no. 383 /March 2021 on amending and supplementing the technical rules for the implementation of National Public Health Programs; proposal for changes to the national online platform, Alerte.ms that is used by laboratories to report aggregated data to the Ministry of Health (the total number of samples tested, the number of tested samples in the last 24 hours, the number of persons tested, the reagent stocks). Starting April 2022, the fellow was the national coordinator of the National Program for NAAT/RT-PCR testing and sequencing and was responsible for the fulfilment of the responsibilities stipulated in the Order of the Ministry of Health 964/2022 regarding the approval of the 'Technical norms for the realisation of national public health programs'. With respect to the COVID-19 situation, the fellow was also involved in advising the DPHA on redistribution of the collected samples to other laboratories in case of exceeding the test capacity, based on data collected on their capacity and availability, and in advising the DPHA on interpretation of discordant results between rapid antigenic testing and RT-PCR testing for COVID-19 or between PCR results from different laboratories for the same patient.

7.4 Member of the 'Technical Commission for the evaluation of the capacity of the specialised units that perform RT-PCR testing for the detection of SARS-CoV-2 and sequencing for characterisation of SARS-CoV-2'

Starting January 2022 (Order of Ministry of Health 122/2022), the fellow was involved as a technical expert in the 'Technical Commission for the evaluation of the capacity of the specialised units that perform RT-PCR testing for the detection of SARS-CoV-2 and sequencing for characterisation of SARS-CoV-2'. The Commission was established by Order of the Ministry of Health 94/2021. The fellow's activity involved participation in weekly work meetings, elaboration of proposals for the modification of some normative acts in the field of competence, as well as evaluation of testing units that requested the evaluation/re-evaluation of the RT-PCR/sequencing capacity, and selection of participating laboratories in the National Surveillance Program. During this process, new laboratories request evaluation/re-evaluation of the RT-PCR/sequencing capacity and their documentation was sent to the Technical Commission on a weekly basis for approval of participation in the National Surveillance Program. The Technical Commission has, on average, a two-week intervals for evaluation and response.

Training modules related to the assignment/projects

Management, Leadership and Communication in Public Health Module: During the module, the fellow learnt about team management, team building, negotiation, personality traits, conflict management, making decisions in emergency situations, methods for project management, and communicating effectively with public health authorities.

Educational outcome

Teodora improved her knowledge on lab organisation, dealt with practical and complex challenges regarding funding, communication, establishing workflows, method validation and quality control. She developed project management skills and gained experience in planning and organising projects, as well as communicating to motivate the team, solve conflicts, and give feedback.

8. Communication

Publications related to the EUPHEM fellowship

1. Chivu-Economescu M, **Vremera T**, Ruta SM, Grancea C, Leustean M, Chiriac D, et al. Assessment of the Humoral Immune Response Following COVID-19 Vaccination in Healthcare Workers: A One Year Longitudinal Study. *Biomedicine*, 2022; 10(7):1526. <https://doi.org/10.3390/biomedicines10071526> (published)
2. **Vremera T**, Furtunescu F, Iancu LS, Rafila A, Leustean M, David A, et al. Detection of anti-SARS-CoV-2-Spike/RBD antibodies in vaccinated elderly from residential care facilities in Romania, April 2021 (manuscript submission eurosurveillance-D-22-00154)
3. **Vremera T**, Furtunescu FL, Leustean M, Rafila A, David A, Radu I, Cornienco AM, et al. Detection of anti-SARS-CoV-2-Spike/RBD antibodies in vaccinated elderly from residential care facilities in Romania, April 2021. *Front. Epidemiol*, 2022, 2:944820. doi: 10.3389/fepid.2022.944820 (published)

Reports

1. Report to Ministry of Health 'Preliminary results of the study Evaluation of the immune status in medical personnel vaccinated against COVID-19'
2. Report to Ministry of Health 'Results of the study Evaluation of the immune status of the elderly, vaccinated against COVID 19, from residential centers'
3. Report for outbreak investigation at the Socola Institute of Psychiatry Iași, Iași County, Romania, 2021
4. Report for outbreak investigation of acute gastroenteritis of possible Norovirus origin in Râșnov City, Brașov County, Romania, 2021
5. Report for training at Instituto de Salud Carlos III (Carlos III Health Institute), Madrid, Spain

Conference presentations

1. **Teodora Vremeră**, Mihaela Leustean, Florentina Furtunescu, Denisa Janta, Luminița Smaranda Iancu, Adriana Pistol. Seroprevalence study of SARS-CoV-2 infection in Romania, 2020. ESCAIDE, 2021, online, poster presentation
2. **Teodora Vremeră**, Mihaela Leustean, Adina David, Adina Gatea, Ciprian Ilie, Iuliana Radu, Ana Maria Cornienco, Florentina Furtunescu, Adriana Pistol, Luminița Smaranda Iancu. Assessment of immune response in elderly persons from residential care facilities following COVID-19 vaccination in Romania, 2021. ECCMID, 2022, Lisbon, Portugal, poster presentation

Other presentations

1. **Teodora Vremeră**, Florentina Furtunescu. Seroprevalence studies in the COVID-19 pandemic; perspectives, 9th RoVaccin National Conference, 26–27/03/2021, online, oral presentation
2. **Teodora Vremeră**, Adriana Pistol, Simona Ruță, Mihaela Chivu Economescu, Camelia Grancea, Mihaela Leuștean, Adina David, Adina Gâtea, Ciprian Ilie, Iuliana Radu, Ana Maria Cornienco. Preliminary results of the study on the evolution of the antibody profile in vaccinated medical staff, National Conference of Microbiology and Epidemiology, 4–6/11/2021, online, oral presentation
3. Mihaela Chivu, **Teodora Vremeră**. Post-vaccination immune response in Romanian medical personnel, 10th RoVaccin National Conference, 01–02/04/2022, online, oral presentation
4. **Teodora Vremeră**. Setting-up genomic surveillance for antimicrobial resistance at National Institute for Public Health (NIPH) Romania, Project Review Module, 29/08/2022 – 02/09/2022, Lisbon, Portugal, oral presentation.

Other training modules

1. EAN GIS-mini module, 09–10/04/2022, Rome, Italy

9. Other activities

9.1 Participation in the project, 'Maintenance of Basic Surveillance System Implementation Activities and Response to Avian, Pandemic and Seasonal Influenza in Southeast European Countries'

The project was founded by The Albanian Foundation Southeast European Centre for Surveillance and Control of Infectious Diseases' (SECID) and was focused on ensuring the support for four molecular biology laboratories at the level of Regional Centre for Public Health (RCPH) Bucharest, Cluj, Iași and Timișoara involved in RT-PCR testing for COVID-19 during the pandemic. The main objectives were: enhancing the RT-PCR testing capacity for the four laboratories belonging to the National Institute of Public Health in order to increase their efficiency in epidemic outbreaks and surveillance capacity; to ensure that the minimum biosafety requirements regarding personnel equipment are respected in all NIPH PCR-laboratories in order to avoid their contamination; training and technical supervision for the laboratory staff in order to ensure standardisation and uniformity of the results.

The fellow was involved in the following activities: preparing the list of necessary laboratory materials for SARS-CoV-2 RT-PCR laboratories belonging to NIPH, including pipettes and consumables; contacting national distributors with regards to the list of necessary laboratory materials for SARS-CoV-2 RT-PCR; evaluating price offers and product characteristics for the list of necessary laboratory materials for SARS-CoV-2 RT-PCR in order to have a good cost-benefit ratio; evaluating the necessity for personal protective equipment for molecular biology laboratory personnel involved in RT-PCR testing for SARS-CoV-2 within the four Regional Public Health Centers and sending the list of PPE to the coordinators of the project; participating in lab visit for technical supervision at the RCPH Iași alongside a representative from INCDMM Cantacuzino.

9.2 Participation in NIPH application for financing from the Global Fund to Fight AIDS, Tuberculosis and Malaria

Given that the NIPH Romania has four molecular biology laboratories at the level of Regional Centre for Public Health (RCPH) Bucharest, Cluj, Iași and Timișoara that were involved in RT-PCR testing for COVID-19 during the pandemic, there is a need for an integrated laboratory information management system (LIMS) for the four laboratories. Also, given its location and the fact that the RCPH laboratory in Bucharest has the highest testing capacity, it was decided to further implement and develop the sequencing capacity in this setting. The National Institute of Public Health applied for financing to the Global Fund in order to purchase: a laboratory information management system for the four RCPH Bucharest, Cluj, Iași and Timișoara, and a sequencing system for the RCPH Bucharest. Although laboratory personnel were not officially part of the project team, given the nature of the project, the fellow together with the laboratory coordinator were asked to give counselling regarding the existing laboratory infrastructure and the necessity report.

The fellow was involved in preparing the necessary documents for submission to the Global Fund of the financing application for NIPH laboratories. The work involved had two main parts:

- a. Justifying the need for implementing sequencing capacity at RCPH Bucharest and a LIMS in the four RCPH labs. The fellow took part in the following activities: the preparation of the Justifying Note regarding the necessity of the investment, outlining the opportunity of developing a sequencing laboratory at the NIPH, introduction of a Laboratory Management Information System and the expected benefits; participation in completing the Laboratory Sequencing Capacity Needs Assessment form; writing of a report containing information regarding the following aspects: national sequencing strategy, human resources availability at the NIPH laboratories, the current infrastructure of the NIPH laboratories, existing equipment at the NIPH laboratories, bioinformatics capacity of the NIPH laboratories, and accreditation of sequencing lab.
- b. Establishing the desired sequencing system to be implemented, the costs and the characteristics. The fellow took part in the following activities: evaluating offers and product characteristics; the preparation of the necessity report for the procurement of sequencing equipment; and the preparation of the necessity report for the procurement of Laboratory Management Information System.

9.3 Focal point to the Laboratory Task Force for emerging and re-emerging pathogens second meeting (21–23 June 2022, Antalya, Türkiye)

The declared aim of the meeting was to review the progress of the Lab Task Force in its second year and to foster close collaboration between the laboratory focal points and WHO Collaborating Centers (CC), to identify needs and opportunities to improve countries' preparedness and capacity for laboratory response to emerging and re-emerging pathogen outbreaks in the WHO European Region, taking into account lessons identified from the response to COVID-19. The main topics of the meeting were: WHO Europe COVID-19 laboratory response, setting EVD laboratory network, results of the national diagnostic capacity assessment for emerging and re-emerging pathogens, Biosafety and Biosecurity, WHO Collaborating Center for laboratory preparedness and response for emerging and re-emerging pathogens, and biorisk, biosafety and biosecurity training, existing EQA mapping, WHO procurement of critical reagents and diagnostics for emerging and re-emerging pathogens, potential role of collaborating centers in procurement, legislation regarding sample transport and shipment, WHO Global Genomic surveillance strategy for pathogens with pandemic and epidemic potential, integration of capacities developed during COVID-19 pandemic, training needs and opportunities, and laboratory readiness.

The fellow participated in round tables and open discussions on the following topics: COVID-19 WHO Reference laboratories contribution to regional response and lessons learnt, ways to improve the Lab Task Force networking, needs for biosafety and biosecurity improvement, EQA needs, countries' access to diagnostics, ways countries can implement WHO Global Genomic surveillance strategy, maintenance of COVID-19 lab capacities built and what kind of interface/integration with the health system is needed, training gaps and needs, essential needs for readiness, developing a roadmap to further strengthen regional capacity for diagnostic of emerging and re-emerging pathogens.

10. EPIET/EUPHEM modules attended

1. Introductory Course part 1, (28/09/2020 to 16/10/2020), virtual
2. Introductory Course part 2 - Operational Research inject days, (9–10/11/2020), virtual
3. Outbreak Investigation, (07–11/12/2020), virtual
4. Multivariable analysis, (15–19/12/2020), virtual

5. Introductory Course part 3, (26/04/2021 to 07/05/2021), virtual
6. Rapid Assessment and Survey Methods, (5–16/05/2021), virtual
7. Project Review 2021, (23–27/08/2021), virtual
8. Biorisk and Quality Management, (17–18/01/2022), virtual
9. Vaccinology, (14–18/02/2022), virtual
10. Time Series Analysis, (4–8/04/2022), ISS, Rome, Italy
11. Management, Leadership and Communication in Public Health, (13–17/06/2022), ECDC, Stockholm, Sweden
12. Project Review 2022, (29/08/2022 to 02/09/2022), Lisbon, Portugal

10. Other training

1. ESCAIDE, 24–27/11/2020, Online
2. ESCAIDE, 16–19/11/2021, Online
3. ECCMID, 23–26/04/2022, Lisbon, Portugal
4. Theoretical and practical training in next generation sequencing techniques at INCDMM Cantacuzino, 11–17/08/2021, Bucharest, Romania
5. Internship in: Emerging viruses, Cellular and molecular pathology, and Molecular virology Departments, Ștefan S. Nicolau Institute of Virology, 13–28/09/2021, Bucharest, Romania
6. Onsite training in sequencing technique at CRGM Dolj, Diagnosis of genetic diseases, rare genetic diseases and infectious diseases by using state-of-the-art sequencing technologies (NGS), 22–24/11/2021, Bucharest, Romania
7. Training at Instituto de Salud Carlos III, 16/05/2022 – 03/06/2022 Madrid, Spain
8. WHO meeting, European Region Laboratory Task Force for High Threat Pathogens, 21–23/06/2022, Antalya, Türkiye
9. Basics in Bioinformatics, 27–29/06/2022, Online
10. Introduction to Microbial Genomics, 14–15/07/2022, Online

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 the activities and projects conducted by Teodora Vremeră at the National Institute for Public Health (NIPH), Bucharest, Romania. During the two years of the fellowship, Teodora has shown a high level of competency. This portfolio is the reflection of her dedication, resilience and hard work. The laboratory and epidemiological projects covered a diverse range of disease programmes involving multidisciplinary work and teamwork on all levels such as with physicians, laboratory technicians, epidemiologists, statisticians, government officials and public health officers. This shows the strength of the fellow and her ability to work within a multifunctional environment. During the two years, she has not only achieved her primary objectives but contributed to the response to the COVID-19 pandemic in Romania. In addition to the COVID-19 response, she has played an important role in building the laboratory capacity at the NIPH. Moreover, Teodora has expanded her research knowledge and analytical skills by participating in different surveillance and research projects that allowed her to apply her new competences. Her activities were complimented by training modules providing theoretical and practical knowledge and skills. Finally, I would like to comment on Teodora's personal attitude toward the fellowship. She was an independent and hard worker, eager to learn, which is shown by her internship at the ISCIII. She was able to work and adapt to the difficulties that the SARS-CoV-2 pandemic brought to the NIPH.

The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all her tasks to a very high standard and with a professional attitude. We wish the fellow every success in her future career and congratulate the training site for the successful training of the fellow.

Supervisor's conclusions

The fellow's work was primarily focused on management of laboratory testing and reporting during the COVID-19 pandemic, and organising the NIPH molecular biology laboratory in Bucharest. Research projects were mainly focused on evaluating the immune response after COVID-19 vaccination in particular groups, such as elderly people in residential care facilities and healthcare workers. Her previous experience, at the Regional Public Health Centre Iași and as lecturer at the Grigore T. Popa University of Medicine and Pharmacy in Iași, have been useful to Teodora to understand concepts related to the role of the microbiology laboratory in public health, both in surveillance and in the investigation of epidemic outbreaks, but also for the work of teaching concepts and communication. This two-year fellowship was all the more useful as Teodora was faced with a new job at the National Institute of Public Health in Bucharest, where the requirement was to integrate microbiology into the epidemiologist's way of thinking and working, the epidemiologist-microbiologist tandem being essential in the concept of public health. Finally, I would like to laud Teodora's seriousness, hard work and perseverance to complete her projects and to successfully meet the requirements of this program which is so useful for young specialists in Romania.

Personal conclusions of fellow

The EUPHEM program provided me with new insights into Public Health Microbiology and Epidemiology. Being a fellow during the pandemic represented a challenge that enabled me to strengthen my communication, organisational and management skills. I had the opportunity to apply my previous knowledge in microbiology in public health settings, while also gaining new skills in fields such as whole genome sequencing, outbreak investigation, surveillance and statistical analysis. I was involved in a variety of projects that allowed me to develop experience in scientific communication, as well as collaborating with colleagues from other institutions and fields of competence.

I am thankful for this experience that has broadened my understanding of the role that the public health microbiology needs to fulfill.

Acknowledgements of fellow

I would like to thank my frontline coordinator, Silvia Herrera Leon for her invaluable support, feedback and good advice. Thank you to my supervisors, Luminita Smaranda Iancu and Adriana Pistol not just for all their guidance, scientific support, flexibility and involvement during the fellowship, but also for the freedom they allowed me in choosing and managing the projects.

I would also like to thank my colleagues from the NCCDSC and the NIPH Laboratory for their constant support, collaboration and coaching. I would like to thank the colleagues from the District Public Health Authorities who collaborated in projects and outbreak investigations.

I would like to thank the staff at the Carlos III Health Institute in Madrid, Spain, who hosted me, and were so welcoming and open to work with me and let me observe them working, especially their guidance and training in BSL-3, sequencing techniques and sequence data analysis. Also, I would like to thank the colleagues from the Ștefan S. Nicolau Institute of Virology for their support in sequencing and viral culture training and participation in projects.

Also, I would like to thank the colleagues from the INCDMM Cantacuzino and CRGM Dolj for their support in sequencing training. Thank you to my Cohort 2020 for the support and lovely experiences. Last, but not least, I would like to thank ECDC lecturers, facilitators, and the administrative team for the training and support they provided.