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Livestock, food chain and public health risk assessment

Animal and Plant Health Agency (APHA), Biomathematics and Risk Research workgroup,
United Kingdom,
Irina Smeu and Rachel A Taylor

Abstract

The EUropean FOod Risk Assessment (EU-FORA) Fellowship work programme 'Livestock, food chain and public health risk assessment', founded by EFSA was proposed by the Animal and Plant Health Agency (APHA), United Kingdom (UK). A scientist working in the field of food safety was selected to work within the Department of Epidemiological Sciences, under the guidance of an experienced risk assessor. The programme was structured in four different modules that covered a wide range of aspects related to risk assessment (RA). Taken together, all modules ensured a broad overview of the various methodologies, tools and applications of RA. Thus, the learning-by-doing working programme in RA allowed the fellow to develop her knowledge in RA, to diversify her competencies and to extend her scientific network for future collaborations in the field of RA.

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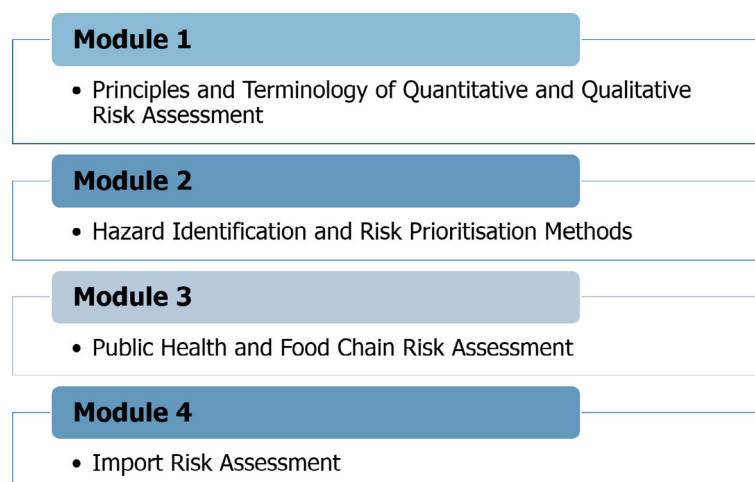
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1.   Introduction

This Technical Report represents a description of the EUropean FOod Risk Assessment (EU-FORA) Fellowship work programme 'Livestock, food chain and public health risk assessment', founded by the European Food safety Authority (EFSA). It was proposed by the Animal and Plant Health Agency (APHA), UK, one of the four executive agencies working for the Department for Environment, Food and Rural Affairs (Defra) and also on behalf of the Scottish Government and Welsh Government. The agency is responsible for safeguarding animal and plant health in the UK, providing support for the delivery of their animal health and welfare and bee health policies. Within the EU-FORA fellowship, the fellow, Dr. Irina Smeu from the National R&D Institute for Food Bioresources – IBA Bucharest in Romania, was placed at the APHA, within the Biomathematics and Risk Research (BRR) workgroup, part of the Department for Epidemiological Sciences (DES). It is a nationally and internationally recognised group of risk analysts, modellers and statisticians providing high quality scientific evidence for policy formulation and outbreak response, as well as specialist support to research and operations in the area of animal health. The work programme was supervised by Dr. Rachel Taylor, Senior Risk Analyst within the BRR workgroup. The programme consisted of four different modules based on on-going risk assessment (RA) project work and previous research interests at APHA, including the development of several RAs supported and funded by EFSA to underpin significant RA research work and European Commission policy support.

2.   Description of work programme

The EU-FORA work programme 'Livestock, food chain and public health risk assessment' developed by APHA was structured in four different modules that covered a wide range of aspects related to RA. Taken together, all modules ensured a broad overview on the various methodologies, tools and applications of RA. Each module was organised into various related activities that were addressed step by step. Over the course of the year, Dr. Taylor monitored the progress of the programme and managed the evolution of the project's activities. Weekly meetings analysed in greater detail the progress of each module's deliverables and outcomes according to the programme timeline. Furthermore, specialists were chosen to co-supervise each module based on their experience and relevance.

The work programme with the included modules is presented in Figure 1.

Module 1
- Principles and Terminology of Quantitative and Qualitative Risk Assessment

Module 2
- Hazard Identification and Risk Prioritisation Methods

Module 3
- Public Health and Food Chain Risk Assessment

Module 4
- Import Risk Assessment

Figure 1: Schematic presentation of the work programme

2.1.   Aims

Each module of the 'Livestock, food chain and public health risk assessment' work programme represented an independent RA project and had specific deliverables and outcomes, as follows:

Module 1 aimed to consolidate the RA knowledge of the fellow gained through the EFSA training, by guidance and practice in understanding the basic principles of qualitative and quantitative RA, the RA methodology and the different tools that are often used to perform RA. During this module, the fellow attended various courses and training opportunities in order to strengthen their RA knowledge.

Module 2 focused on the understanding of available risk ranking tools for exotic animal diseases cross-bordering Europe and how they can be incorporated into the decision making process. The fellow attended various meetings of different governmental groups, and had a close collaboration with Defra, which facilitated progress on this module. A review paper on risk ranking tools for animal diseases has been submitted for publication.

Module 3 addressed different RA models and techniques that are available to relate *Salmonella* isolates identified in food products with those that are prevalent in causing human salmonellosis. For this purpose, a collaboration with Public Health England (PHE) was formed as part of the work programme, as it allowed the use of whole genome sequencing (WGS) data on isolates of *Salmonella* from food commodities and human cases. Different levels of genetic relatedness were identified, allowing the ranking of food isolates by order of public health risk.

Module 4 focused on the RA process from start to finish through the scenario of onward transmission of *Leishmania* parasites if entry were to occur into the UK. The module involved working alongside risk assessors for developing the risk pathways for the pathogen of interest, which offered a rapid learning of RA methodologies applied within RA situations.

2.2. Activities/methods

Module 1: Principles and Terminology of Quantitative and Qualitative Risk Assessment

The first module of the working programme was co-supervised by Dr. Robin Simons, Lead Risk Analyst within the BRR Workgroup, APHA. The module was dedicated to structured lectures and practical sessions on RA methodologies for both qualitative and quantitative RA. The lectures were part of the Royal Veterinary College (RVC)'s Master of Science (MSc) course in Veterinary Epidemiology, held at the London campus of the RVC. The training consisted of both theoretical and practical sessions. The practical exercises provided experience in how to produce a qualitative RA report and how to replace descriptive analysis of the risk pathways and qualitative risk estimates with their mathematical description and numerical risk estimates.

During the one year fellowship, the fellow also attended meetings of various governmental groups such as the National Emergency Epidemiology Group (NEEG), the Human-Animal Infections and Risk Surveillance Group (HAIRS) and the Veterinary Risk Group (VRG) from Defra. The NEEG coordinates and reports on the epidemiology of exotic notifiable disease outbreaks to describe and anticipate disease frequency and distribution, providing epidemiological advice and assessment on the determinants, level and distribution of disease to the National Expert Group (NEG) (Scottish Government, 2017). The HAIRS is a multiagency and cross-disciplinary horizon-scanning group, comprising numerous governmental agencies such as PHE, Defra, APHA, Food Standards Agency (FSA) and the Department of Health and Social Care. The group identifies and discusses infections with potential for interspecies transfer (Welsh and Morgan, 2005). The VRG is a UK group managed and delivered by APHA and directly supported by a network of risk management teams. Its role is to identify, assess, escalate and prioritise new and re-emerging animal-related threats in the UK, in order to decrease their impact to society and economy (Kosmider et al., 2017). Thus, the attendance at these meetings represented an important training in RA, especially in outbreak or high-impact situations, which acted as a support for carrying out the following activities. Various RA situations which were presented in these meetings offered the chance to identify key elements in the control and prevention of animal diseases and to learn how various RA methodologies are applied to real situations. It also served to indicate how RA is used to support policy and the roles risk assessors and risk managers play in these situations.

In addition to the scheduled activities, the fellow participated in various meetings and consultations with other colleagues over the entire period of the EU-FORA fellowship programme which had numerous advantages for the fellow. The hosting institution provided additional training which played an important role in improving the fellow's knowledge of RA (Table 1).

Table 1: Supporting activities organised or facilitated by the hosting site, Animal and Plant Health Agency, during the EU-FORA fellowship

Type of event	Title	Date
Workshops	Workshop on the use of pig movement data for modelling and demographics	3.10.2018
	2019 APHA Modelling Symposium: 'Global Thinking: Modelling pathogen risk and spread across borders'	7.2.2019
Seminars	Epidemiology training day	6.11.2018
	Videoconference on generic risk models, in collaboration with EFSA and Wageningen Bioveterinary Research	15.1.2019
	Department of Epidemiological Sciences seminar day: 'Epidemiology as a Collaborative Science'	30.4.2019
	Science Engagement Group (SEG) seminars	Monthly
	Department for Epidemiological Sciences Taster Club presentations	Fortnightly
Other activities	Civil Service Learning online courses	3.10.2018–8.10.2018
	Science Open Day, APHA Weybridge	7.11.2018
	Career Q&A session with Dr. Francesca Gauntlett	13.11.2018
	FutureLearn online course: 'Animal viruses'	3.12.2018–11.1.2019
	DataCamp online courses	3.12.2018–30.4.2019
	Training session: 'Leadership skills'	19.2.2019

The EU-FORA training programme was supported by 4 training sessions provided by EFSA: a 3-week induction training at EFSA premises in Parma, Italy and 1-week training modules at the Austrian Agency for Health and Food Safety (AGES) in Vienna, Austria, the German Federal Institute for Risk Assessment in Berlin, Germany and the Hellenic Food Authority in Athens, Greece.

Furthermore, the training programme was completed with participation in the Parma Summer School 2019 'Risk–benefit in food safety and nutrition', organised at the EFSA's premises on the 11–13 of June 2019. The event was coordinated by EFSA, the University of Parma and the School of Advanced Studies on Food and Nutrition, with the collaboration of the Catholic University Sacro Cuore of Piacenza, the Technical University of Denmark, the National Food Agency, Sweden, the University of Barcelona and the Instituto Superiore di Sanità. The course broadened the fellow's knowledge and understanding of the risk–benefit approach in food safety and nutrition and highlighted the importance of a close collaboration between risk assessors and benefit assessors in order to ensure that the generated data can be used in a broader risk–benefit assessment context.

Module 2: Hazard Identification and Risk Prioritisation Methods

Module 2 was co-supervised by Dr. Helen Roberts, Equine, Pets and New and Emerging Diseases, Science and Risk Adviser, within the Exotic Disease Control team of Defra. Defra is a UK ministerial department supported by 33 agencies and public bodies and is responsible for safeguarding the natural environment, promoting the food and farming industry and sustaining the rural economy (Defra, 2019).

This module was focused on an extensive study of risk ranking methods and tools for prioritising animal diseases. There were explored various tools which are maintained and designed specifically for the UK to prioritise pathogens of highest risk, on a regular basis, and which feed into the specific contingency plans within the Outbreak National Response. The International Disease Monitoring (IDM) 'Risk of Incursion' tool was closely studied by the fellow. The tool deals with rapid RAs for animal health, being currently used in the assessment of risk incursions for the UK (Roberts et al., 2011). Thus, a case study was assessed by the fellow, taking the IDM 'Risk of Incursion' tool as a template to analyse the risk of incursion of various animal diseases into Romania through an associated livestock or product of animal origin. For this purpose, 2017 international trade data for Romania were obtained from COMEXT, a freely available online reference database for detailed statistics on international trade in goods run by Eurostat, and the Trade Control and Expert System (TRACES) European Union (EU) database (Eurostat, 2017; European Commission, 2019).

Furthermore, various EU risk ranking tools for animal diseases were studied and the ones available online were tested in order to identify their advantages and limitations. Several generalised risk ranking

frameworks proposed by various international agencies were also assessed, in order to identify their general recommendations for a prioritisation approach of animal diseases in the selected risk ranking tools. These activities facilitated the completion of a comprehensive overview of various tools developed within the EU over time to rank animal diseases. The study entitled 'Best practices in risk ranking animal diseases: An analysis of ten risk ranking tools' has been submitted for publication.

Horizon scanning methods were also explored within module 2 for assessing future risks for animal and public health. These activities were co-supervised by Dr. Paul Gale, Senior Risk Analyst within the BRR workgroup. The fellow was introduced to the International Forward Look (IFL), a programme developed at the request of the Government Chief Scientific Adviser, in partnership with Government Office for Science. IFL represents a cross-government approach which joins up horizon-scanning scientists and risk assessors from various governmental departments for identifying, flagging and anticipating emerging global natural threats which could require a response from government departments working overseas. Since July 2015, a group of scientists from various government agencies such as the Met Office, British Geological Survey, PHE and APHA perform weekly a natural hazard identification document for government departments. To support this, a Microsoft Excel®-based summary was created by the fellow, containing information on animal health supplied by the World Organisation for Animal Health (OIE) international surveillance system and alerts through the OIE World Animal Health Information System (WAHIS), an internet-based computer system which processes data on animal health in real time and informs the international community. Thus, data on animal diseases and their serotypes, countries of origin, status of the report, date of the event, affected animal species, number of affected animals, outbreak status and other observations were centralised, along with the maps of outbreak locations, for feeding into the weekly natural hazard risk identification document. This activity allowed the fellow to learn a routine approach that highlights the current situation of emerging global natural threats in order to improve the situational awareness of decision-makers.
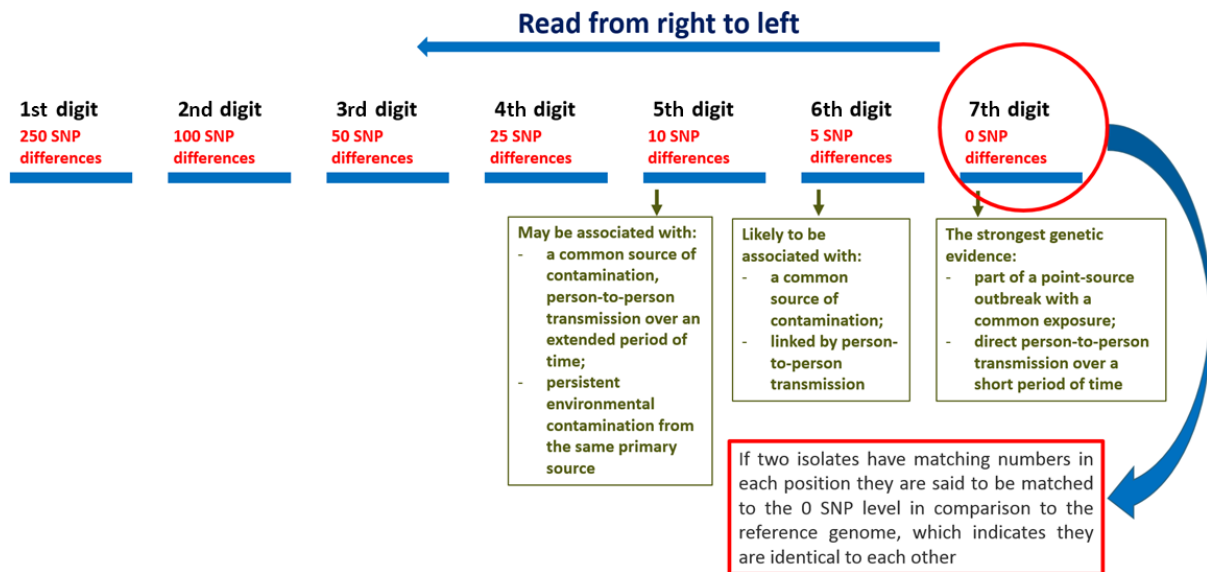
Module 3: Public Health and Food Chain Risk Assessment

Module 3 was co-supervised by Dr. Robin. Simons, Lead Risk Analyst within the BRR Workgroup on behalf of APHA and Dr. Lesley Larkin, Surveillance Lead, Gastrointestinal Infections, Tuberculosis, Acute Respiratory, Gastrointestinal, Emerging/Zoonotic Infections and Travel Health Division (TARGET), on behalf of PHE. The work was carried out between the two governmental agencies, APHA and PHE, and involved a 2-week secondment at PHE in Colindale, London. PHE is an executive agency of the Department of Health and Social Care and a distinct organisation with operational autonomy. PHE is the key provider for public health surveillance data and information to parametrise aspects of public health.

Non-typhoidal Salmonellae are major zoonotic pathogens which cause a significant global public health concern. The European Centre for Disease Prevention and Control (ECDC) noted that salmonellosis is the second most commonly reported gastrointestinal infection in the EU/European Economic Area (EEA). The Annual Epidemiological Report for 2016 noted an EU/EEA notification rate of 20.4 cases per 100,000 population, where the highest notification rate of salmonellosis was noticed among young children 0–4 years, with 89.9 cases per 100,000 population, seven times higher than in adults 25–64 years (ECDC, 2019).

In April 2014, WGS was implemented by PHE for the characterisation of isolates of *Salmonella* (McLauchlin et al., 2019). Since 2015, WGS is the primary typing tool used for public health surveillance. *Salmonella* serovar determination is predicted based on the *Salmonella* eBURST group (eBG) or sequence type (ST) (Achtman et al., 2012; Ashton et al., 2016) as a replacement for traditional serotyping. PHE currently holds databases on *Salmonella* isolates, including more than 1,000 isolates from food and approximately 50,000 isolates from cases of human salmonellosis. The activities of this module aimed to use WGS data on isolates of *Salmonella* from food commodities and enumerate the number of cases of human salmonellosis reported, analysed at different levels of genetic relatedness.

The method employed by PHE is single nucleotide polymorphisms (SNP) typing. A bioinformatics application, SnapperDB, has been developed to quantify SNP relatedness and derive an isolate level nomenclature termed the 'SNP Address' (Dallman et al., 2018). This applies multi-threshold single linkage clustering to describe an isolate's position in the population structure of a given *Salmonella* eBG. Single-linkage clustering is performed at seven descending thresholds of SNP distance: 250, 100, 50, 25, 10, 5 and 0. This clustering results in a discrete seven-digit code where each number represents the cluster membership at each descending SNP distance threshold. Thus, clusters of cases that are microbiologically linked can be detected using the 'SNP address' to indicate how closely related genetically an isolate is to other isolates in the database (Figure 2).

Read from right to left

1st digit	2nd digit	3rd digit	4th digit	5th digit	6th digit	7th digit
250 SNP differences	100 SNP differences	50 SNP differences	25 SNP differences	10 SNP differences	5 SNP differences	0 SNP differences

May be associated with:
- a common source of contamination, person-to-person transmission over an extended period of time;
- persistent environmental contamination from the same primary source

Likely to be associated with:
- a common source of contamination;
- linked by person-to-person transmission

The strongest genetic evidence:
- part of a point-source outbreak with a common exposure;
- direct person-to-person transmission over a short period of time

If two isolates have matching numbers in each position they are said to be matched to the 0 SNP level in comparison to the reference genome, which indicates they are identical to each other

Figure 2: Schematic description of a Single Nucleotide Polymorphism (SNP) address

Data provided by the Gastrointestinal Bacteria Reference Unit's web-based result reporting system, Gastro Data Warehouse (GDW), was used to facilitate the detection and assessment of clusters identified by whole genome sequencing on 2016–2018 human and food isolates of *Salmonella*. The food isolates were ranked by considering the *Salmonella* serotype, the food category, the reason for sampling and the country of origin of the food isolate. Based on SNP addresses, clinical isolates identical or with less than 10 SNP differences were linked to some of the food commodities, demonstrating how higher resolution SNP typing could efficiently be used for surveillance and global tracking of important food-borne pathogens, by having an increased discriminatory power over traditional typing techniques (Waldram et al., 2018).

Module 3 also considered the role of quantitative microbiological risk assessments (QMRAs) in the area of food-borne pathogens, such as *Salmonella*. APHA has extensive expertise in the development of farm-to-consumption QMRAs, including leading the development of a QMRA for EFSA for *Salmonella* in pigs, (Hill et al., 2010). The fellow studied this model and then conducted a review to obtain the input data necessary to parameterise the model for Romania. Thus, data including information regarding Romanian pig farms, pig population, meat processing and meat consumption were obtained from the official websites of the Romanian authorities (Ministry of Agriculture and Rural Development, the National Institute of Statistics, the National Sanitary Veterinary and Food Safety Authority). As all these documents were in Romanian, this specific task would have been particularly difficult for APHA staff. Furthermore, the fellow was introduced to R, version 3.4.4 (R Core Team, 2018) and used it to analyse and plot various maps of these input data (Figure 3). These maps contribute to the RA by visualising relevant data to aid understanding by users without an in-depth knowledge of the subject matter, generating a level of transparency and facilitating the investigation of interventions at different points of the food chain.
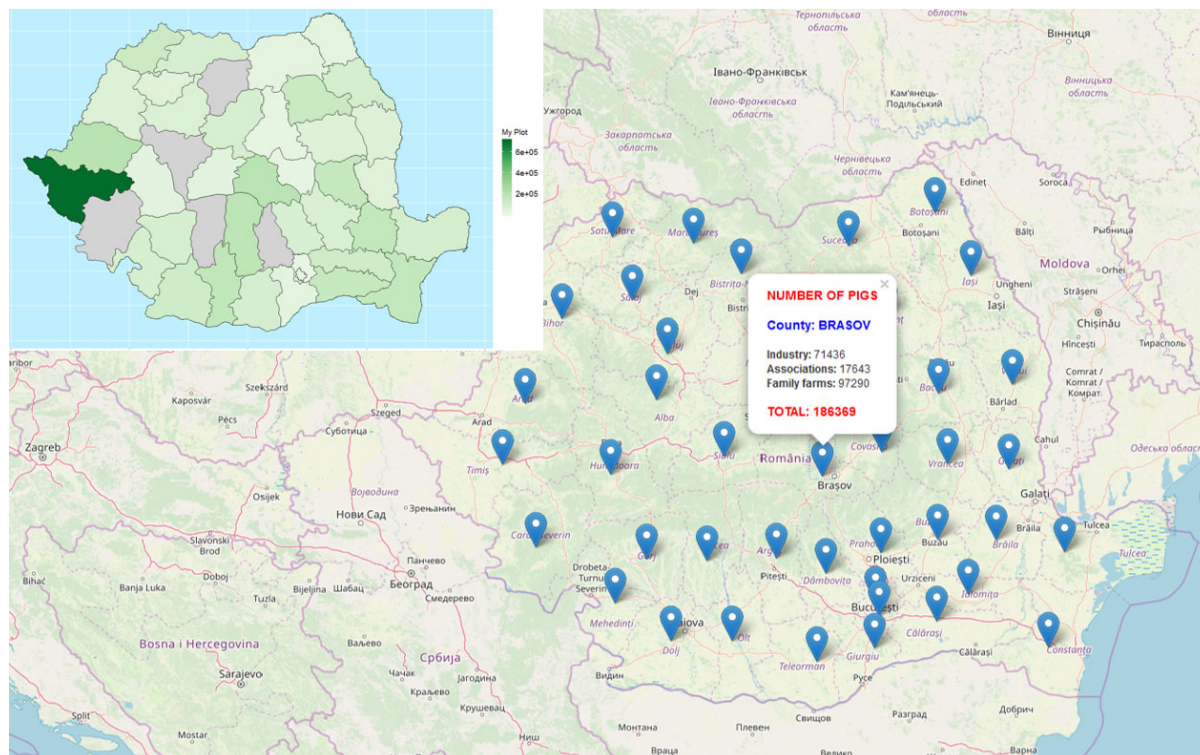
Figure 3: Mapping the 2017 Romanian pig livestock population using R (ggplot2 package, 2019)

Module 4: Import Risk Assessment

The fourth module of the working programme was co-supervised by Verity Horigan, a Risk Analyst in the BRR workgroup within APHA and specialist in microbial and food safety RAs.

This module was focused on the production of a qualitative RA which addressed the likelihood of introduction and onward transmission of *Leishmania* parasites within the UK. This assessment represented a case study for the EU 'COHESIVE – One Health Structure In Europe' project, within The One Health European Joint Programme (JIP2 COHESIVE, 2018; OHEJP, 2018).

Leishmaniasis is caused by the protozoan *Leishmania* parasites (over 20 *Leishmania* species) which are transmitted by the bite of infected female phlebotomine sandflies. The epidemiology of leishmaniasis depends on the characteristics of the parasite and sandfly species, the local ecological characteristics of the transmission sites, current and past exposure of the human population to the parasite, and human behaviour. Over 90 sandfly species are known to transmit *Leishmania* parasites and some 70 animal species, including humans, have been found as natural reservoir hosts of *Leishmania* parasites (WHO, 2019). Thus, there is the potential that this disease could enter new regions due to multiple pathways, namely entry via infected humans, pets or vectors.

Within this study, the fellow analysed the risk of onward transmission of leishmaniasis in the UK, taking into account biogeographic and epidemiological consequences in relation to the risk of leishmaniasis introduction into the UK. The potential transmission cycles and various risk pathways were identified and described, based on the available literature, and a qualitative RA was performed. Thus, this module provided the chance to work alongside staff of a national risk research group while performing a RA from start to finish, and thus represented the best opportunity in understanding and practising the RA principles outlined during the previous modules.

3. Conclusions

The EU-FORA 'learning-by-doing' programme enabled a fast and extensive knowledge and experience of RA. An overview of the major RA methodologies and various risk assessment and risk ranking tools was facilitated by the 'Livestock, food chain and public health risk assessment' working programme alongside the BRR workgroup within APHA, UK.

The interdisciplinary approach of the working programme as well as its diversity of the research fields will provide a complementary perspective to future cross-disciplinary research projects and future collaborations.

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Abbreviations

AGES	Austrian Agency for Health and Food Safety
APHA	Animal and Plant Health Agency
BRR	Biomathematics and Risk Research workgroup

Defra	Department of Environment, Food and Rural Affairs
DES	Department for Epidemiological Sciences
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EU-FORA	European Food Risk Assessment Fellowship Programme
FSA	Food Standards Agency
GDW	Gastro Data Warehouse
HAIRS	Human-Animal Infections and Risk Surveillance Group
IFL	International Forward Look
MSc	Master in Science
NEG	National Expert Group
NEEG	National Emergency Epidemiology Group
OIE	World Organisation for Animal Health
OHEJP	One Health European Joint Programme
PHE	Public Health England
QMRA	Quantitative Microbiological Risk Assessments
RVC	Royal Veterinary College
SNP	single nucleotide polymorphism
TARGET	Tuberculosis, Acute Respiratory, Gastrointestinal, Emerging/Zoonotic Infections and Travel and Migrant Health Division
TRACES	Trade Control and Expert System
VRG	Veterinary Risk Group
WGS	Whole Genome Sequencing
WAHIS	World Animal Health Information System
WHO	World Health Organization