SAPIENZA
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The One Health approach: case studies between vector and food-borne diseases

Scuola di Biologia e Medicina Molecolare
Dipartimento di Sanità Pubblica e Malattie Infettive
Corso di Dottorato in Malattie Infettive, Microbiologia e Sanità Pubblica

Laura Amato
Matricola 1841176

Tutor esterno
Paolo Calistri

Tutor interno
Stefano D'Amelio

A.A. 2021-2022

Foreword

The global occurrence and connectedness of high-impact diseases such as African swine fever, COVID-19, and avian influenza, with the overuse and/or misuse of antimicrobials that has led to the emergence of antimicrobial resistance, as well as food insecurity and safety, human-driven socio-economic changes driving climate change, and the unsustainable population growth and land-use, is shaping a world in which outbreaks of infectious diseases and spillover events are frequent, and to be considered more common in the future (Evans & Leighton, 2014; Gruetzmacher et al., 2021). The links between animals, plants, humans, and overall environment health are now more important than ever (Gruetzmacher et al., 2021). As a response to various significant global outbreaks in recent history, the global health management focus is changing to mitigate health threats in a horizontal, transdisciplinary, and integrative way (Evans & Leighton, 2014), but the changes are slow.

If we want to reverse the trend, the implementation of One Health could be the key factor. One Health has already been progressively incorporated into decision-making by Governmental and non-Governmental organizations (Kaiser, 2021). Moreover, because of the SARS-CoV-2 pandemic, the One Health approach, which was already well-known in the scientific community, has now become a trend and a 'pass-par-tout' for new projects and, consequently, financing opportunities.

Let's make the most out of the attention recently drawn to this approach, to implement a real paradigm shift and not waste away this momentum.

Abstract

The One Health (OH) approach intends to develop multi-sectoral collaborations to improve the health of people, animals, and the environment, and has been claimed to be central to facing actual global health challenges. Two experiences focusing on the OH approach are presented, exploring the implementation of a OH surveillance on vector-borne and food-borne diseases.

The experience of the MediLabSecure projects has led to a survey on early warning indicators, to be used in surveillance activities against relevant vector-borne diseases. Results showed that the collection of such indicators varies greatly in the 22 non-European countries involved. For example, information on animal population density is collected in all the countries, while information on wildlife is rarely collected. In the human sector, data on disease frequency or occurrence are frequently collected, as it happens for the presence of vectors in the area, which was the most collected indicator for the vector sector. At the same time, the collection of indicators related to climate and environment has to be strengthened, given the impact of these factors on arboviruses' presence and transmission. Moreover, besides being fundamental in the implementation of OH early warning surveillance strategies, data sharing using digitalized databases was in place only in a few cases. Nevertheless, to propose effective solutions appropriate to the context, the interpretation of the results should be guided by the understanding of the background.

Within the context of the OHEJP MATRIX, another survey was performed: the purpose was the understanding and the mapping of surveillance activities in place against four food-borne pathogens, in all the sectors involved in four whole food production chains. The survey involved European countries and showed a very heterogeneous situation between countries and pathogens. To show this heterogeneity, results have been graphically mapped and displayed. As expected, the situation with the most differences between countries was observed in the wild boar meat food chain concerning HEV, which is an emerging threat in Europe and for which surveillance activities are still not harmonized.

The two case studies described the settings for further actions. The next suggested step in the implementation of the OH approach should be pursued through additional country-based studies, to verify the most suitable target areas for the application of the OH, and prioritize the efforts.

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List of abbreviations

AH - Animal Health
AMR - Antimicrobial Resistance
CCHFV - Crimean-Congo haemorrhagic fever virus
CHIKV - Chikungunya virus
DENV - Dengue virus
EC – European Commission
EFSA – European Food Safety Authority
ET - Emerging Threats
EU – European Union
FAO – Food and Agriculture Organisation of the United Nations
FBZ – Food-borne Zoonoses
FS - Food Safety
HEV - Hepatitis E virus
ISS – Istituto Superiore di Sanità
IZSAM – Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise
MLS – MediLabSecure
MSs – Member State(s)
OIE – The World Organisation for Animal Health
OH – One Health
OHEJP – One Health European Joint Programme
OHS - One Health Surveillance
PH – Public Health
RVFV - Rift Valley fever virus
TNA - Training Need Assessment
UK – United Kingdom
VBD(s) – Vector Borne Disease(s)
WHO – the World Health Organisation
WP(s) – Work Package(s)
WNV - West Nile virus
YFV - Yellow fever virus
ZIKV - Zika virus

Introduction

Once upon a time, there was One Health

The "One Health" concept is not new. There have been many precedents to One Health (OH) throughout history, which did not go by this name and happened in times when health, science, and the world were very different (Zinsstag et al., 2020). The concept of OH did not arise from a single source; rather it "represents a basic condition of life on earth, repeatedly re-discovered and further explored throughout human history" (Evans & Leighton, 2014).

One Health in history

The interplay and links between different natural systems (animals, water, humans, land, etc.) have been culturally acknowledged through the centuries up to the modern era. The same 'doctor' used to treat both human and animal diseases in ancient cultures, such as Babylonian, Egyptian, Greek, Roman, and Arabic, and this can still be seen today in certain traditional pastoral cultures (Evans & Leighton, 2014; Mantovani, 2008; Zinsstag et al., 2005). Besides OH being present in the historical record of Western thought, over the centuries many 'visionary individuals' have shown the interactions between animal, human, and ecosystem health, and their impact (Evans & Leighton, 2014).

In the past, the Greek physician Hippocrates (460 BCE – 367 BCE) proposed a connection between a clean environment and public health (Evans & Leighton, 2014). Subsequently, the concept of comparative medicine was introduced by Aristotle (384 BCE – 322 BCE), who studied the commonalities between different species, including people and other mammals, and included the description of several animal diseases in his 'Historia Animalium' (Evans & Leighton, 2014).

On the contrary, in the medieval period, human medicine evolved separately from animal medicine, mainly for religious reasons: comparative medicine was strongly discouraged in light of the 'Christian fundamentalism', focusing on the demonstration that the nature of mankind was modeled in the likeness of God (Mantovani, 2008; Mantovani & Macrì, 2004).

In the Renaissance, comparative medicine was taken again into consideration, with enlightened researchers in Europe engaged in the management of livestock diseases, and that investigated both medical and veterinarian issues (Mantovani & Macrì, 2004).

Jumping forward to the 18th century, an Italian physician named Giovanni Maria Lancisi (1654 –1720) suggested a role for the environment in the spreading of diseases to humans and animals (Evans & Leighton, 2014): he studied malaria outbreaks in the area surrounding the city of Rome and, describing the pathogenesis of the disease, and the close correlation between its onset and the swampy waters of the Tiber River, he proposed the draining of marshes for its eradication (Paleari et al., 2021); he was not acknowledged, and it took another century and a half for his hypothesis on the relationship between environment (i.e. swamps), disease, and mosquitoes to be considered (Paleari et al., 2021). Also, advocating for animal depopulation and quarantine strategies, he is considered a pioneer in the management of rinderpest in cattle (Evans & Leighton, 2014).

Until the 18th century, veterinary medicine was not included in the universities, unlike human medicine, but mostly practiced by 'equerries' (Zinsstag et al., 2005). The first veterinary faculty was founded in Lyon, France, in 1762, by Claude Bourgelat (1712–1779), who was criticized for suggesting human medical science as the basis for veterinary medicine (Evans & Leighton, 2014; Zinsstag et al., 2005). Even so, human and animal medicine were practiced separately until the 20th century (Centers for Disease Control and Prevention (CDC), 2016).

The veterinary field of public hygiene was implemented shortly after, following the work of Louis-René Villermé (1782–1863) and Alexandre Parent-Duchatelet (1790–1835), also in France (Evans & Leighton, 2014). Only in the 19th century, the microbiological revolution and the advent of cellular pathology pushed for the development of comparative medicine (Zinsstag et al., 2005).

Critical public health measures were made following the discoveries of the German physician and pathologist Rudolf Virchow (1821–1902) on the zoonotic potential of *Trichinella spiralis* in swine (Carlton Gyles, 2016; Schultz, 2008). Virchow invented the term 'zoonosis' to indicate an infectious disease that is passed between humans and animals and showed the link between animal and human medicine (Carlton Gyles, 2016; Centers for Disease Control and Prevention (CDC), 2016). Moreover, according to Virchow, health conditions were affected also by environmental factors (Evans & Leighton, 2014). He is also quoted as saying: *"Between animal and human medicines there are no dividing lines – nor should there be. The object is different but the experience obtained constitutes the basis of all medicine"* (Evans & Leighton, 2014).

One of Virchow's students, the Canadian Sir William Osler (1849–1919), continued to encourage the integration of human and animal health teaching, in the 1870s, both medical students at McGill College and veterinary students at the Montreal Veterinary College (Carlton Gyles, 2016; Evans & Leighton, 2014). For his works, Sir William Osler is considered the father of modern medicine (Evans & Leighton, 2014).

In the 20th century, two scientists of the United States have been recognized for their forward approach to what one day would become the 'One Health' concept: James Steele (1913-2013) and Calvin Schwabe (1927–2006) (Evans & Leighton, 2014).

Steele founded in 1947 the veterinary public health unit within the future Centers for Disease Control and Prevention, which involved public health education as a new veterinary field (Evans & Leighton, 2014). Also, the role played by animals in the epidemiology of zoonotic diseases was acknowledged by Steele, who promoted the interconnection between public health and animal health (Centers for Disease Control and Prevention (CDC), 2016). The creation of a ground-breaking programme in veterinary preventive medicine at the School of Veterinary Medicine at the University of California, Davis, was made by Schwabe (Evans & Leighton, 2014), who also invented the term 'One Medicine' (Zinsstag et al., 2005). He strongly advocated for collaboration between professionals in human and veterinary public health to address zoonotic disease concerns: studying rinderpest in cattle in East Africa, he illustrated the added values of the 'one medicine' compared to the traditional approach to the disease (Carlton Gyles, 2016; Centers for Disease Control and Prevention (CDC), 2016; Evans & Leighton, 2014; Zinsstag et al., 2005).

Moreover, in 1948 a veterinary public health programme was implemented by the World Health Organisation (WHO), stressing the need to close the gap between the two disciplines (Mantovani, 2008). An additional next step in this direction was accomplished in 1978 with the introduction of 'primary health care', which requires collaborations amongst different professionals, during the WHO General Assembly (Mantovani, 2008).

A unique situation is represented by the evolution, in the second post-war period, of the public health sector in Italy: in 1945, the High Commissioner for Hygiene and Public Health was established, which also included veterinary services. This organization is reflected in the structure of the current Italian Ministry of Health, which still includes the veterinary services (Ministero della Salute, 2014).

One Health in the 21st Century

In the past twenty years, the OH concept is receiving increasing attention not only because of the emergence and re-emergence of diseases transmitted to humans from an animal reservoir, but also because of the increasing awareness of the global challenges that require a broader approach (Amato et al., 2020).

The current OH concept is a restructuring of health (Evans & Leighton, 2014). Within this reform, environmental factors have been integrated as new components of ecosystem health (highlighting the fundamental connections between animals, humans, and the environment) (Carlton Gyles, 2016). From the One Medicine concept, which put attention to treating diseases, One Health evolved through the development of awareness on health promotion (Carlton Gyles, 2016). In Figure 1, the milestones in the global recognition of One Health during the 21st century are summarized.

- 2004: The Wildlife Conservation Society publishes the 12 Manhattan Principles
- 2007: The American Medical Association passes the One Health resolution promoting partnership between human and veterinary medicine
- 2007: The One Health approach is recommended for pandemic preparedness
- 2008: FAO, OIE, and WHO collaborate with UNICEF, UNSIC, and the World Bank to develop a joint strategic framework in response to the evolving risk of emerging and re-emerging infectious diseases
- 2008: One Health becomes a recommended approach and a political reality
- 2009: The One Health Office is established at CDC
- 2009: USAID establishes the Emerging Pandemic Threats program
- 2009: Key recommendations for One World, One Health™ are developed
- 2010: The Hanoi Declaration, which recommends broad implementation of One Health, is adopted unanimously
- 2010: The Tripartite Concept Note is published
- 2010: Experts identify clear and concrete actions to move the concept of One Health from vision to implementation
- 2010: The United Nations and the World Bank recommend adoption of One Health approaches
- 2010: The European Union reaffirms its commitment to operate under a One Health umbrella
- 2011: The 1st International One Health Congress is held in Melbourne, Australia
- 2011: The 1st One Health Conference in Africa is held
- 2011: The High Level Technical Meeting to Address Health Risks at the Human-Animal-Ecosystem Interface builds political will for the One Health movement
- 2012: The Global Risk Forum sponsors the first One Health Summit
- 2013: The 2nd International One Health Congress is held in conjunction with the Prince Mahidol Award Conference

Figure 1 - Milestones in the global recognition of One Health (Gibbs, 2014)

Pillar of the foundation of the One Health approach has been the publication of the "Manhattan Principles" in 2004 by the Wildlife Conservation Society. On September 29, 2004, a symposium titled "Building Interdisciplinary Bridges to Health in a 'Globalized World'," organized by the Wildlife Conservation Society took place at Rockefeller University in New York City; 12 priorities were set to combat health threats to human and animal health. These priorities, known as the Manhattan Principles, called for an international, interdisciplinary approach to prevent disease and formed the basis of the "One Health, One World™" concept, a trans-disciplinary approach, or simply "One Health" (Centers for Disease Control and Prevention (CDC), 2016; Cook et al., 2004; Gruetzmacher et al., 2021). Since then, the OH approach has been pursued by many international bodies, and the Manhattan Principles were followed by many additional international developments.

In 2008 the guidance document "Zoonotic Diseases: A Guide to Establishing Collaboration between Animal and Human Health Sectors at the Country Level" was developed in the WHO branches of South-East Asia Region and Western Pacific Region (WHO, 2008). Also in 2008, a consultation document on "Contributing to One World, One Health - a strategic framework for reducing risks of infectious disease at the animal-human-ecosystem interface" (FAO et al., 2008), jointly prepared by the Food and Agriculture Organisation (FAO), the World Organisation for Animal Health (OIE), WHO, the United Nations Children's Fund (UNICEF), the World Bank and the United Nations System for Influenza Coordination (UNSIC), was discussed during the International Ministerial Conference on Avian and Pandemic Influenza (Egypt, 25th–26th October 2008) (Calistri et al., 2013). The report highlighted that control and prevention of emerging zoonoses is in everyone's interest and requires long-term investment from private and public sources (Gibbs, 2014). The Strategic Framework paper (FAO et al., 2008), besides focussing on emerging infectious diseases at the animal-human-ecosystems interface, identified six specific objectives (Calistri et al., 2013):

1. To develop international, regional, and national surveillance capacity, making use of international standards, tools, and monitoring processes;
2. To ensure adequate international, regional, and national capacity in public and animal health—including communication strategies—to prevent, detect and respond to disease outbreaks;
3. To ensure national emergency response capacity, as well as a global rapid response support capacity;
4. To promote inter-agency and cross-sectoral collaboration and partnership;
5. To control HPAI and other existing and potentially re-emerging infectious diseases;

6. To conduct strategic research.

The document was shortly followed in 2010 by the "Tripartite Concept Note", cooperatively developed by FAO, OIE, and WHO, on "Sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces" (FAO et al., 2010), which is acknowledged as the major milestone towards OH global implementation after the Manhattan Principles. The economic benefits of the OH approach were also assessed by the World Bank, and the results were published in a document in 2012 (World Bank, 2012).

A few years later, in 2019, the joint efforts of FAO, OIE, and WHO resulted in the tripartite guide to address zoonotic diseases (WHO et al., 2019). The document was conceived as a collection of successful case studies of the application of the OH approach, highlighting the lesson learned and the good-practice standards. Moreover, it represents a pillar for the implementation of multi-sectoral collaboration at a national level, but also in guiding effective communication, coordination, and collaboration across sectors to mitigate the effects of the threats arising from the human-animal-environment interface (WHO et al., 2019).

The same year, the "Berlin Principles on One Health" restructured and expanded the Manhattan Principles in the light of the global fundamental changes of the previous years (Gruetzmacher et al., 2021). The Climate and Environmental Foreign Policy Division at the German Federal Foreign Office and the Wildlife Conservation Society convened the One Planet, One Health, One Future conference in Berlin, October 25th, 2019 (Gruetzmacher et al., 2021). Before the conference, a multidisciplinary group of experts (including experts in policy, sociology, philosophy, economics, ecology, meteorology, and human and veterinary medicine) prepared a Call to Action, the "Berlin Principles on One Health" (Gruetzmacher et al., 2021). These new fundamentals are an update of the Manhattan Principles: they tackle ecosystem health and integrity, but also address new pressing issues, such as pathogen spillover, climate change, and antimicrobial resistance (Gruetzmacher et al., 2021). It is noteworthy how the discussion of the Berlin Principles predicts the COVID-19 outbreak by several months, confirming their urgency.

One Health in Europe

In most European countries, the veterinary services, and therefore veterinary public health, are framed under the umbrella of the agricultural administration. A few exceptions are represented by Italy (as mentioned) and Austria, in which the veterinary sector depends on the Health Ministries (Mantovani & Macrì, 2004). This model was considered beneficial and therefore was adopted also by the European Commission (EC): public health, animal health, animal welfare, and food safety are comprised within the DG SANTE (DG SANCO, n.d.). This particular structure could facilitate cross-sectoral initiatives.

On a policy level, the EC (European Commission, 2019) compiled the European Green Deal in late 2019. The policy has the goal to *"transform the EU into a modern, resource-efficient and competitive economy"* (European Commission, 2019). The central part of the Green Deal is the "Farm to Fork" strategy (European Commission, 2020), with which policy-makers are addressing and re-thinking completely food production systems currently in place, implementing more sustainable productions chains (Figure 2). Because of its attention to the environment, the strategy has been associated with OH.

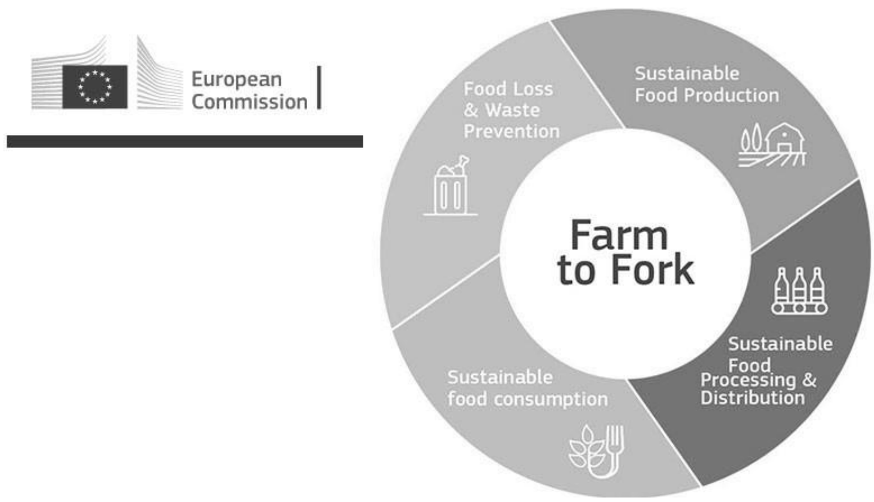

Figure 2 - Components of the Farm to Fork strategy (European Commission, 2020)

Intending to promote OH in Europe, the EC has been stimulating several projects and initiatives enhancing collaborations across sectors. The initiatives have been covering different areas of application and are addressed to many beneficiaries, Europeans and not Europeans. Two examples are investigated in the present document: the MediLabSecure 2 project[1], and the One Health European Joint Programme (OHEJP) MATRIX[2].

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[1] *MediLabSecure Project is supported by the European Commission (DEVCO: IFS/2018/402-247).*

[2] *The One Health European Joint Programme (OHEJP) is a research programme of the EU framework "Horizon 2020"*

Defining One Health

This kaleidoscope origin and evolution explains also why it is very difficult to use a single definition of One Health. At present, no consensus has been reached on a universally accepted definition of OH (Evans & Leighton, 2014). Consequently, the concept of OH must follow the evolution of the relationship between and within its components: animals, humans, and the planet they share. The concept takes into consideration the WHO definition of "health" as a state of complete physical, mental, and social wellbeing and not merely the absence of disease or infirmity (WHO, 1948).

Gibbs (2014) collected several definitions of the approach currently in use (Figure 3). A broader and more comprehensive definition is the one given by the One Health Initiative, which considers the One Health concept as a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for people, animals, and the environment (One Health Initiative, n.d.).

Definitions of One Health

'One Health is the collaborative effort of multiple health science professions, together with their related disciplines and institutions – working locally, nationally, and globally – to attain optimal health for people, domestic animals, wildlife, plants, and our environment.'
One Health Commission

'A collaborative, international, cross-sectoral, multidisciplinary mechanism to address threats and reduce risks of detrimental infectious diseases at the animal-human-ecosystem interface.'
Food and Agriculture Organization

The **World Organisation for Animal Health**, while not specifically defining One Health, endorses the approach as 'a collaborative and all-encompassing way to address, when relevant, animal and public health globally. This collaboration should not be limited to only the international level, but must be translated as a new and fundamental paradigm at national levels'.

The **One Health Global Network** considers that the aim of One Health is to 'improve health and wellbeing through the prevention of risks and the mitigation of effects of crises that originate at the interface between humans, animals and their various environments'.

The **One Health Committee of the World Small Animal Veterinary Association** comments that 'One Health or One Medicine proposes the unification of the medical and veterinary professions with the establishment of collaborative ventures in clinical care, surveillance and control of cross-species disease, education, and research into disease pathogenesis, diagnosis, therapy and vaccination. The concept encompasses the human population, domestic animals and wildlife and the impact that environmental changes ('environmental health') such as global warming will have on these populations.'

The **One Health Initiative** considers One Health to be 'a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans, animals, and the environment'.

Figure 3 – Definitions of One Health as collected by (Gibbs, 2014)

Simplistically, the components of the One Health approach are human health, animal health, and environmental health (Kaiser, 2021) (Figure 4). In practice, two OH approaches have been observed by Schmiege et al. (2020) in studies applying OH: the "classical" and the "extended" OH approach (Schmiege et al., 2020). The "classical OH approach" addresses the "management of the disease threats to humans and animals"; the second referred to as the "extended OH approach" looks into "the close interrelationship between humans and animals with ecosystems, environmental health, pathogens, and the broader social, cultural, and economic factors" (Schmiege et al., 2020). In the same study, a lack of a clear definition of "the environment" was observed, and the classical approach resulted to be the natural choice at the early stages. The extended approach needs time to be implemented, to address also the social, cultural, economic, and/or climatic issues (Schmiege et al., 2020).

The OH approach could be applied to almost any area covering complex health issues and requiring a close collaboration across sectors, stakeholders, and countries (WHO Europe, 2021). Other OH activities do not involve zoonotic diseases. According to the One Health Initiative, these actions could be comprised in the area of comparative and translational medicine (One Health Initiative, n.d.). Figure 5 summarizes the scope of OH according to the One Health Initiative (One Health Initiative, n.d.).

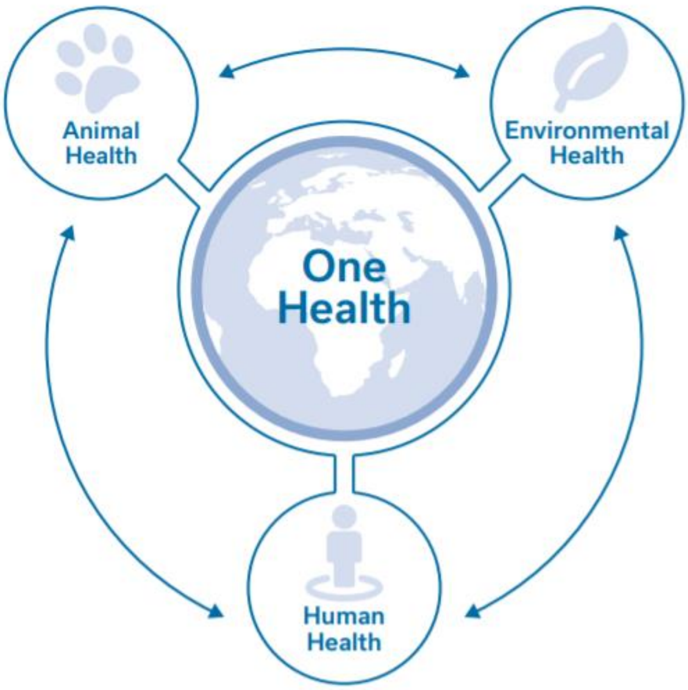

Figure 4 - Components of One Health (Kaiser, 2021)

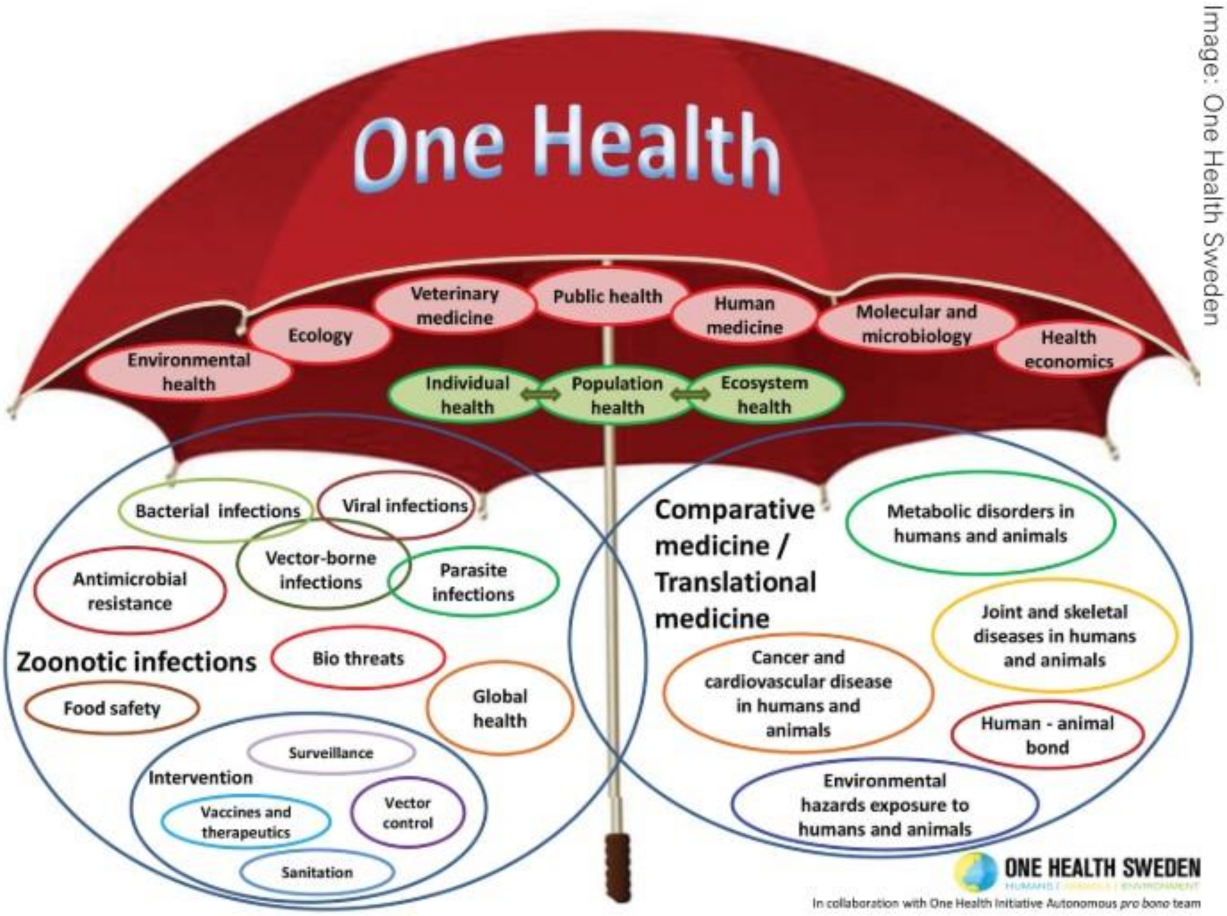

Figure 5 - The scope of OH (One Health Initiative, n.d.)

One Health: where are we?

National success stories in the implementation of OH strategies proved that the approach has worked in specific situations and contexts (Dente et al., 2018). However, concerns on the effective implementation of OH have been presented by many parts (Gibbs, 2014).

The rapid emergence and popularity of the approach have attracted funding and attention, but might not be followed by consistent results in its applications. To tackle this, initiatives like the Network for Evaluation of One Health (NEOH) (an international COST-funded network) were born, to promote the evaluation and comparison of OH activities, as well as informed decision-making and resource allocation. Its recommendations are outlined in a handbook for the evaluation of OH (Rüegg et al., 2018).

In the following pages, two case studies applying the OH approach are presented. The two refers to the extended and classical approaches (Schmiege et al., 2020), respectively: vector-borne diseases (VBDs) are taken into consideration involving also the climate and environment features in the MediLabSecure project, while in the OHEJP MATRIX it is referred to the OH approach in the sense of cross-sectoral surveillance on zoonosis in animals, food, and humans.

1. One Health and Vector-borne diseases: the experience of MediLabSecure

Why arboviruses and One Health

To better address the challenges posed by vector-borne diseases (VBDs) emerging at the animal-human interface in countries and regions not previously affected, potentially causing large epidemics, a "One Health" approach has been regarded as the best method for a long time (Calistri et al., 2013). VBDs have a complex life cycle often involving human and animal hosts, and, being transmitted by vectors, are strongly influenced by the surrounding environment; therefore, their surveillance and control could intuitively benefit from the OH approach (Dente et al., 2018).

Previous projects

Public Health networking projects are not new to the European Commission Directorate-General for Health and Food Safety (DG SANTE, former DG SANCO until 2014). The trend of networking projects addressing Mediterranean countries started many years before MediLabSecure. The main previous projects that laid the foundation for MediLabSecure2, are hereby briefly outlined.

EpiSouth Project (2006-2010) - "Network for Communicable Disease Control in Southern Europe and Mediterranean". 27 countries of the Mediterranean and Balkan regions were incorporated into the network on epidemiological issues, aiming to increase surveillance, communication and training on communicable diseases (The EpiSouth Project, n.d.). Some of the main outcomes of the project were: training modules on applied epidemiology, publication of quarterly and weekly bulletins on different issues, a pilot website with a secured section for cross-border epidemic intelligence with alerts originating from partners, directory of institutions involved in the network, directory of human and veterinary public health officials, four strategic documents on training, cross-border epidemic intelligence, vaccine-preventable diseases and migrants, and cross-border emerging zoonoses with focus on Mediterranean area (The EpiSouth Project, n.d.). A need for the improvement of national preparedness and response networks, according to the International Health Regulations, was identified by the network (Declich et al., 2010; Dente et al., 2018).

EpiSouth Plus (2010 – 2014): The natural continuation of EpiSouth was 'EpiSouth Plus', which aimed at increasing the health security in the Mediterranean Region by enhancing the preparedness to, and improve the detection of, public health threats at national and regional levels (The EpiSouth Project, n.d.).

MediLabSecure (2014 – 2018): Aiming to increase surveillance and monitoring within the Mediterranean Basin and the Black Sea regions of emerging arboviral diseases, the MediLabSecure (MLS) project was started. This network linked 55 laboratories and 19 public health institutions and/or ministries of health, throughout 19 non-EU countries (Figure 6) (Dente et al., 2018).

The OH project was developed through the transdisciplinary interaction of four sectors (or sub-networks: human virology, animal virology, medical entomology, and public health) to enhance preparedness and response against emerging arboviral diseases, and to improve integration of surveillance across sectors (Dente et al., 2018).

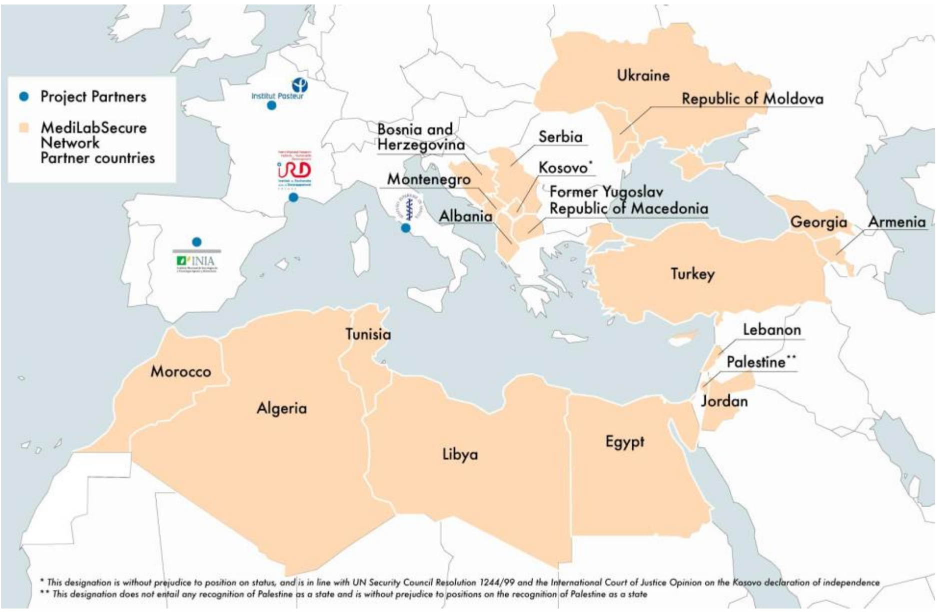

Figure 6 – MediLabSecure (2014-2018) partners and beneficiary countries

Of particular interest among the results of the MLS (2014-2018), a conceptual framework was developed with the purpose to analyze surveillance systems in place for West Nile virus (WNV), Chikungunya virus (CHKV), Dengue virus (DENV), and Rift Valley fever virus (RVFV) (Dente et al., 2018). The results highlighted that there was consistency between the descriptive criteria proposed in the conceptual framework and what was reported in studies and programmes relating to integrated surveillance of the selected arboviral diseases. These criteria can facilitate the identification and description of One Health surveillance activities that are in practice (Dente et al., 2018).

MediLabSecure, 2nd phase

Activities implemented within the countries of the consortium of the first MediLabSecure project provided for relevant results which were summarized and discussed in a Strategic Document: "Integrated surveillance and risk assessment for arbovirus infections: recommendations for enhancing One Health in the Mediterranean Region" (Dente, Ranghiasci, et al., 2019).

Given the promising results, the project was funded for additional three years (2018-2021[3]), and the second MediLabSecure (MLS2) started in December 2018. In addition to the first phase, five countries of the Sahel region (North Africa) were included: Burkina Faso, Mali, Mauritania, Niger, and Senegal. The 22 countries of the study area have been grouped into five regions, namely Balkans (Albania, Bosnia and Herzegovina, Kosovo, Montenegro, Republic of North Macedonia, and Serbia), Black Sea (Armenia, Georgia, and Turkey), Middle-East (Jordan, Lebanon, and Palestine), North Africa (Algeria, Egypt, Libya, Morocco, and Tunisia), and Sahel (Burkina Faso, Mali, Mauritania, Niger, and Senegal) (Figure 7).

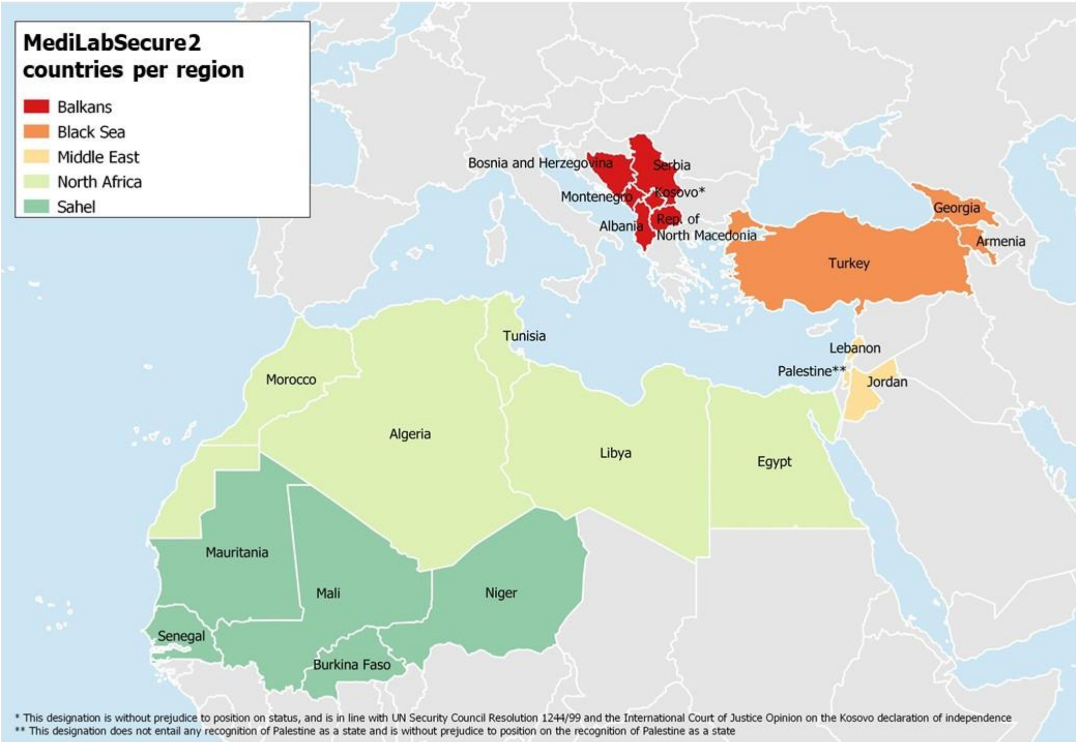

Figure 7 – Beneficiary countries of the MLS2 project, per regions

[3] *At present, January 2022, the project is still ongoing; in this regard, see pg. 47, "The way forward: impact of the pandemic"*

The Sahel region represents a major source of security threats, uncontrolled migration, and unstable countries, which affects the European Union (EU) (Dentice, 2018). To create stability and solve critical issues within this region, various strategies need to be implemented, which bring together different stakeholders and affected parties (Dentice, 2018). Falling within these broader Sahel regional strategies, the MLS2 project is also supported by the EU Chemical, Biological, Radiological and Nuclear (CBRN) Risk Mitigation Centres of Excellence (CoE) initiative (European Union, n.d.). The EU CBRN CoE provides support to, amongst others, the Sahel partner countries in improving risk management and mitigation by training, implementation of regional and national action plans, risk assessment, and field exercises (European Union, n.d.).

The MLS2 project gathers more than 170 multidisciplinary experts, from 114 laboratories and national institutions. These include animal virologists, human virologists, medical entomologists, public health epidemiologists, veterinary services epidemiologists, and modelers. The main goal of MLS2 is to promote the implementation of prevention and control strategies against VBDs under a OH approach. Under this umbrella, six Work Packages (WP) are pursuing the enhancement of capacity building, diseases surveillance, and networking (Figure 8):

- WP0 – coordination
- WP1 – human virology
- WP2 – animal virology
- WP3 – medical entomology
- WP4 – human and veterinary public health[4]
- WP5 – environmental characterization and analysis[5]

[4] *WP4 (Public Health and Veterinary Services) is held by ISS; IZSAM joined the project as a sub-contractor, therefore it is not listed as a "partner".*
[5] *The WP is also known as "Early Warning System & Modelling".*

Figure 8 – Working groups and partners (MediLaWbSecure : Partners, n.d.)

Work-Package 4

The Work-Package 4 (WP4) is focussed on the cross-sectoral field of Public Health. It is led by Istituto Superiore di Sanità (ISS), for Human Public Health, and supported by Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise (IZSAM), for the Veterinary Public Health component.

WP4 specifically promotes activities on early detection and integrated risk assessment. As WP4 involves, besides human and veterinary public health, the sectors of human and animal virology, entomology, and climate and environment, the One Health approach is fully respected. Within the WP, ISS is in charge of operational studies on integrated surveillance, and multisector risk assessment exercises, while IZSAM performs Training Need Assessments (TNA) and targeted epidemiological training.

2018's OH events

Activities of the MLS2 project started in December 2018, with two events organized by WP4: a OH scientific conference that took place in Rome (MediLabSecure, 2018a), and a OH workshop organized in Teramo (MediLabSecure, 2018b), both in Italy. The invitees to the events were the contact points of the public health and animal health sector, officially appointed to represent their institutions in the MLS2 network.

During the OH conference (MediLabSecure, 2018a), participants had the opportunity to share their national strategies, lessons learned, and constraints, and to identify and discuss the main needs and gaps to be addressed, to strengthen integrated surveillance and control of arbovirus infections. The focus was also given to the prioritization of regional and cross-border strategies and actions (MediLabSecure, 2018a). On the other hand, the workshop

(MediLabSecure, 2018b) had the objective to discuss and analyze the main gaps and needs at national and regional levels, for the implementation of integrated surveillance systems for VBDs in these countries. The participants highlighted, among gaps and needs, that some of the surveillance systems currently in place were not adequate, and scarcity of integration between the involved systems persists.

Training needs assessment

In the framework of the project, a TNA was initially planned as a phase to be delivered before each Regional meeting by IZSAM. However, on-site TNA visits were not possible and the first TNA was performed with a web-based survey and submitted to the 8 countries participating in the first Regional meeting (Tunisia, Algeria, Morocco, Mauritania, Senegal, Mali, Niger, Burkina Faso). The online questionnaire was composed of two sections, the first addressing generic questions on training systems in place in the various countries (essential to identify the training needs related to the integrated surveillance on arboviruses as Rift Valley fever virus), and the second to gather information on specific working areas (e.g. existing regional/national/local surveillance systems and other information sources, etc.). As a follow-up, a face-to-face four-hour session on epidemiology was performed during the first Regional meeting (Dakar, 20-24 January 2020). The session was conducted preferring a high level of interaction with participants, providing several practical examples, stimulating questions and discussion for each topic.

The survey on indicators for early warning surveillance:

Introduction

One Health surveillance could be described as the systematic collection, validation, analysis, interpretation of data, and dissemination of information collected on humans, animals, and the environment to inform decisions for more effective, evidence- and system-based health interventions (Amato et al., 2020; Stärk et al., 2015).

With limitations, integrated surveillance systems for arbovirus infections have been implemented in several countries (Dente, Riccardo, et al., 2019; Riccardo et al., 2018; Vrbova et al., 2010). It appears, however, that in the majority of the countries, even when the different sectors involved (i.e., human, animal, entomological, and environmental) collect surveillance data, rarely this information is shared between sectors in such a timely manner to be able to plan and implement preventing measures (Amato et al., 2020).

The topic, relevant for the MLS2 project, has been previously investigated during the first phase of the project, employing a scoping review to identify and examine surveillance systems for West Nile virus (WNV), Chikungunya virus (CHKV), Dengue virus (DENV), and Rift Valley fever virus (RVFV) (Dente et al., 2018). Moreover, in three countries of the network (Serbia, Tunisia, and Georgia), the presence of integrated surveillance systems in place has been assessed: early warning activities have not been reported as operationally prioritized (Dente, Riccardo, et al., 2019). Implementation of the early warning capacity is needed throughout the area (Dente et al., 2020; Riccardo et al., 2018).

The utilization of early warning indicators has been reported as an effective measure to implement prevention and control measures, thus reducing the severity and impact of arbovirus epidemics (Consultative Group for RVF Decision Support, 2010; Nguku et al., 2010). The vulnerability of countries or geographical zones to the introduction and spread of VBDs can be stressed out by specific indicators, which could provide crucial information to design and plan preventing actions (Ben Hassine et al., 2017; Fullerton et al., 2014).

To deal with this, studies have already been performed to predict the risk of VBDs transmission using climate data (Anyamba et al., 2009; Ezanno et al., 2015; Lowe et al., 2014, 2017), sectoral information from animals (P. Munyua et al., 2010; P. M. Munyua et al., 2016), humans (Boaz et al., 2019; Corberán-Vallet & Lawson, 2014; Rotejanaprasert et al., 2018) and vectors (Kjær et al., 2019; M. U. Kraemer et al., 2015; M. U. G. Kraemer et al., 2019).

With the purpose of investigating this topic in more depth, WP4 of the MLS2 implemented a survey, which has been carried out using an online questionnaire. To this aim, a set of surveillance indicators was identified, that could assist in increasing regional early-warning capacity and verified, through a survey, their collection at the national level (Amato et al., 2020).

Materials and methods

Literature review and the selected indicators

Attention was put on seven emerging and re-emerging arboviruses which could represent a priority for the various geographical areas of interest included in the MLS2 network (Figure 9): Crimean-Congo haemorrhagic fever virus (CCHFV), Chikungunya virus (CHIKV), Dengue virus (DENV), Rift Valley fever virus (RVFV), West Nile virus (WNV), Yellow fever virus (YFV), and Zika virus (ZIKV).

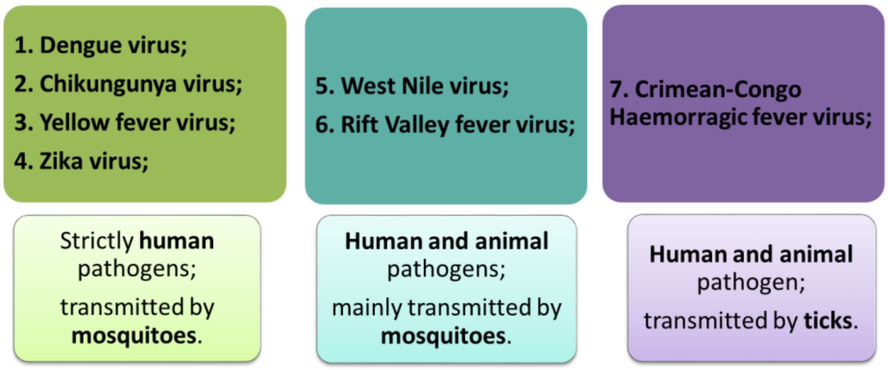

Figure 9 – Priority arboviruses in the study area and features

Making use of indicators enhances data communication and comparisons between different datasets, and summarizes important information (Hammond et al., 1995). Therefore, a literature review was performed to identify possible indicators to be used in early warning surveillance. Both peer-reviewed than not peer-reviewed literature was included (Ben Hassine et al., 2017; CDC et al., 2019; ECDC & EFSA, 2018; Fullerton et al., 2014; Lowe, 2017; Moreland et al., 2018; P. M. Munyua et al., 2016; Paz & Semenza, 2013). The potential indicators would be used to highlight vulnerabilities of MLS2 countries to the selected VBDs.

The work of Fullerton et al. (2014) for the United Nations University was particularly helpful: by describing a vulnerability assessment to Dengue, it was highlighted how relevant factors may act through different spatial and temporal scales and may be represented by both qualitative and quantitative data (Fullerton et al., 2014). Indicators are useful for summarizing large volumes of data into practical formats for decision-makers (Fullerton et al., 2014). The identification of indicators to describe different components was guided by a vulnerability framework, and the selection of data to measure these indicators was based on the quality and availability of global datasets identified from publicly accessible data repositories online (Fullerton et al., 2014).

When selecting the indicators for the MLS2 study, it was taken into consideration that they should have certain basic characteristics (Garriga & Foguet, 2010): they should be 1) available (measurable at no/reasonable cost); 2) understandable (exactly defined to be easily accepted by those who are likely to use it); 3) accurate (supported by reliable information); 4) scalable at different administrative levels; 5) relevant (responsive to changes); 6) regularly updatable; and 7) integrative among the environmental, social, and economical aspects. These criteria were used as guidelines, but not strictly applied, as some indicators were selected despite not meeting all the principles, given their relevance to the topic.

Four to six potential indicators were identified for each sector involved in surveillance activities of the selected arboviruses (the sectors involved were: medical entomology, public health, and, in case of zoonotic pathogens, animal health). Moreover, seven indicators were identified for the common climate and environment sector. MLS2 experts in medical entomology, human and animal virology, public health, and veterinary public health reviewed the selected indicators and the list was finalized (Amato et al., 2020).

The indicators selected for the questionnaires on the humans and animals' sectors were categorized as "general" (therefore falling into the "public health" or "animal health" category), or "pathogen-specific" (therefore related to the specific pathogen) (Table 1). For the questionnaire on vectors, no general indicators were identified. Some pathogen-related questions were also adjusted based on which vector is involved in the cycle (i.e. mosquitoes or ticks). Lastly, indicators of the common section on climate and environment were only general, and not pathogen-specific (Amato et al., 2020).

Sector	Indicator category	Specific indicator
Animal	Animal Health	Animal population density
		Animal movements and trade - pastoralism and transhumance
		Animal movements and trade - import and export
		Animal movements and trade - wildlife migrations
		Global public datasets on Animals
	Pathogen-related	Animal disease occurrence
		Animal disease seroprevalence
Human	Public Health	Population density
		Population age distribution
		Global public datasets on Humans
	Pathogen-related	Disease frequency or occurrence - new notified cases/outbreaks (according to National case definition) per year
		Disease frequency or occurrence - number confirmed laboratory cases (according to National case definition) per year
		Disease frequency or occurrence - persons with detected antibodies (seroprevalence)
Vector	Pathogen-related	Vector presence
		Vector abundance/density
		Vector seasonality
		Vector infection rate
		Global public datasets on Vectors
Animal / Human / Vector	Climate and Environment	Temperature
		Precipitations
		Meteorological stations
		Vegetations
		Land use
		Land cover
		Soil Type
		Global public datasets on climate and environment

Table 1 - Selected potential indicators for early warning (expanded from Amato et al., 2020)

The questionnaires

To gather information about the utilization of the selected indicators for their potential use for early warning activities in the MLS2 network, one online questionnaire was implemented in three forms, namely vector, human, and animal version. The questionnaires were compiled on Google Form©. To improve comprehension, relevance, structure, and time needed to respond, the questionnaires were reviewed by a limited group of external experts (Amato et al., 2020).

The three questionnaires contained common features and sector-specific questions for each pathogen, to which one section was dedicated to each. The animal questionnaire included only zoonotic pathogens (CCHFV, RVFV, and WNV) (Table 2), and a list of relevant species that was presented for each indicator (Table 3).

Investigated pathogens	In which questionnaires
Chikungunya virus	HUM, VECT
Crimean-Congo haemorrhagic fever virus	ANIM, HUM, VECT
Dengue virus	HUM, VECT
Yellow fever virus	HUM, VECT
Rift Valley fever virus	ANIM, HUM, VECT
West Nile virus	ANIM, HUM, VECT
Zika virus	HUM, VECT

Table 2 - Investigated pathogen per questionnaire

Animal species or category	General indicators	CCHFV-specific indicators	RVFV-specific indicators	WNV-specific indicators
Cattle	X	X	X	
Goats	X	X	X	
Sheep	X	X	X	
Equids	X			X
Camels	X	X	X	
Wild ruminants	X	X	X	
Wild animals (except wild ruminants)	X	X	X	
Wild birds	X	X		X

Table 3 – Animal species and categories investigated

At the beginning of each questionnaire, personal information was collected, including the expert's affiliation to one or more MLS2 Work-packages. At the beginning of each section, a question asking whether the specific pathogen was relevant to the experts' country. A definition of 'relevance' was given as follows: "an endemic or epidemic pathogen in the country, or an emerging pathogen not yet identified in the country" (Amato et al., 2020). If the pathogen was considered relevant, the experts were able to provide information on the collection of the indicators for that specific pathogen; if the pathogen was not considered relevant, they were able to skip to the next section (Amato et al., 2020). For each relevant pathogen, whenever an indicator was reported as collected by the respondents, another question regarding the storage modalities of the information was asked.

In addition, the availability of global public datasets (and their use) was enquired in the three questionnaires for datasets related to public health, animals, and vectors, respectively. Finally, the last section of each questionnaire was applied to all sectors, and dedicated to the indicators of climate and environment. As a final point, in a similar way to the sector-specific part, the availability and use of global public datasets on climate and environment was investigated.

Dissemination

In May 2019, the questionnaires were disseminated to 110 officially appointed contact points of the MLS2 22 countries: the version on vectors was sent to entomologists (22 experts); the version on humans to human virologists and human public health professionals (44 experts); and the version regarding animals to animal virologists and veterinary services professionals (44 experts). This approach was applied to ensure each of the versions be completed by experts with relevant experience. Completed questionnaires were collected until September 2019. Information was then analyzed using MS Excel 2016©.

Results

Questionnaire responsiveness

At least one completed questionnaire was returned by 21 out of the 22 MLS2 countries. Breaking down the responsiveness (returned questionnaires), the vector questionnaire was returned on 20 occasions out of the 22 originally sent questionnaires; the animal, by 30 occasions out of the 44 originally sent questionnaires; and the human by 28 occasions out of the 44 originally sent.

Depending on the MLS2 country, in certain cases public health sectors are separated into different districts/country regions, causing the collection of multiple responses for the same sector and country (in two cases, more than a single reply was received). Therefore, 81 questionnaires were returned (Table 4): all of them were considering zoonotic pathogens (CCHFV, RVFV, and WNV), while 50 questionnaires looked at only non-zoonotic pathogens (CHIKV, DENV, YFV, and ZIKV).

Sector	N. returned questionnaires
Vector	20
Animal	31
Human	30

Table 4 - Returned questionnaires per sector

The highest responsiveness was recorded in the Balkans area (90%), while the Sahel countries only returned 52% of the questionnaires, indicating low responsiveness (Figure 10 and Table 5).

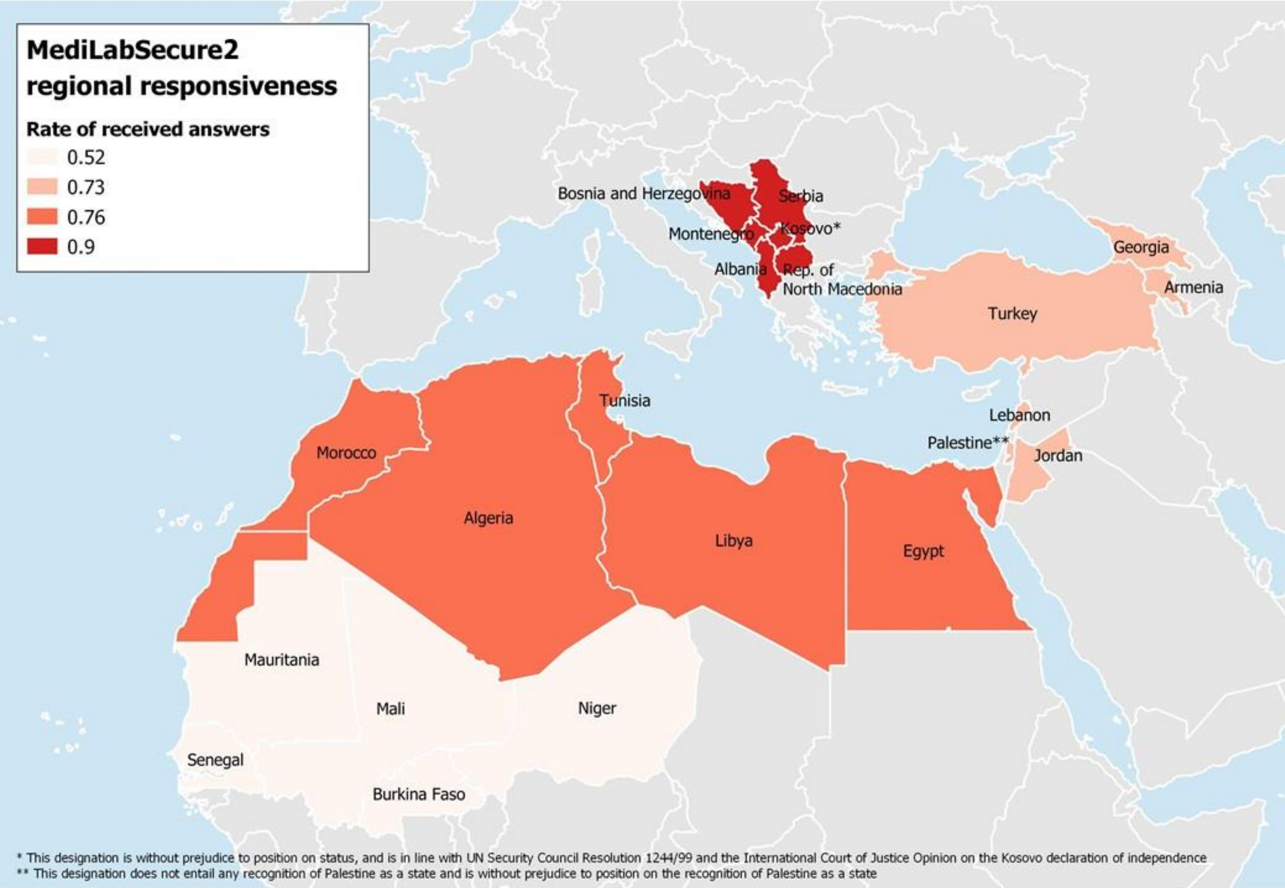

Figure 10 - Regional responsiveness to the questionnaire

Region	**Countries**	**Experts**	**Answers**	**Rate of returned questionnaires**
Balkans	6	30	27	90%
Black Sea	3	15	11	73%
Middle-East	3	15	11	73%
North Africa	5	25	19	76%
Sahel	5	25	13	52%
Total	22	110	81	74%

Table 5 – MLS2 regional responsiveness to the questionnaires

Pathogens Relevance

National Level

What emerged from the questionnaires is that WNV was perceived as the most relevant zoonotic pathogen in the overall study area, followed by CCHFV and RVFV. Specifically, WNV was relevant for 73% (59/81) of the respondents, CCHFV for 63% (51/81), and RVFV for 49% (40/81) (Table 6). Among the non-zoonotic pathogens, DENV was perceived as the most important in the study area as it was considered relevant for 62% (31/50) of the respondents (Table 6). Less relevant non-zoonotic pathogens were CHIKV at 46% (23/50), ZIKV at 40% (20/50), and YFV at 38% (19/50). Percentages of relevance per individual pathogen in the overall study area and within the different sectors are reported below in Table 6.

Pathogens	**Overall relevance in the study area**	**Vector**	**Human**	**Animal**
Crimean-Congo Haemorrhagic Fever virus	51/81 (63%)	14/20 (70%)	20/30 (67%)	17/31 (55%)
Chikungunya virus	23/50 (46%)	11/20 (55%)	12/30 (40%)	*not relevant*
Dengue virus	31/50 (62%)	13/20 (65%)	18/30 (60%)	*not relevant*
Yellow fever virus	19/53 (38%)	8/20 (40%)	11/30 (37%)	*not relevant*
Rift Valley fever virus	40/81 (49%)	11/20 (55%)	13/30 (43%)	16/31 (52%)
West Nile virus	59/81 (73%)	18/20 (90%)	22/30 (73%)	18/31 (61%)
Zika virus	20/53 (40%)	9/20 (45%)	11/30 (37%)	*not relevant*

Table 6 - Investigated pathogens and perceived relevance by sectors – adapted from (Amato et al., 2020)

Regional Level

The regional relevance of the investigated pathogens was analyzed[6]. Within the regionally grouped data, WNV was the most relevant pathogen for the respondents from the Balkans and North Africa; for Black Sea region respondents, CCHFV was the most important pathogens amongst those investigated; in the Middle East region, DENV was considered very relevant, whereas all respondents from the Sahel region considered RVFV as the most important pathogen amongst the proposed options. The following figures summarize regional relevance, overall (Figure 11) and in the three sectors (Figure 12, Figure 13, Figure 14).

[6] *Most of the results are presented geographically grouped in the five areas for the privacy of the respondents. The breakdown of countries into regions has been detailed on pg. 19.*

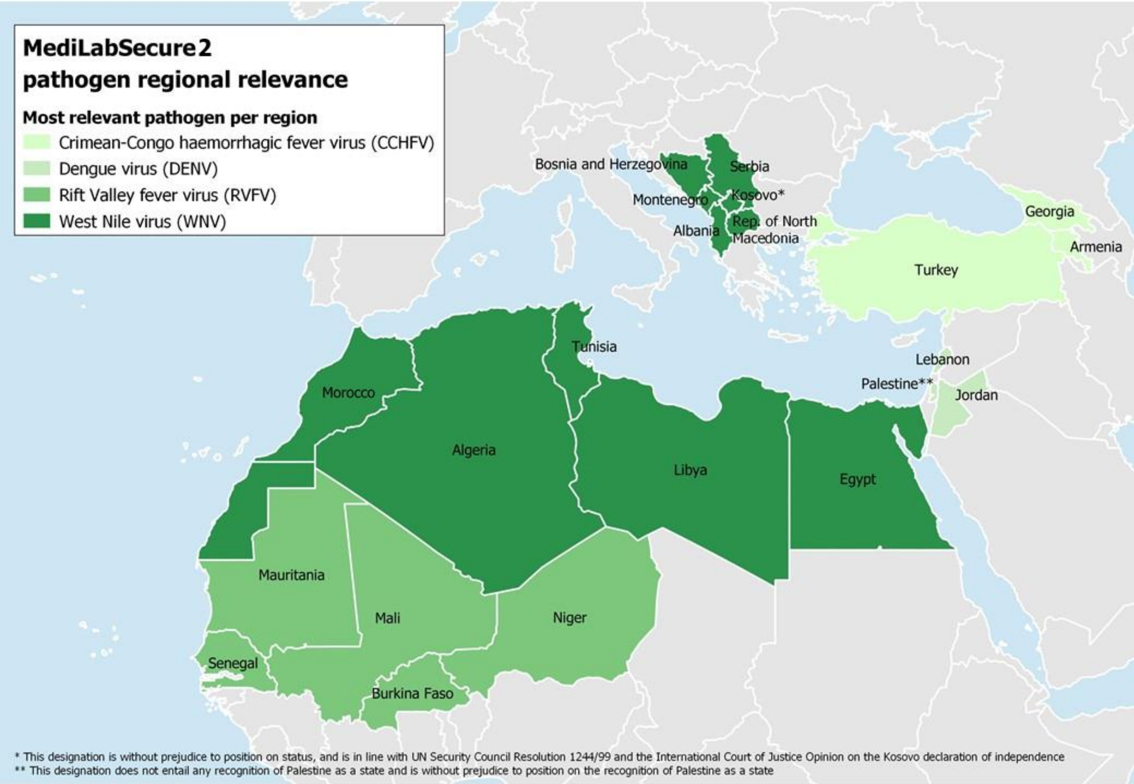

Figure 11 – Pathogen relevance on the overall received questionnaires, per region.

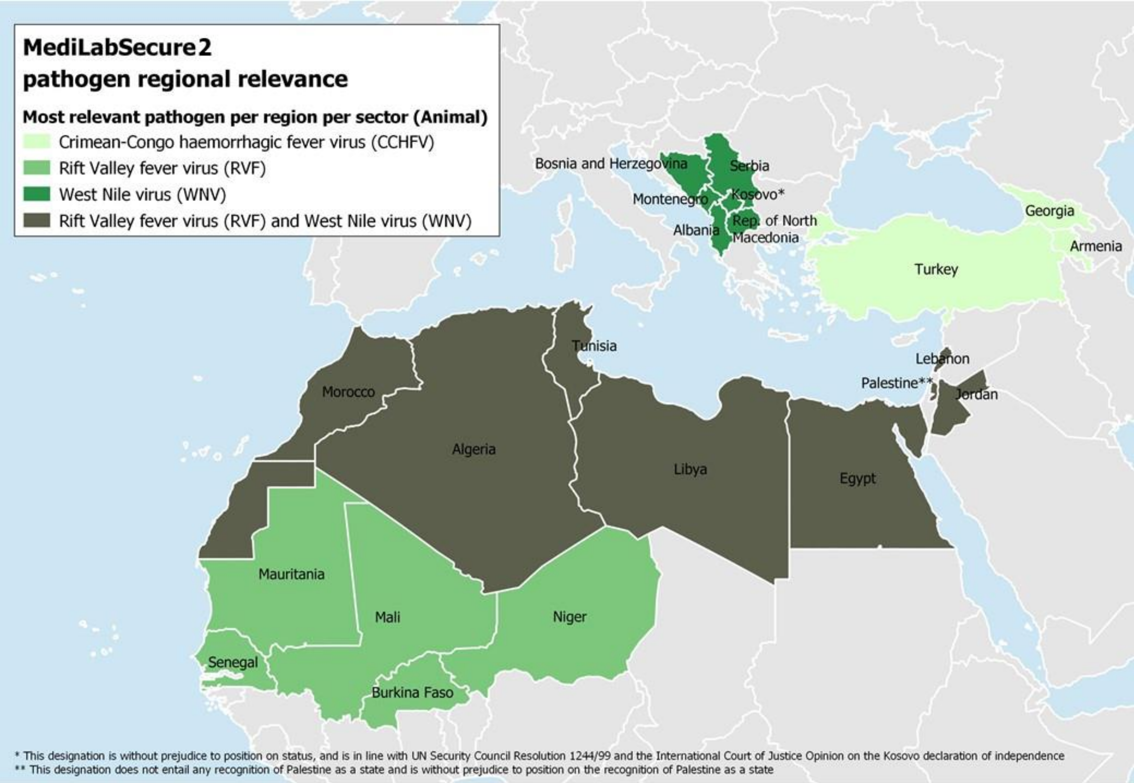

Figure 12 – Pathogen relevance on the received Animal questionnaires, per region.

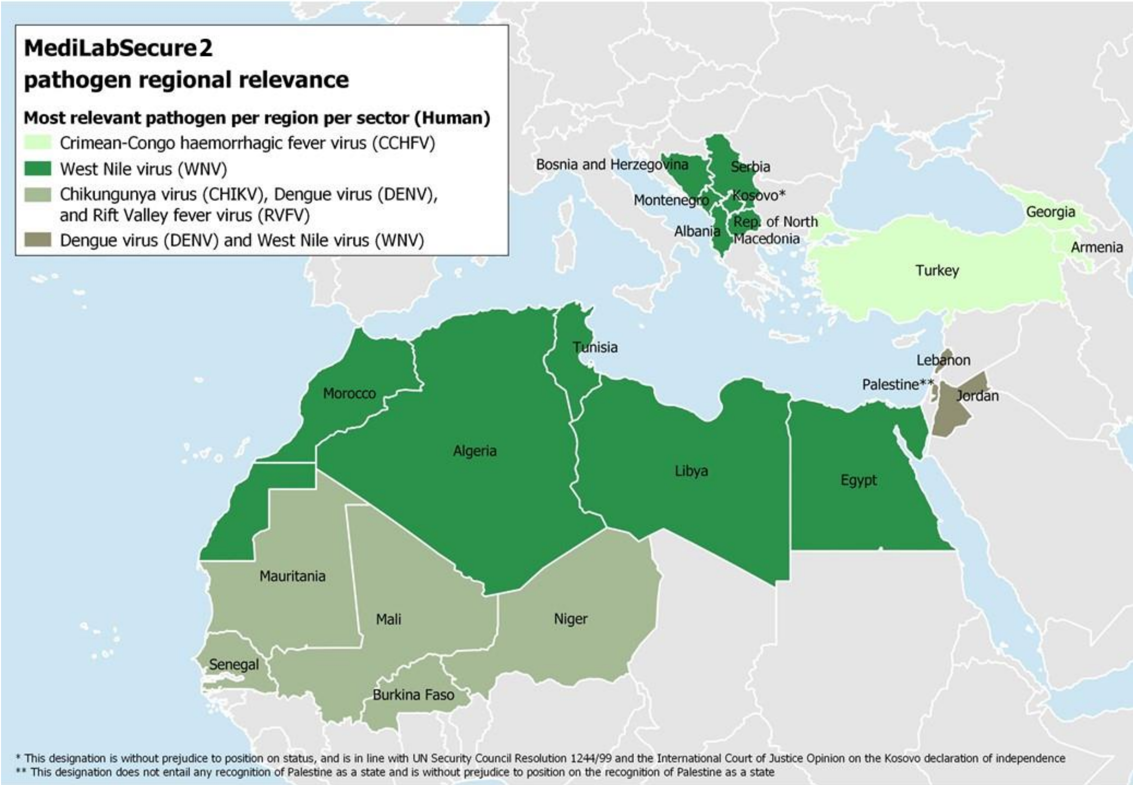

Figure 13 - Pathogen relevance on the received Human questionnaires, per region.

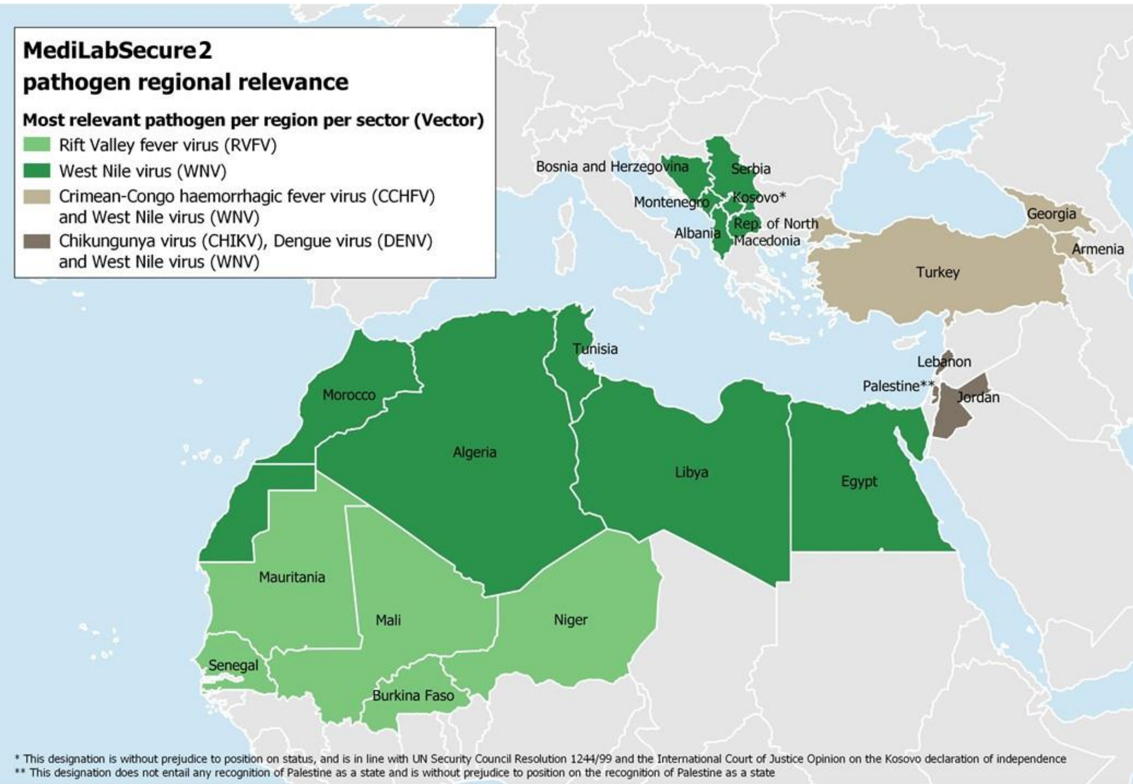

Figure 14 - Pathogen relevance on the received Vector questionnaires, per region.

Surveillance systems in place

For each sector, the routinely collection of the identified indicators was analyzed.

ANIMAL – In 100% of the returned questionnaires, the information regarding animal population density was collected for cattle, goats, and sheep, and in lesser cases for equids and camels; whilst for wild species, this data were rarely collected. Animal movements data were reported to be collected in 97% of the returned questionnaires relevant to import and export, in the 65%, for pastoralism and transhumance practices, and in the 16% of the returned questionnaires for wild animals migrations (Table 7).

The indicators of animal disease occurrence and animal disease seroprevalence, are collected by pathogen-type from 74% to 47% in the returned questionnaires (Table 7). For WNV, the two most collected pathogen-specific indicators involve equids, while for CCHFV and RVFV they refer to cattle, goats, and sheep.

Since each indicator was applied to each relevant species, in Table 7 the indicators rate are reported only for the highest collected species of interest (i.e. for Animal population density, 100% refers to the collection of the indicator in cattle, which was the highest returned indicator in all the received questionnaires).

Collection of possible indicators (animals)	**General indicators**	**Pathogen-specific indicators**		
		WNV	**CCHFV**	**RVFV**
Animal population density	31/31 (100%)	-	-	-
Animal movements and trade - pastoralism and transhumance	20/31 (65%)	-	-	-
Animal movements and trade - import and export	30/31 (97%)	-	-	-
Animal movements and trade - wildlife migrations	5/31 (16%)	-	-	-
Animal disease occurrence *	-	14/19 (74%)	8/17 (47%)	11/16 (69%)
Animal disease seroprevalence *	-	12/19 (63%)	8/17 (47%)	10/16 (63%)

** The indicator was considered "collected" when the answer was "yes" in at least one of the species present*

Table 7 – Collection of indicators per relevant pathogen, animal sector – extended and adapted from Amato et al., 2020)

HUMAN - The results from the human sector questionnaires show that population density and population age distribution data are collected in almost all cases (Table 8). To evaluate disease frequency or occurrence, the most frequently collected data are new cases (new notified cases or outbreaks, according to the national case definition, per year) and laboratory cases (number of confirmed laboratory cases, according to national case definition, per year).

Collection of possible indicators (humans)	General indicators	Pathogen-specific indicators						
		WNV	**CCHFV**	**DENV**	**RVFV**	**CHIK**	**YFV**	**ZIKV**
Population density	27/30 (90%)	-	-	-	-	-	-	-
Population age distribution	27/30 (90%)	-	-	-	-	-	-	-
Disease frequency or occurrence - new notified cases/outbreaks (according to National case definition) per year	-	20/22 (91%)	18/20 (90%)	14/18 (78%)	10/13 (77%)	7/12 (58%)	9/11 (82%)	8/11 (73%)
Disease frequency or occurrence - number confirmed laboratory cases (according to National case definition) per year	-	19/22 (86%)	17/20 (85%)	13/18 (72%)	10/13 (77%)	6/12 (50%)	8/11 (73%)	8/11 (73%)
Disease frequency or occurrence - persons with detected antibodies (seroprevalence)	-	13/22 (59%)	11/20 (55%)	9/18 (50%)	7/13 (54%)	4/12 (33%)	5/11 (45%)	6/11 (55%)

Table 8 – Collection of indicators per relevant pathogen, human sector – extended from Amato et al., 2020)

VECTOR - The most frequently collected indicator in the entomology sector is "vector presence," regardless of the involved pathogen, while data on "vector infection rate" are rarely gathered (Table 9). No general indicators were investigated in these questionnaires.

Collection of possible indicators (vectors)	**Pathogen-specific indicators**						
	WNV	**CCHFV**	**DENV**	**RVFV**	**CHIK**	**YFV**	**ZIKV**
Vector presence	12/18 (67%)	7/14 (50%)	11/13 (85%)	5/11 (45%)	11/11 (100%)	8/8 (100%)	9/9 (100%)
Vector abundance/density	8/18 (44%)	2/14 (14%)	9/13 (69%)	4/11 (36%)	9/11 (82%)	6/8 (75%)	7/9 (78%)
Vector seasonality	8/18 (44%)	4/14 (29%)	10/13 (77%)	3/11 (27%)	9/11 (82%)	6/8 (75%)	7/9 (78%)
Vector infection rate	6/18 (33%)	3/14 (21%)	1/13 (8%)	1/11 (9%)	1/11 (9%)	1/8 (13%)	1/9 (11%)

Table 9 - Collection of indicators per relevant pathogen, vector sector – extended and adapted from Amato et al., 2020)

Presence of digitalized databases

Whenever the indicator under consideration was reported as collected by the respondents, another question regarding the data storage modalities was asked. The possible answers were:

a. Digitalized national database interoperable or integrated with other sectors' databases;
b. Digitalized national database;
c. Non digitalized national database;
d. Local or regional database;
e. Other;
f. I don't know.

Table 10 summarizes the rate at which each collected indicator was reported to be stored in a digitalized national database (taking into account responses *a* and/or *b*), on the overall number of questionnaires returned (for general indicators) or on the questionnaires which stated that the pathogen of interest was relevant (pathogen-specific indicators).

Data stored in a digitalized national database	**General indicators**	**Pathogen-specific indicators**						
		WNV	**CCHFV**	**DENV**	**RVFV**	**CHIK**	**YFV**	**ZIKV**
ANIMAL								
Animal population density	71.0%	-	-	-	-	-	-	-
Animal movements and trade - pastoralism and transhumance	45.2%	-	-	-	-	-	-	-
Animal movements and trade - import and export	80.6%	-	-	-	-	-	-	-
Animal movements and trade - wildlife migrations	9.7%	-	-	-	-	-	-	-
Animal disease occurrence *	-	47.4%	41.18%	N/A	50.0%	N/A	N/A	N/A
Animal disease seroprevalence *	-	47.4%	23.53%	N/A	43.8%	N/A	N/A	N/A
HUMAN								
Population density	70.0%	-	-	-	-	-	-	-
Population age distribution	73.3%	-	-	-	-	-	-	-
Disease frequency or occurrence - new notified cases/outbreaks (according to National case definition) per year	-	63.6%	50.0%	44.4%	53.8%	33.3%	54.5%	45.5%
Disease frequency or occurrence - number confirmed laboratory cases (according to National case definition) per year	-	63.6%	50.0%	44.4%	53.8%	33.3%	45.5%	45.5%
Disease frequency or occurrence - persons with detected antibodies (seroprevalence)	-	40.9%	35.0%	33.3%	30.8%	25.0%	27.3%	36.4%
VECTOR								
Vector presence	-	11.1%	7.1%	7.7%	9.1%	9.1%	12.5%	11.1%
Vector abundance/density	-	5.6%	7.1%	7.7%	0.0%	9.1%	12.5%	11.1%
Vector seasonality	-	5.6%	0.0%	7.7%	0.0%	9.1%	12.5%	11.1%
Vector infection rate	-	5.6%	7.1%	0.0%	0.0%	0.0%	0.0%	0.0%

** The indicator was considered "collected" when the answer was "yes" in at least one of the species present*

Table 10 - Percentage of questionnaires stating data of the selected indicators are stored in a digitalized national database (animal, human, vector).

Climate and environment

Seven indicators were investigated transversally in all the questionnaires. As they were cross-cutting across the sectors, they also have been analyzed altogether. The questions included the collection of the indicator and its storage modalities.

Table 11 shows the rates, per geographical area, of the collection and storage in a digitalized national database. Meteorological stations were investigated in terms of presence/absence, and location; therefore, were not considered in the abovementioned analysis.

Temperature and precipitations resulted to be the indicators most frequently collected (from 72.7% to 100% in the five regions), and for which a national digitalized database was reported to exist most frequently. On a regional level, the most heterogeneously collected indicator seems to be vegetation, which ranges from 68.4% of the collection in North Africa to 14.8% of the Balkan region. The presence of national digitalized databases for indicators of the Climate and Environment resulted scattered in the study area (Table 11).

Region	**Results**	**Indicators**					
		Temperature	**Precipitations**	**Vegetation**	**Land use**	**Land cover**	**Soil type**
Balkans	Collection	85.20%	85.20%	14.80%	40.70%	18.50%	33.30%
	Digit. Stored	55.60%	51.90%	0.00%	14.80%	11.10%	18.50%
Black Sea	Collection	81.80%	72.70%	27.30%	36.40%	27.30%	27.30%
	Digit. Stored	18.20%	27.30%	18.20%	27.30%	9.10%	9.10%
Middle-East	Collection	81.80%	90.90%	54.50%	63.60%	54.50%	45.50%
	Digit. Stored	63.60%	72.70%	45.50%	54.50%	36.40%	27.30%
North Africa	Collection	89.50%	89.50%	68.40%	57.90%	57.90%	63.20%
	Digit. Stored	63.20%	68.40%	42.10%	36.80%	36.80%	31.60%
Sahel	Collection	84.60%	100.00%	46.20%	38.50%	38.50%	46.20%
	Digit. Stored	46.20%	69.20%	38.50%	23.10%	30.80%	38.50%

Table 11 – Climate and environment indicators collection and digital storage, per regional area

Other suggested indicators

Regarding other possible indicators to be collected for early warning purposes, the respondents to the vector version of the questionnaire mentioned insecticide resistance, presence of virus in birds (for WNV), and traps distribution. Also, regarding CCHFV, one respondent answered "ticks vs hosts", which leaves room for interpretation. In the animal questionnaires, mentioned additional indicators were: human cases, specific parameters of the outbreak (as mortality and morbidity), and vector species. Lastly, in the human version of the questionnaire, the respondents suggested: seroprevalence studies, other community events, identification of the circulating viral strain (for Dengue virus), specific information on cases (as geographical region, occupation, recent travel, clinical status, etc.), socio-demographic information, entomology, meteorological data, and animal data.

Global public datasets

Global public datasets were investigated in each one of the three questionnaires, both specifically to the sector considered than regarding climate and environment.

No examples of datasets in use were reported from the respondents from public health and human virology sectors. Some examples of datasets were reported, but the information was not completed by a website or platform (for instance: "Insecticide resistance database Irmaper", or "STATAGRI: Database for animal statistics", or "MLD mosquito list"). Also, additional answers reported some indicators to be found in a dataset, but not the dataset itself (for instance: "Temperature, precipitation", or "Wind, precipitation, pressure, and temperature", or "Climate data for GIS"), thus indicating there might have been a certain level of misunderstanding of the question.

Global public datasets regarding climate and environment were investigated cross-sectoral, and half of the overall respondents (41/81, 50%) stated that they are aware but do not use any public global dataset, while 30% of them (24/81) do not know. Regarding the 20% of the respondents (16/81) who knows and uses global public datasets to enhance surveillance capacity, 4/16 (24%) belong to the vector sector, 6/16 (38%), and 6/16 (38%) to the human and animal sectors respectively. The global public datasets reported to be in use are reported in Table 12.

Sector	Name	Website
Vector	Vectormap	https://www.vectormap.org
	ECDC vectornet vector maps	https://www.ecdc.europa.eu/en/disease-vectors/surveillance-and-disease-data
	Global biodiversity information facility (gbif)	https://www.gbif.org
Animal	OIE WAHIS	https://wahis.oie.int/
	ADNS **	https://ec.europa.eu/food/animals/animal-diseases/animal-disease-information-system-adis_en
	Genbank	https://www.ncbi.nlm.nih.gov/genbank/
Climate and environment*	Worldclim	https://www.worldclim.org/
	Modis	https://modis.gsfc.nasa.gov/about/
	Soilgrids	https://soilgrids.org/
	Unsd	https://unstats.un.org/home/

** Please note that this question was asked in the three versions of the questionnaires;*
*** Now "ADIS"*

Table 12 - Global public datasets reported to be in use in the investigated countries

Level of cross-discipline of the involved experts

On a final note, the level of cross-discipline of the involved experts was assessed based on their affiliation to one or more MLS2 Work-packages.

In the three questionnaires, most of the answers were received from an expert belonging to the specific WP of the sector (Table 13) (e.g., expert affiliated to the WP of animal virology responding to the animal questionnaire); particularly, in the animal and human questionnaires, the most represented experts were the virologists (animal virology, 16/31; human virology, 9/31, respectively).

Regarding the answers to the animal questionnaire, the experts with cross-sectoral affiliations were 4/31 (12,9%); amongst the experts involved in the human questionnaire, the intermingling was higher, up to 9/30 (30%), most of which with the entomology sector (8/30); vice-versa, out of the experts that replied to the vector questionnaire, 5/20 (25%) stated to be involved in the activities of WPs of medical entomology, public health, and human virology, while 2/20 (10%) in animal virology and veterinary services.

Questionnaire	MLS2 Work-package member	N. answers	N / tot
Animal	Animal virology	16	51.6%
	Veterinary services	4	12.9%
	Animal virology and veterinary services	6	19.4%
	Animal virology, veterinary services, and Medical Entomology	1	3.2%
	Animal virology, veterinary services, Medical entomology, and human virology	2	6.5%
	Animal virology and human virology	1	3.2%
	Not assessed	1	3.2%
Human	Human virology	9	30.0%
	Public health	7	23.3%
	Human virology and public health	4	13.3%
	Human virology, public health, and medical entomology	7	23.3%
	Human virology and medical entomology	1	3.3%
	Human virology, public health, medical entomology, and animal virology	1	3.3%
	Not assessed	1	3.3%
Vector	Medical entomology	13	65.0%
	Medical entomology and human virology and public health	4	20.0%
	Medical entomology and animal virology and veterinary services	2	10.0%
	Medical entomology and public health	1	5.0%

Table 13 – MLS2 Work-package membership of the experts replying to each questionnaire

Discussion

As stated by Leta et al. (Leta et al., 2018), arboviral diseases are indeed a global public health threat considering that 215 countries/territories are potentially suitable for the most important arboviral disease vectors (*A. aegypti* and *A. albopictus*) and more than half of these areas are reporting cases of Zika, Dengue fever, Chikungunya, Yellow fever, and/or Rift Valley fever.

The pathogens' relevance perceived by the respondents of the survey is in accordance with their diffusion in the region. WNV is the most widely distributed arbovirus on the planet (Kramer et al., 2008); RVFV is relevant mainly for African countries, even if it is suggested that other regions of the MLS2 network are suitable for potentially competent RVFV vectors and may be considered at risk of introduction through uncontrolled movements of infected animals from infected neighbouring countries (EFSA Panel on Animal Health and Welfare (AHAW), 2013). CCHFV, clearly acknowledged in the Black Sea and Balkans regions as a priority, is not considered relevant by the respondents from both the Middle East and North Africa, despite its main vector being present in both regions, and virological and serological evidence was highlighted in some of those countries (WHO, n.d.). The results for YFV suggest that it is perceived as the least important pathogen, perhaps in light of the widespread and effective vaccination programs in progress for 50 years (Wilder-Smith, 2017). Overall, the relevance ranking of pathogens is the same within the three sectors, demonstrating that shared priorities exist and that there is strong potential for integrated strategies. This is not completely true in the case of Middle-East countries: DENV was the non-zoonotic pathogen considered more relevant, while amongst the zoonotic WNV and RVF were equally relevant.

According to the information gathered by the survey, the collection of indicators suitable for early warning is in place with a range of different situations in the MLS2 network countries. At this stage, it would be possible, albeit challenging, to identify opportunities for targeting disease threats upstream (prevention at the source, or via early detection and effective response) to support the reduction of occurrence and impact of arboviruses transmission (Berthe et al., 2018).

From the questionnaire results, information on animal population density is collected in all the involved countries for some domestic species, supplying national authorities with important data for animal disease surveillance. However, wildlife information is rarely gathered: surveillance programs in wildlife are needed and desirable, not only to investigate the health status of wildlife populations, but also to investigate a potential reservoir of infection and, therefore, to prevent the spillover in domestic animals and humans (Morner et al., 2002).

Data on disease frequency or occurrence in humans (both either suspected cases or lab confirmed) are collected by the majority of the countries involved. On the other hand, less effort is dedicated to seroprevalence studies, despite their potential importance in areas where the disease has been not reported yet.

Vector presence predictably resulted as the most collected vector indicator. On the contrary, vector infection rate was the most difficult to gather in the case of mosquitos-transmitted pathogens, while for CCHFV (transmitted by ticks) the least collected indicator is vector abundance/density. Therefore, vector species-specific differences should be taken into consideration when interpreting these results. This said, a limitation of the present study is the use of the same indicators regardless of the vector species involved (for example, does data on "vector abundance/density" have the same significance for ticks rather than for mosquitoes?). Moreover, different people and/or different laboratories of the same institution may focus on specific vector species (i.e., mosquitoes or ticks); as a result, addressing the questionnaire to only one of them may have limited the collection of information or biased the results. However, to mitigate this risk, we strongly recommended the MLS2 contact points share the questionnaire with relevant colleagues when appropriate. Information on vector seasonality is instead less available, although by analyzing the collection of this indicator by country and by pathogen, coherent explanations might be found (e.g., endemicity of the pathogen in the concerned country with the assumption that the vector is abundant throughout the year). Nevertheless, a lack of awareness on the importance of some indicators for the monitoring of certain pathogens could also explain their unsuccessful collection.

A final section in all the questionnaires allowed for the collection of information on indicators relevant to climate and environment (temperature, precipitations, meteorological stations, vegetation, land use, land cover, and soil type). The preliminary analysis of this information shows that this collection should be strengthened, especially in light of the increasing environmental and climate impact on the diffusion of arboviruses. This section was compiled by experts from all the sectors involved in the survey; despite the possibility to answer "I don't know", the collected answers could have been not 100% accurate.

Data sharing is fundamental in the context of the implementation of OH strategies, and there is no efficient and effective data sharing without a digitalized database at the national level, for the effective communication of data amongst the involved sectors. From the survey, it emerged that data sharing is in place only in a few cases amongst the MLS2 countries.

Interestingly, when asked to present additional indicators not mentioned in the survey, the experts mentioned also other sectors' indicators, denoting a slow but progressive exit from the silo thinking. When looking at the MLS2 affiliation of the experts that returned the questionnaires, it appears that some multi-discipline experts are part of the Network, in particular across public health/human virology and medical entomology. On the other hand, experts from the veterinary services and animal virology showed limited multidisciplinary expertise, being involved at a lower level in other WPs' activities. This finding is influenced by the different organizations of the sectors in the countries.

Based on the returned questionnaire, the utilization of the global public dataset on climate and environment to enhance national early warning capacity for arboviral diseases is quite low in the investigated study area. Few examples were reported also for datasets of the three sectors. In light of the importance of environmental and climate in the transmission of several infectious diseases, including arboviral, awareness on the availability of environment and climate information should be improved in all the sectors involved, and their utilization enhanced to reinforce early warning strategies with a One Health approach.

Collecting data through an online questionnaire proved to be the most convenient and effective solution to quickly gather information from the MLS2 region. However, this method has some disadvantages: it was not possible to verify the quality (completeness, uniformity, etc.) of data collection in place, nor to investigate individual special cases discovered with the study.

Having assessed that each of the sectors involved in the surveillance was collecting indicators for the most relevant arboviral infections in the MLS2 region, the next step would be to verify if a specific selection of appropriate indicators amongst those presently collected can provide the ability to predict or allow for early warning, especially in terms of a One Health perspective ("integrated early warning"). The piloting of such a type of integrated approach could help to understand if integrated early warning represents the weak spot of the OH, until more effort will be put into setting up all the requirements needed to operationalize such a system. Among others, the need to increase the performance of the system is crucial in terms of sensibility and specificity through the integration of data from different sources and Institutions. This is only possible with the presence of shared or closely connected information systems, procedures, and indicators.

However, when interpreting the results, it has to be taken into account the extreme variability of the study area, which comprises countries very different from each other from a socio-economic point of view. For instance, the Sahel area (which was investigated with the participation of Burkina Faso, Niger, Mali, Mauritania, and Senegal), is one of the poorest areas of the planet. In this region, 80% of its people live in extreme poverty (with less than $1.90 a day), and the SARS-CoV-2 pandemic has exacerbated this situation (Diagana, 2020). The current economic growth is not sufficient to improve the living condition of the area (Diagana, 2020). The scarcity of infrastructures poses a serious limitation for the public health sectors, let alone the implementation of cross-sectoral surveillance activities. The regional context could also have had an impact on the answers to the questionnaires. On the other hand, the Middle-East region (investigated in Palestine, Lebanon, and Jordan), has experienced multiple and occasionally overlapping security challenges even before the 2011 Arab uprisings (Kamrava, 2019). This chronic insecurity has many causes and many consequences, one of the latter is the limitation in the development of public health infrastructures, which in turn constrains the integrated response capacity to cross-sectoral health threats. In North Africa, socio-economic limitation persists and varies between countries: in Libya, Egypt, Tunisia, Algeria, and Morocco, different levels of surveillance activities are in place, but underlying organizational situations may have influenced the data collection of the study. Lastly, in the Balkan and Black-sea areas (investigated countries: Albania, Bosnia and Herzegovina, Kosovo, Montenegro, Republic of North Macedonia, and Serbia; Armenia, Georgia, and Turkey) the results showed that existing capacities of the public health systems are not used at the maximum of their potential, and cross-sectoral activities are still difficult to implement.

In all the countries of the study, supplementary investigations would be needed to identify specific gaps and possible areas of intervention, to implement the OH approach operationalization when dealing with the surveillance of arboviruses and other common health threats.

Conclusions

A certain grade of collection of surveillance data (indicators) is already in place in the MLS2 countries. Their collection should be strengthened and the gaps on critical indicators addressed (i.e., vector infection rate and wildlife information). It would be now worthwhile to proceed with further assessments which could help to clarify the reliability of the indicators collected and the feasibility of the implementation of an integrated early warning system for arboviral infections. Since some relevant indicators are already being collected, this would not demand extra resources but, on the contrary, its operationalization could lead to savings.

Deep studies in promising countries could help to address the problem and would represent the chance to pilot integrated early warning systems using data already being collected and to promote the collection of critical data not yet gathered. This would reflect what was stated by Berthe et al.: "One Health is a sound management approach, fully aligned with the definition of 'health,' and good practice for its predicament on the use of increasingly scarce resources, therefore improving efficiency and efficacy" (Berthe et al., 2018).

The way forward: impact of the pandemic

Since February 2020, the advent of the SARS-CoV-2 pandemic severely impacted the activities of the project and forced a halt in the networking component. Not only was it not possible to travel and meet with colleagues (a fundamental aspect of a networking project), but also the appointed experts of many countries were personally involved in their country's emergency responses to the pandemic, and were therefore not available to follow up on other ongoing activities, even if online.

With the dual intent of postponing the core activities (i.e., those planned in the initial project) of the project and supporting the beneficiary countries of MLS2 in the COVID-19 response, a project extension was submitted and approved by the European Commission. A new Work Package was established to follow COVID-19 related activities, while the core activities were almost completely discontinued. The canceled or postponed activities of WP4 include 1) the second phase of the survey on early indicators, with site visits in selected countries for an in-depth analysis of the surveillance systems in place, 2) on-site TNA addressed to the countries not involved in the first Regional meeting, and 3) subsequent epidemiology training on the identified needs. Some of these have been/are currently being performed via online tools. Therefore, at the time of writing, the project is still ongoing and it is supposed to finish by the 7th July 2022.

2. One Health and food-borne diseases: a glimpse from the OHEJP MATRIX

OHEJP: an interdisciplinary, integrative, and international approach

The One Health European Joint Programme (OHEJP), a research programme that started in 2018 within the EU framework programme Horizon 2020, and coordinated by the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) falls within the European initiatives to promote OH (Bundesinstitut für Risikobewertung, 2022).

The OHEJP (01/2018-12/2022) has been established with several aims. The strengthening of the ongoing relationships between European institutes, through transdisciplinary activities on food-borne zoonoses (FBZ), emerging threats (ET), and antimicrobial resistance (AMR) carried out within dedicated Joint Projects, is the primary aim (One Health EJP, 2019). Simultaneously, there is the ongoing effort to develop a European OH platform, to satisfy the needs of the stakeholders and national and European decision-makers (Bundesinstitut für Risikobewertung, 2022).

The project brings together 22 Member States (MSs) and 44 partners, each one with separate tasks to perform: scientific data, guidelines, epidemiological studies, and tools will be produced for their use by national and EU authorities and institutions for health risk assessments and the evaluation of preventive and intervention measures (Bundesinstitut für Risikobewertung, 2022; One Health EJP, 2019). A priority of the project is the dissemination of information, which should be proficient and continuous, from the researchers to the scientific community, the stakeholders, and the relevant authorities (ANSES, 2017; Bundesinstitut für Risikobewertung, 2022).

The "interdisciplinary, integrative and international approach to One Health" is fundamental to dealing with FBZ, ET, and AMR. The experts involved in the project represents the underlining fabric of the research network (One Health European Joint Programme, 2019).

MATRIX: "Connecting dimensions in One-Health surveillance"

The strengthening and implementation of collaborations and dissemination between sectors involved in surveillance activities on AMR, ET, and FBZ, was the focus of the earlier round of the integrative projects. This was the starting point of the OHEJP MATRIX. The project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 773830 (One Health EJP, 2020b).

MATRIX has the goal to continue what had been started in terms of integrative surveillance along the food chain, revision of the measures in place, to propose guidelines to reinforce or create One Health Surveillance (OHS) collaborations (One Health EJP, 2020b). The project especially focuses on cross-sectoral OHS in practice, analyzing already existing programmes of this kind and enhancing them. It is based on the premise of the need for a problem-based approach that could use real-life cases; however, any country has a peculiar reality; therefore, proposed solutions, tools, guidelines, etc., should be adaptable to different settings (One Health EJP, 2020b). This problem-oriented approach is the strong point of the project: it is reflected by the implementation of activities and tasks along specific hazard-tracks. This, in turn, allows for the identified solutions to be applicable and useful for as many hazards as possible (One Health EJP, 2020b).

The name MATRIX takes inspiration from the matrix composed of the different sectors involved in OHS, and the four hazard tracks of the project (*Campylobacter*, *Salmonella*, *Listeria*, and Emerging Threats), interacting with each other in a cross-disciplinary way. MATRIX was launched the 1st of January 2020. Having been strongly impacted by the SARS-CoV-2 pandemic, in terms of the availability of resources and staff to carry on the planned activities, an extension has been granted. The project will be concluded at the end of 2022.

Work-package 2 and the mapping of the surveillance chain

Work-package 2 (WP2) focus is on best practices and multi-sectoral collaboration. WP2 leader is IZSAM and deputy-leader is the Danish Statens Serum Institut.

The work of WP2, and more in general of the MATRIX project, connects to the results obtained by two projects of the first round of OHEJP, ORION and COHESIVE (One Health EJP, 2018b, 2020a), intending to put them into practice and carry on the dissemination. Moreover, the WP's activities are focused on cross-sectoral collaboration, to implement the operationalization of OHS in Europe. The development of best practices in the form of guidelines has the objective to facilitate the implementation of effective strategies for multi-sectoral collaborations.

While facilitating OH collaborations across sectors, WP2 has the purpose to deliver a common framework by means, amongst other tasks, of the identification of best practices for data collection, analysis, and dissemination in the framework of surveillance activities.

In this context, WP2 first task (WP2-T1) was implemented to provide a "mapping of the surveillance chain across all sectors for each hazard-track", for at least one country per hazard-track. The work performed for WP2-T1 has been reported within the first Deliverable of WP2, D-WP2.1, submitted in December 2021. At the time of writing, the document is under revision by the MATRIX Consortium, and it will be made publicly available on the Zenodo platform (European Organization For Nuclear Research, 2013). In alignment with the dissemination intention of the OHEJP Projects, the results will likely be published in a paper. The main task's outcomes and conclusions are hereby reported.

WP2-T1: Mapping of the surveillance chain across all sectors for each hazard-track

Introduction

The OHEJP MATRIX Project's activities are focused on three specific pathogens (*Campylobacter, Listeria, Salmonella*), plus one not-specific hazard-track, named Emerging Threats.

According to the last EFSA's Zoonoses report (EFSA and ECDC, 2021b), the two most notified zoonoses in humans in 2020 were caused by *Campylobacter* spp. and *Salmonella* spp., campylobacteriosis and salmonellosis, respectively. The trend in the reporting of the two diseases has been stable in the EU in the past four years (EFSA and ECDC, 2021b). For the sole campylobacteriosis, the estimated burden for the Public Health sector hovers around 2.4 billion euros per year (European Food Safety Authority, n.d.-a).

Since *Campylobacter* lives in the intestine of healthy animals, raw poultry meat could be easily contaminated. Therefore, eating ready-to-eat or undercooked foods, that have been in contact with raw poultry meat, is considered the most common source of infection. Campylobacteriosis is considered a priority disease by EFSA: from 2007 to 2020, many scientific opinions and reports have been published on the risk of contamination of poultry meat, risk factors for human health, and control options (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2020; EFSA Panel on Biological Hazards (BIOHAZ), 2010, 2011; Vose Consulting (US) LLC, 2010).

On the other hand, many animals, including livestock, are the reservoirs of *Salmonella* spp.. Unlike campylobacteriosis, salmonellosis could be the result of the consumption of many different food items: eggs, contaminated meat from pigs and poultry (European Food Safety Authority, n.d.-b). At the same time, a significant under-reporting of salmonellosis cases is considered to be happening, given the generally less severe illness, not requiring hospitalization or treatment in many cases. To reduce the rate of cases, every EU member state has implemented *Salmonella*-control programmes in poultry farms (European Commission, n.d.)

Listeria monocytogenes is the cause of listeriosis, a human and animal disease. In vulnerable people (e.g. the elderly, pregnant women, and immunocompromised individuals) the infection could turn into a severe disease and lead to hospitalization, and, more rarely, death (EFSA, n.d.). *Listeria monocytogenes* was the most frequently reported pathogen amongst hospitalized cases of all reported zoonoses in 2019 in Europe (EFSA and ECDC, 2021a). Reservoirs of the pathogen are different animal species, including cattle, and small ruminants. A serious risk for food is the persistent contamination of food-processing plants, and often the disease is linked to ready-to-eat food consumption, which happens without additional cooking (Lundén, 2004). Otherwise, the pathogen is more frequently isolated from raw vegetables, smoked fish, meats, and cheese products (EFSA, n.d.). To limit the contamination and prevent the disease, hygiene good practices are fundamental; also, it is essential to maintain effective temperature control along the whole food chain, from the food production to consumers' homes (EFSA, n.d.).

Acknowledged to be an emerging pathogen in Europe, the Hepatitis E virus (HEV) can be transmitted by the faecal-oral route (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017). Commonly, the disease is asymptomatic or self-limiting. Hepatitis E has a low fatality rate; however, in immunocompromised patients, it could lead to chronic infections (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017). Moreover, it could develop into fulminant liver failure in pregnant women, causing a much higher mortality rate (Chilaka & Konje, 2021). Four genotypes (HEV-1 to HEV-4) have been isolated all around the world: HEV-1 and HEV-2 are mostly identified in low-income countries, and have been isolated only in humans; on the contrary, HEV-3 and HEV-4 were found in both humans and farmed or wild animals, in both low- and high-income countries (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017). Amongst other risk factors, the consumption of raw or undercooked pork and wild boar meat has been undoubtedly associated with small outbreaks and sporadic HEV events (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017).

To describe the surveillance activities in place on *Salmonella*, *Campylobacter*, *Listeria* and HEV, in the involved sectors, the present study was implemented.

Materials and methods

The available information from the previous round of OHEJP integrative projects (One Health EJP, 2018a, 2018b, 2020a) regarding surveillance systems in place in terms of food-borne diseases was revised. In particular, the result from the OHEJP NOVA reported in D3.1, "Full mapping of the chain process for three main productions in EU'' (NOVA, 2020), was the example to conceptualize the questionnaires and the mapping (Figure 15). Moreover, the One Health Glossary (One Health EJP ORION, n.d.) developed by the OHEJP ORION helped to settle on a common terminology. Lastly, additional information on surveillance systems was collected from EFSA's outputs (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017).

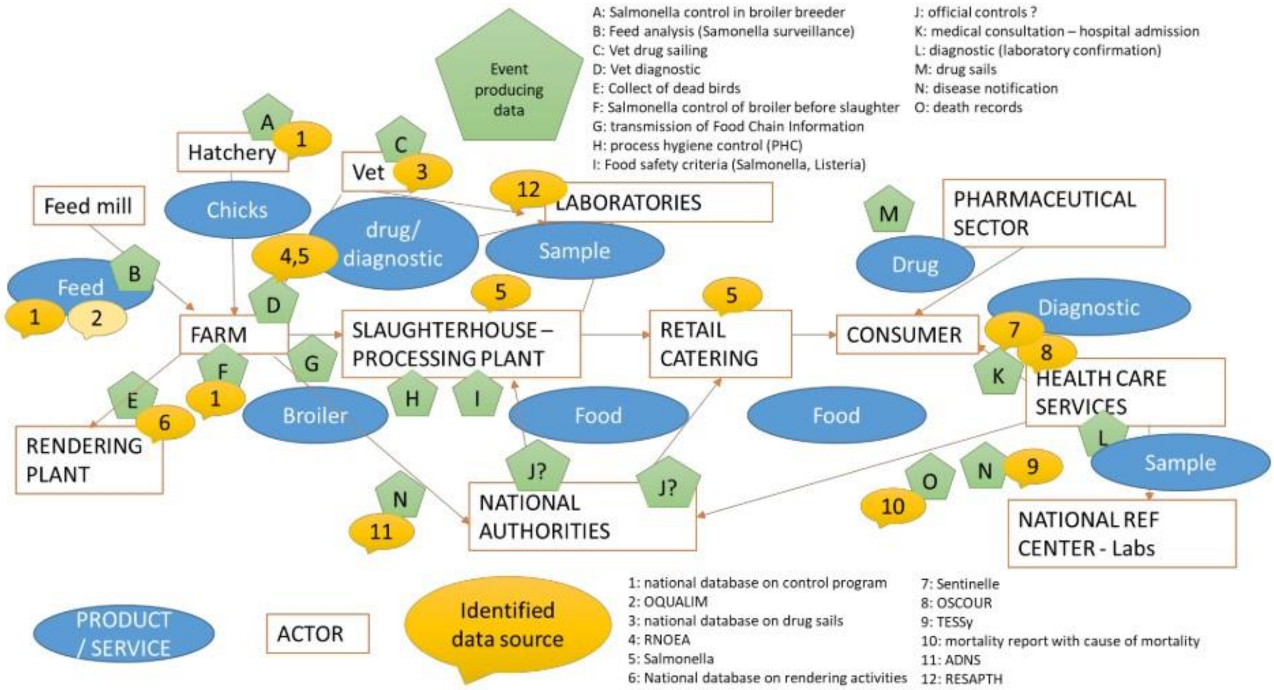

Figure 15 – From D-3.1 Full mapping of the chain process for three main productions in EU (NOVA, 2020)

The four hazard-tracks that are the basis of MATRIX were taken into consideration: *Campylobacter* spp., *Listeria* spp., *Salmonella* spp., and Emerging threats. For previous tasks of MATRIX, antimicrobial resistance had been selected as the emerging threat. Nevertheless, in the case of the mapping study, a pathogen was selected to examine the food chain in all the sectors: Hepatitis E virus (HEV). Then, for each of the four hazard-tracks, a specific food chain to explore was chosen (Table 14).

Hazard-track	**Investigated food chain**
Campylobacter	Poultry meat
Listeria	Dairy products
Salmonella	Pork meat
Hepatitis E virus	Wild boar meat

Table 14 – Investigated hazard-tracks and food chains combinations

To gather the necessary information regarding surveillance systems in place for the whole food chain, to be reported in the mapping, online questionnaires were implemented. Extending the "farm-to-fork" concept (European Commission, 2020) to "farm-to-patient", twelve online questionnaires were developed: one questionnaire per each sector involved in the food chain (namely, animal health - AH, food safety - FS, and public health – PH), per each of the four hazard-track/food chain selection.

The draft version was shared between the WP2 participants, and feedback and suggestions were taken into consideration. The final version of the 12 questionnaires was uploaded on the online survey platform Survey Monkey© and then disseminated. The recipients of the questionnaire were identified utilizing recommendations from MATRIX partners and involved both MATRIX partner and non-partner institutes. The experts were preliminarily contacted and, if their interest in taking part in the survey was confirmed, invited to respond to the questionnaires. The questionnaires were open to replies from November 2020 to April 2021.

Per each country, and each hazard-track, the questionnaire was considered completed when an answer from all the three sectors (AH, FS, PH) had been received. Then, the submitted information was analyzed. Information regarding the involved actors, the sampling context, the collected sample types, the laboratory methods in use, and the available data sources, for the three sectors of each case, were graphically displayed in MS PowerPoint©; the framework which enabled the information to be shown is reported in Figure 16.

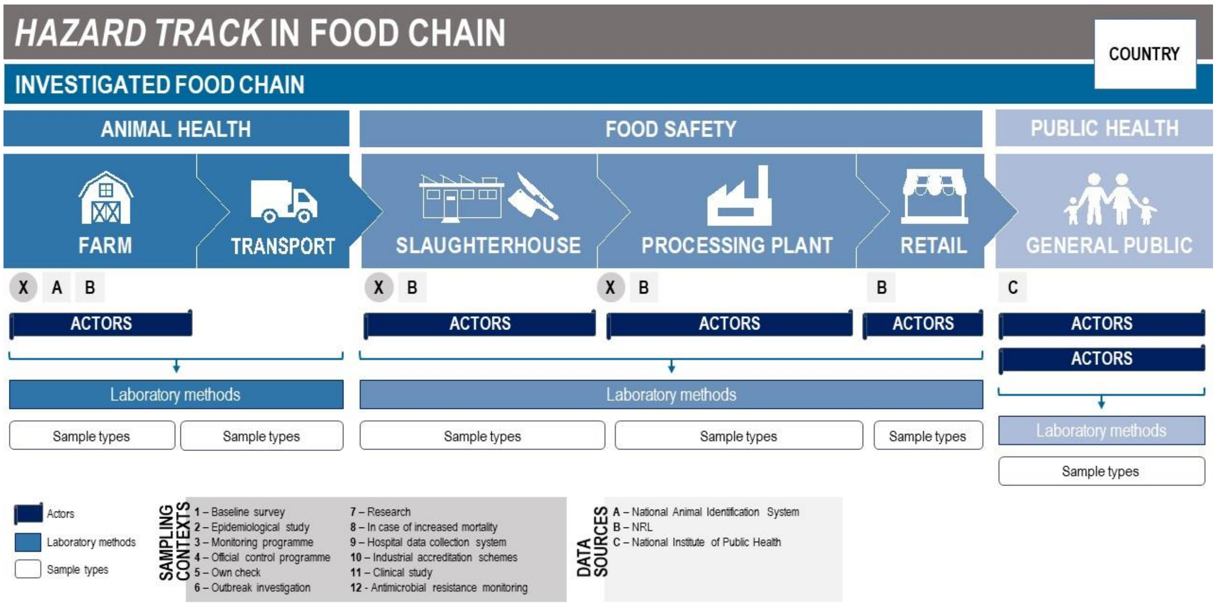

Figure 16 - The framework used for the mapping

Support was asked to hazard-track leaders in the interpretation and comment of the data, as their expertise was judged essential to describe the overall picture. In the case of one hazard-track (HEV), additional support was asked to experts from ISS.

The final results of the survey were reported in the WP2 first Deliverable (D-WP2.1), submitted in December 2021.

Results and discussion

Eight countries participated in the survey, and 14 questionnaires were completed throughout the study period (Table 15). Experts that compiled the questionnaires belonged to 10 MATRIX partner institutes and 5 non-partner institutes.

Surveillance activities in place on *Campylobacter* along the whole poultry meat food chain have been investigated in Germany, France, and Norway. In the case of *Listeria* and dairy products, Italy and Norway participated in the study. Five countries, namely France, Germany, Norway, the United Kingdom, and Spain, sent back questionnaires on *Salmonella* and pork meat food chain. Lastly, HEV surveillance activities were studied in the wild boar meat food chain in Italy, Portugal, the Netherlands, and Norway.

Hazard-Track	**Investigated Food Chain**	**Investigated countries**	**N. submitted questionnaires**
Campylobacter	Poultry meat	France, Germany, Norway	3
Listeria	Dairy products	Italy, Norway	2
Salmonella	Pork meat	France, Germany, Norway, Spain, the UK	5
HEV	Wild boar meat	Italy, Norway, Portugal, the Netherlands	4

Table 15 – Investigated countries per each hazard-tracks and food chains combinations

The Figures showing the mapping resulting from the 14 submitted questionnaires have been reported in Annex I, Figures A1-A14.

I. *Campylobacter spp. in poultry meat food chain*

The overall organization of national surveillance programmes for *Campylobacter* spp. in poultry meat shows several similarities between Germany, France, and Norway, in all three sectors.

Many surveillance activities were reported to be in place in Norway and France at the farm level. Additionally, in Norway, surveillance activities are put in place in case of increased mortality. At hatcheries and during transport, no surveillance activities were reported in France and Norway. By contrast, in Germany, outbreak-related and research activities are in place at the farm and also at the hatchery level.

Several activities are in place also at the slaughter level. Amongst the different sample types collected at this stage, Norway did not report the collection of samples related to production hygiene, or carcass status. On the contrary, equipment and environmental samples were reported only by France. Lastly, faecal or caecal content is being collected at slaughter in all three countries. Given the risk posed by cross-contamination of carcasses with faecal contents, and *Campylobacter* spp. presence in the latter, surveillance activities at this stage are of uttermost importance (Normand et al., 2008; Rosenquist et al., 2003). At the processing and retail stage, surveillance on *Campylobacter* spp. is performed by monitoring, own-check, and research activities in France, while in Germany and Norway official control activities and own-check are coupled with outbreak investigations. The involved actors vary between countries (Figures A1 – A3).

Lastly, in the three countries, surveillance data on human campylobacteriosis are collected with epidemiological studies, outbreak-related, and research activities. Moreover, Norway performs clinical studies.

EFSA's baseline survey reports highlighted risk factors that contribute most to the contamination of poultry-derived food; amongst other recommendations, it has been pointed out that the decrease of risk for human health in terms of contaminated food consumption goes through reducing *Campylobacter*'s prevalence in flocks in Europe (European Food Safety Authority, 2014). Risk mitigation measures applied to the pre-slaughter phase could reduce by half the risk for human health, while if such measures are applied at the meat production process, the risk reduction would be 90%, at least (European Food Safety Authority, 2014). According to EFSA's Scientific Opinion on the risk of broiler meat for human campylobacteriosis in the EU, from 50% to 80% of human cases could be attributed to the chicken reservoir as a whole, while handling, preparation, and consumption of broiler meat may account for 20-30% (EFSA Panel on Biological Hazards

(BIOHAZ), 2010). Therefore, risk mitigation measures are also addressed to the reduction of cross-contamination in the final preparation stages in domestic settings.

II. Hepatitis E virus in wild boar meat food chain

First of all, HEV in wild boars is not notifiable in any of the countries of the study (OIE - World Organisation for Animal Health, n.d.). Therefore, the results of the study should be interpreted under this perspective (Figures A4 – A7). Surveillance activities in animals were reported in terms of monitoring programmes in Norway, research activities in the Netherlands, and monitoring programmes, outbreak investigations, and research in Italy. Nevertheless, surveillance on animal mortality is not conducted in any of the investigated countries. Animal samples collection may vary depending on the purpose (sero-surveillance studies, viral isolation, etc.) and between countries, including blood/serum and/or liver, meat juice, and faeces.

Outbreak investigations and research activities are carried out in Italy also in the three phases (slaughter, game handling establishment, and retail) of the food sector, through the work of researchers and of the official control authorities, and the collection of animal tissue and organs (liver, gallbladder, meat, blood/serum, faeces), meat, meat products, and environmental samples. No specific surveillance activities were reported to be ongoing for HEV in the other three countries, denoting not continuous surveillance along the food chain. A probable explanation might be the fact that HEV is not mentioned in the list of zoonotic pathogens included in Directive 2003/99/EC of the European Parliament (European Parliament, 2003). As a consequence, surveillance activities were expected to be significantly different from country to country. For the same reason, the absence of internationally standardized analytical methods might have an impact on food control activities, which require specific protocols for the detection or quantification of HEV in food products.

In the human public health sector, surveillance activities are carried out with outbreak investigations in Norway, research activities in Portugal, epidemiological studies in the Netherlands, and research, outbreak investigations, clinical and epidemiological studies in Italy. The samples collection includes stool, serum, and plasma. According to EFSA's Scientific Opinion, most HEV cases (80%) identified in the last 10 years were notified from France, Germany, and the UK (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017). Unfortunately, none of these countries participated in the study. However, it has to be noted that the human infection is not notifiable in a harmonized way across all the MSs (European Centre for Disease Prevention and Control, 2019), therefore surveillance activities in place could vary greatly: reported cases are not comparable between countries, and notification is underestimated (EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards) et al., 2017). An Operational Guidance was published by ECDC in 2019 (European Centre for Disease Prevention and Control, 2019), aiming to implement data collection on human cases in the EU / EEA countries. Clinical testing standards and case definitions are provided.

III. Listeria spp. in dairy products food chain

Norway and Italy were the two countries investigated with regards to *Listeria* spp. in dairy products (Figures A8, A9).

At the farm level, the farmer and the official control authorities are responsible for the controls in Italy (monitoring activities, outbreak investigations, and research), while in Norway the activities are carried out by the veterinary technicians and/or the private veterinarians, which perform outbreak investigations and surveillance in case of increased mortality (Figure A8). Miscarriages are investigated in both countries, and the samples collected are very similar between the two.

Numerous different surveillance activities are in place in the food sector in both Norway and Italy. They are performed by the official control authorities in Norway, and also by the food business operators in Italy. Samples collected include surfaces, equipment, refrigerators, and water, in both countries. This type of monitoring is especially important in light of the capacity of the pathogen to survive with adverse environmental conditions, and persist for a long time attached to surfaces (Moghadam & Larsen, 2019).

Regarding surveillance of human listeriosis, many actors are involved in the surveillance. Activities have not been specified, except for the fact that Italy reported a hospital data collection system in place. The same sample types are collected in the two countries (blood, placenta, cerebrospinal fluid).

Within dairy products, *Listeria monocytogenes* is a public health concern (Moghadam & Larsen, 2019). The contamination rate of both milk and cheese products has been thoroughly researched (Moghadam & Larsen, 2019). To decrease the potential for contamination, improving food safety throughout the food chain, the implementation of good manufacturing practices is essential (Moghadam & Larsen, 2019).

In conclusion, a broad range of surveillance activities were reported from the respondents, reflecting the consideration of the pathogen in both countries.

IV. *Salmonella spp. in pork meat food chain*

Salmonella spp. is a widespread pathogen, and food at risk for contamination is numerous. It was selected to investigate the pork meat food chain concerning *Salmonella* spp. to avoid overlapping with previous studies that investigated *Salmonella* spp. in poultry (One Health EJP, 2018a). Five countries participated in the study: France, Germany, Spain, Norway, and the United Kingdom (UK) (Figures A10-A14).

In the animal sector, many activities are implemented at the farm level, carried out by official control authorities, laboratories, farmers, the industry, private veterinarians or technicians, and eventually Research centers or institutions like Universities. Amongst the activities in place, in the UK surveillance activities are performed in case of increased mortality, while in Spain there is specific monitoring on antimicrobial resistance. France was the only country to report surveillance activities (through research) at transport.

For the food sector, activities at the slaughter and processing plants are performed mainly by official control authorities in Spain and Norway; by official control authorities and the private sector in Germany and the UK; by official control authorities, the private sector, laboratories, and the French Pig and Pork Institute in France. Activities in place vary widely between countries, and so do the sample types collected. Also, information on activities performed at the retail stage was provided only by France, Germany, and Spain. In these countries, minced meat and meat preparations/products are subject to monitoring and research activities, outbreak investigations, official control programs, and own-check.

Human salmonellosis is monitored by several actors, from local health authorities to hospital/clinical/reference/local laboratories in different countries. In Germany, activities include outbreak investigation, research, and epidemiological studies. Outbreak investigations are performed also in the UK and France.

Being such a widespread pathogen, it is difficult to identify a single point of exposure along the whole food chain. Therefore, intense surveillance activities are needed throughout the process, literally from feed to fork.

Conclusions

A full map of the activities in place along the whole food chain has been realized and discussed, for the four MATRIX hazard tracks, for at least one country per hazard-track.

A possible bias of the study is the use of questionnaires as the tool to collect the information: in a couple of cases, the appointed expert circulated the draft questionnaire amongst his/her office, before replying, therefore answers in those cases had been revised by colleagues; on the contrary, in most of the cases only one expert completed each questionnaire (sector-based), therefore we acknowledge the possibility that some information may not be complete or up to date.

The information collected described a very heterogeneous situation in terms of surveillance activities in place in different countries. Four countries replied to more than one questionnaire: both France and Germany for *Campylobacter* and *Salmonella*, Italy for *Listeria* and HEV, and Norway to all the four hazard-track/food chain combinations. Hence, it would be interesting a comparison between surveillance activities in place, in the same country, for different pathogens and food products. However, this goes beyond the scope of the present study, and could perhaps be accomplished at a later time.

HEV was selected as the emerging pathogen, and a very different range of surveillance activities was expected to be in place between countries. Nevertheless, it is important to highlight that attention towards this pathogen has been increasing in the past years, and a generalized effort to harmonize the collection of information and consequently to improve surveillance activities is ongoing.

The present results have been submitted as part of D-WP2.1, "Mapping of the surveillance chain for all hazard tracks, and cross-sectoral linkages", in which additional data obtained from the questionnaires implemented in the context of WP2-T1 have been provided. At the same time, also the results obtained from the activities performed for WP2-T2 have been reported in D-WP2.1. Thus, the study part reported in the present document represents the first stage of a process.

Comprehensive knowledge of the surveillance activities in place will enable the identification of cross-sectoral linkages, also in terms of data sharing, already in place or potentially to be enhanced. Moreover, to implement OHS in Europe, data gathered with the study are being used to identify virtuous cases on which to base guidelines to enable the improvement of effective cross-sectoral collaborations.

Final remarks

Two case studies have been present. They belong to two very different projects, but they both highlight important aspects in the implementation of the One Health approach.

The first case concerns the project MLS2 and arboviruses in the Mediterranean area: a Network is implemented to facilitate the establishment of inter-sectoral collaborations when dealing with vector-borne diseases. The study on early warning indicators for their use in inter-disciplinary surveillance activities showed the diversity of situation of the network countries. The survey is being followed by specific country studies, to further investigate the situation, and propose solutions to implement effective cooperation. Concurrently, training need assessments and training sessions to address the identified gaps are being performed.

In the second situation, which relates to the OHEJP MATRIX on food-borne diseases in European countries, a study was implemented to describe and map surveillance activities performed in different countries, for four hazard-track and four different complete food chains. Several differences between the countries emerged from the mapping, including an increasing interest in the selected emerging threat, HEV. The following steps of the project include the identification of links in the food chain between the different sectors, to identify useful outputs to be shared in a OH perspective; the proposal of guidelines on data collection, analysis, and dissemination for multi-sectoral collaboration; finally, the identification of commonalities between the hazard-tracks, and the implementation of a OHS framework to be applied in the countries.

The presented experiences represent the first steps towards OH implementation in two completely different contexts. Such preliminary studies, although presenting mainly qualitative data, are the beginning of a process and are fundamental to assess the settings on which to base the subsequent activities. Exhaustive knowledge of the starting point is crucial not only to assess the needed effort to reach the desired level of inter-disciplinary collaborations, but also to set priorities of intervention, and identify feasible medium to long-term goals that could be achieved to implement the surveillance activities under a OH approach.

As shown by the results of the studies, many efforts are still required to reach a good level of synergies between sectors in surveillance activities against vector-borne and food-borne diseases. This would help with the ultimate goal to strengthen the public health sector and to reunite public health and veterinary public health as a whole under the OH umbrella, back to as they were born (Mantovani & Macrì, 2004).

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Annex

Campylobacter spp. and poultry meat food chain:

- Figure A1 - Mapping of surveillance of *Campylobacter* spp. in poultry meat food chain in France
- Figure A2 - Mapping of surveillance of *Campylobacter* spp. in poultry meat food chain in Germany
- Figure A3 - Mapping of surveillance of *Campylobacter* spp. in poultry meat food chain in Norway

Hepatitis E virus in wild boar meat food chain:

- Figure A4 - Mapping of surveillance of HEV in wild boar meat food chain in Italy
- Figure A5 - Mapping of surveillance of HEV in wild boar meat food chain in Norway
- Figure A6 - Mapping of surveillance of HEV in wild boar meat food chain in the Netherlands
- Figure A7 - Mapping of surveillance of HEV in wild boar meat food chain in Portugal

Listeria spp. in dairy products food chain:

- Figure A8 - Mapping of surveillance of *Listeria* spp. in dairy products food chain in Norway
- Figure A9 - Mapping of surveillance of *Listeria* spp. in dairy products food chain in Italy

Salmonella spp. in pork meat food chain:

- Figure A10 - Mapping of surveillance of *Salmonella* spp. in pork meat food chain in France
- Figure A11 - Mapping of surveillance of *Salmonella* spp. in pork meat food chain in the UK
- Figure A12 - Mapping of surveillance of *Salmonella* spp. in pork meat food chain in Norway
- Figure A13 - Mapping of surveillance of *Salmonella* spp. in pork meat food chain in Spain
- Figure A14 - Mapping of surveillance of *Salmonella* spp. in pork meat food chain in Germany

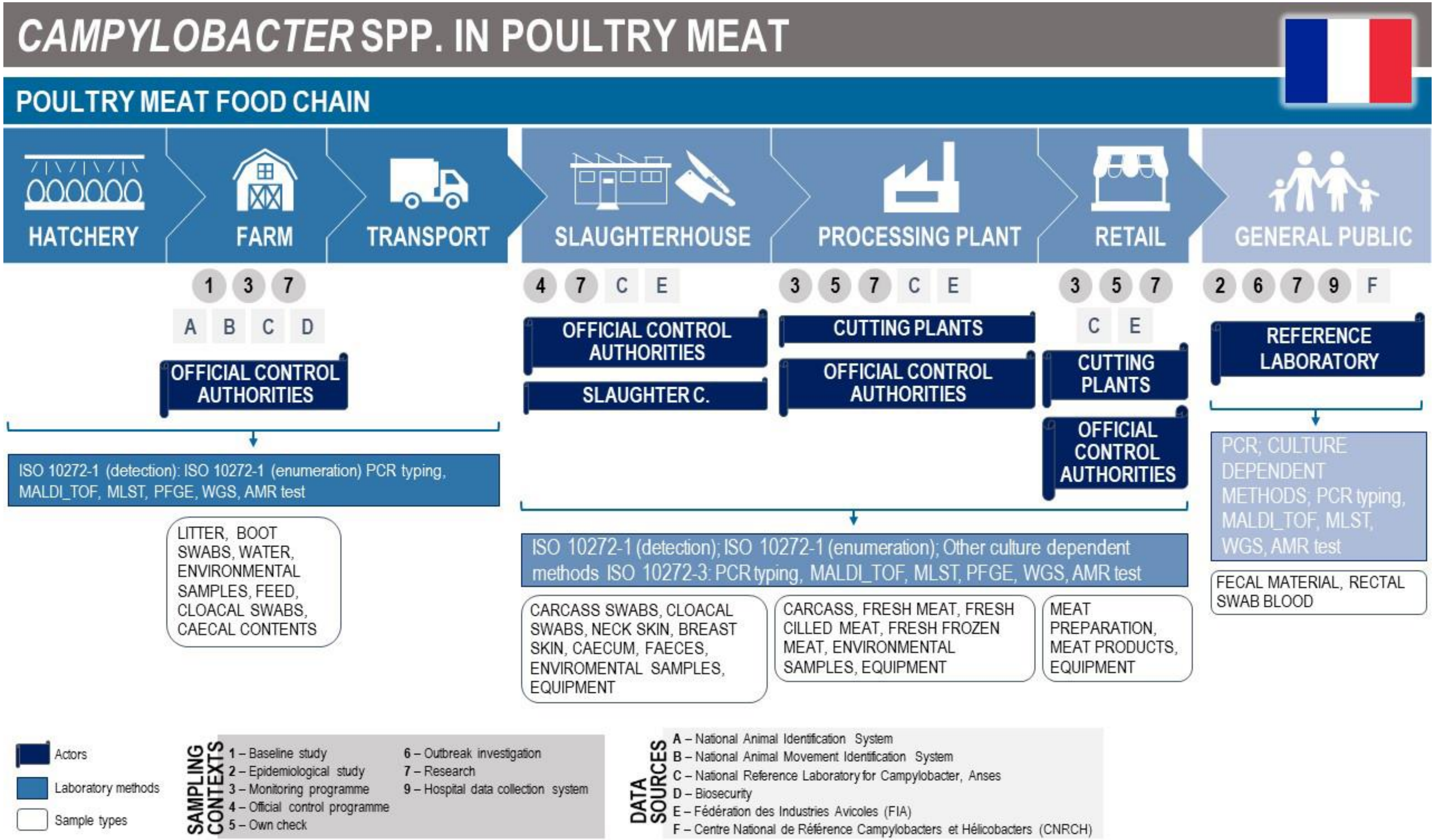

Figure A1 - Mapping of surveillance of Campylobacter spp. in poultry meat food chain in France

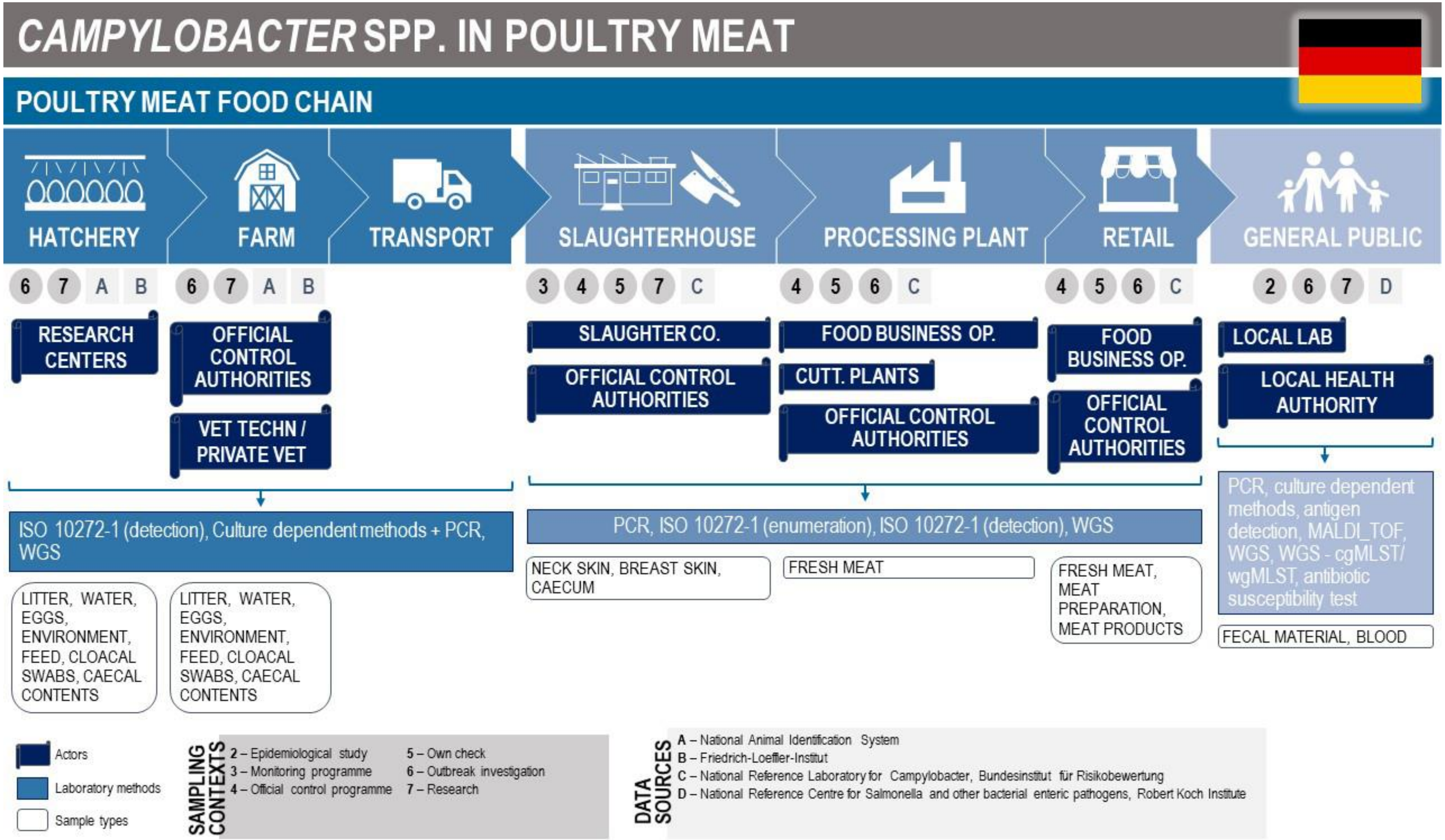

Figure A2 - Mapping of surveillance of Campylobacter spp. in poultry meat food chain in Germany

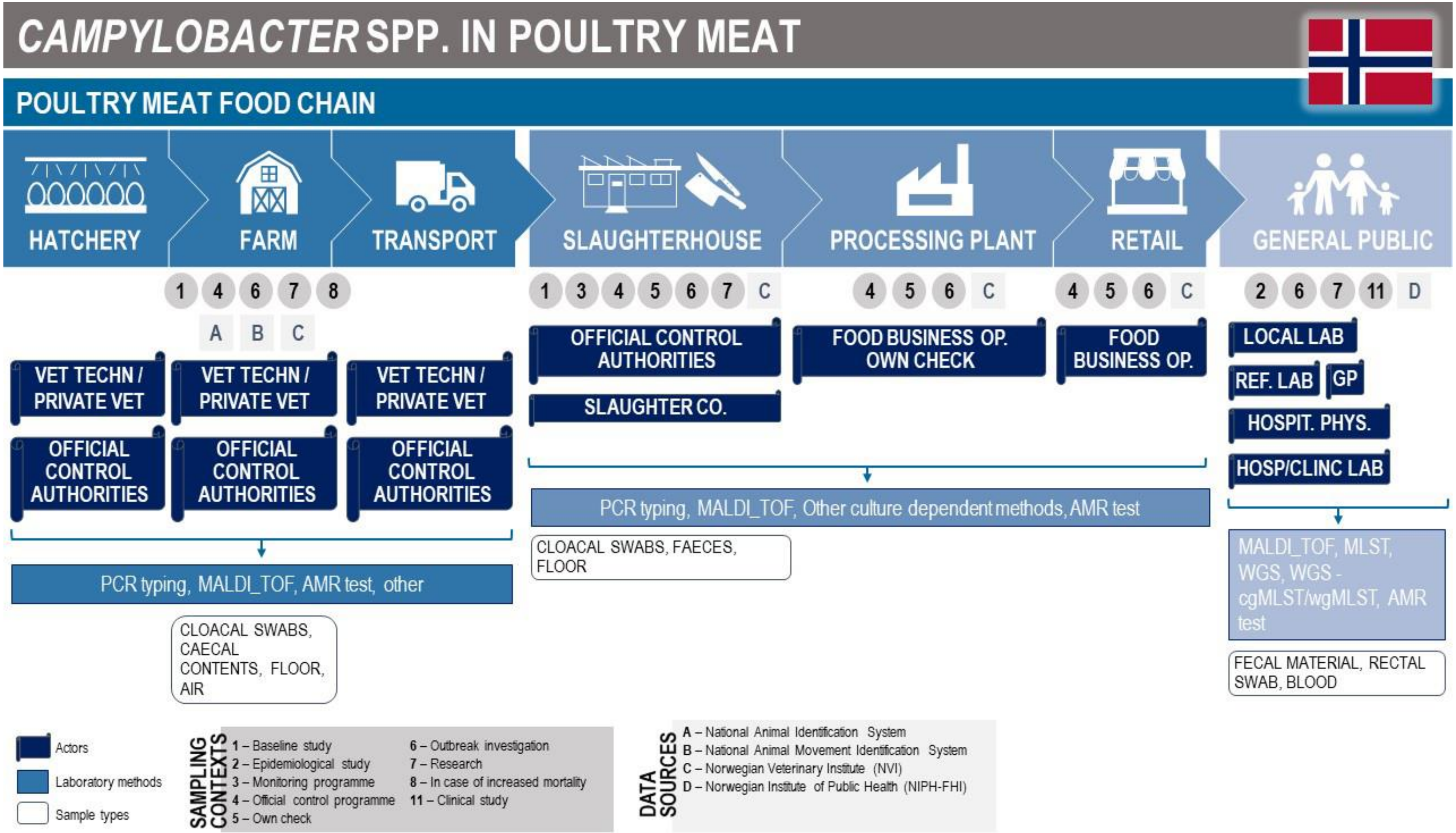

Figure A3 - Mapping of surveillance of Campylobacter spp. in poultry meat food chain in Norway

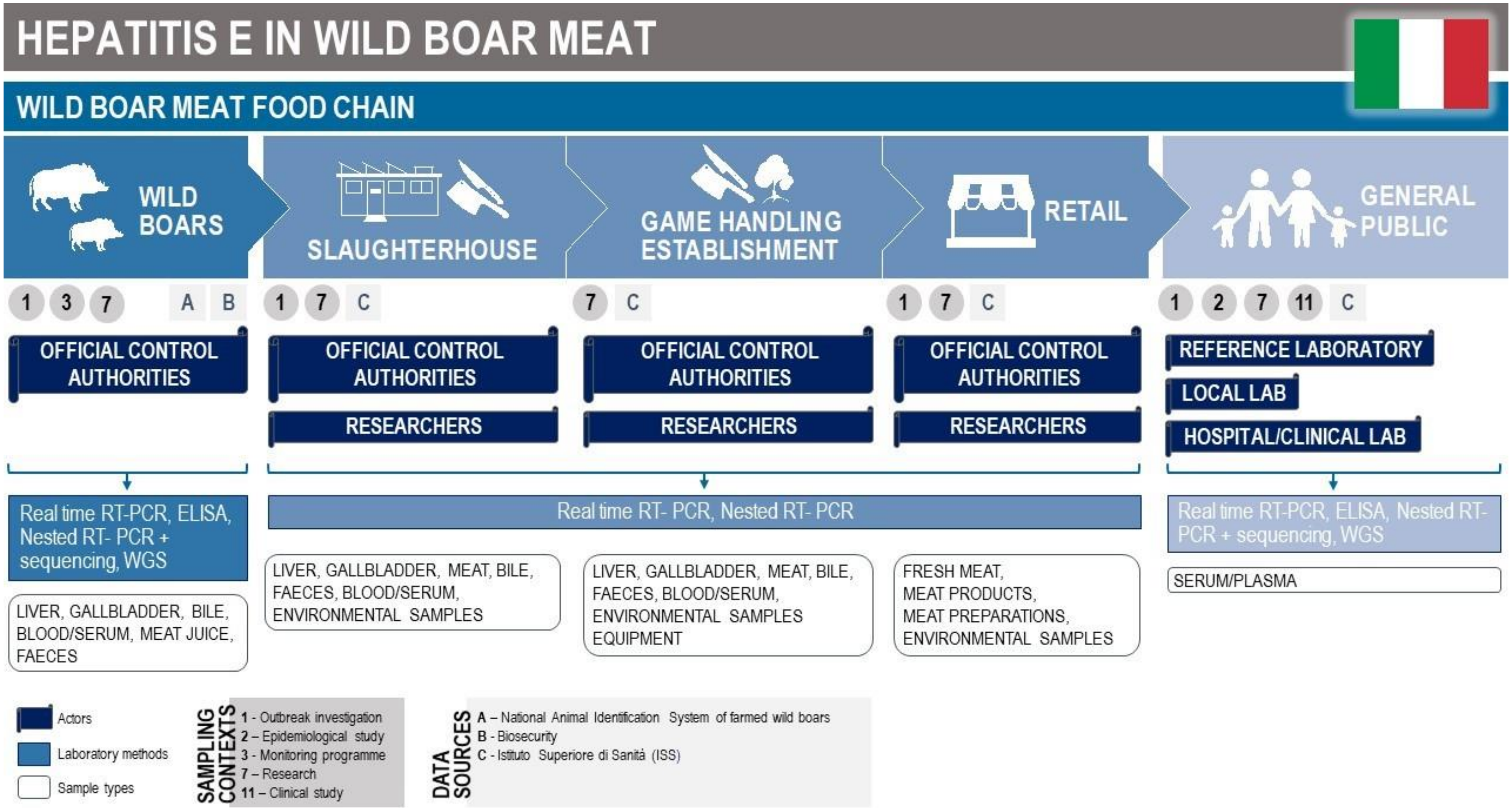

Figure A4 - Mapping of surveillance of HEV in wild boar meat food chain in Italy

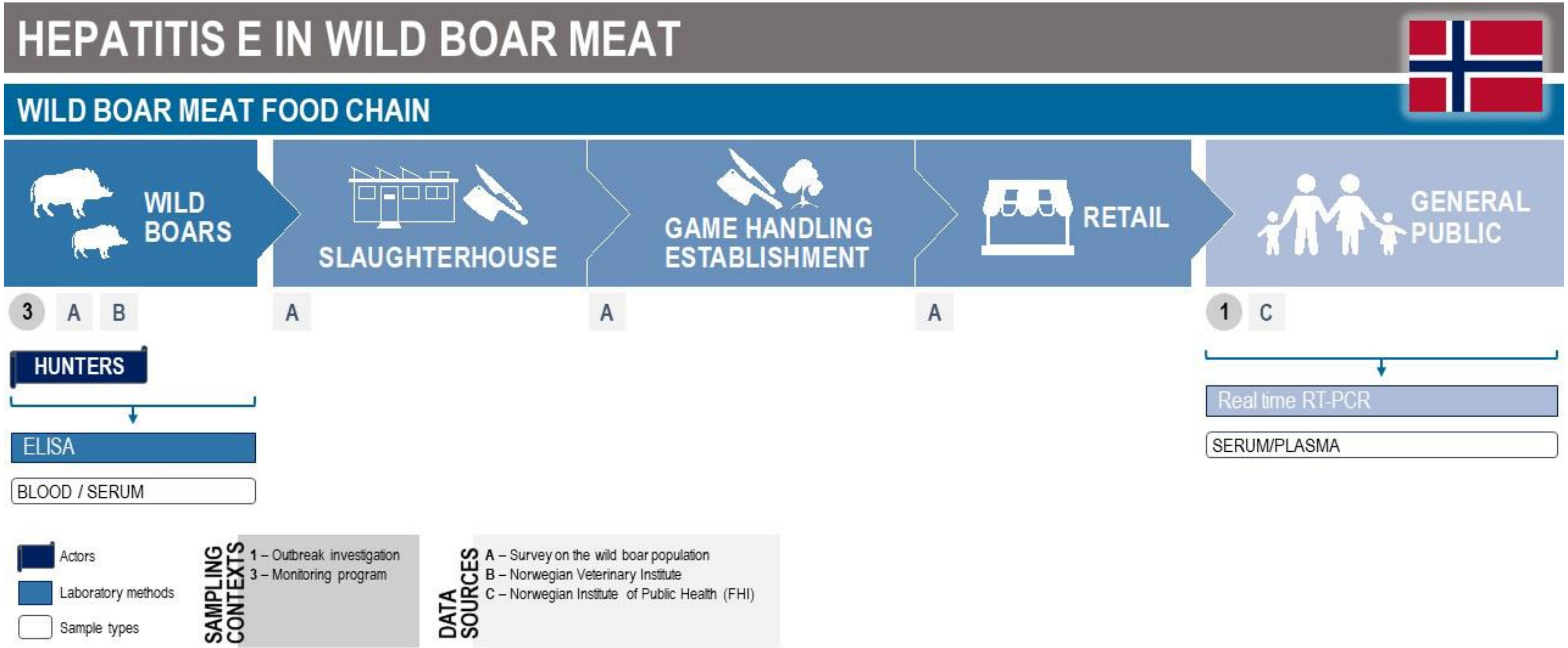

Figure A5 - Mapping of surveillance of HEV in wild boar meat food chain in Norway

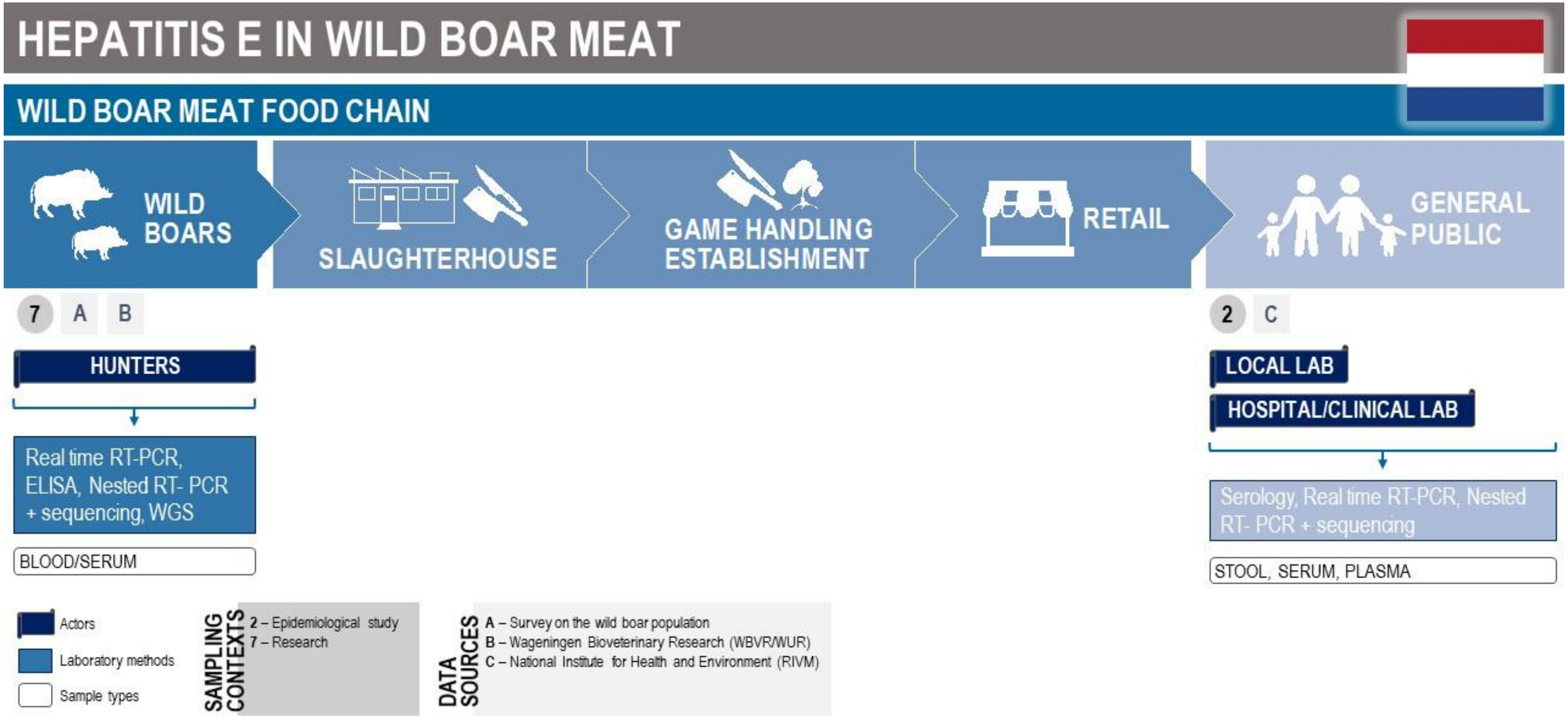

Figure A6 - Mapping of surveillance of HEV in wild boar meat food chain in the Netherlands

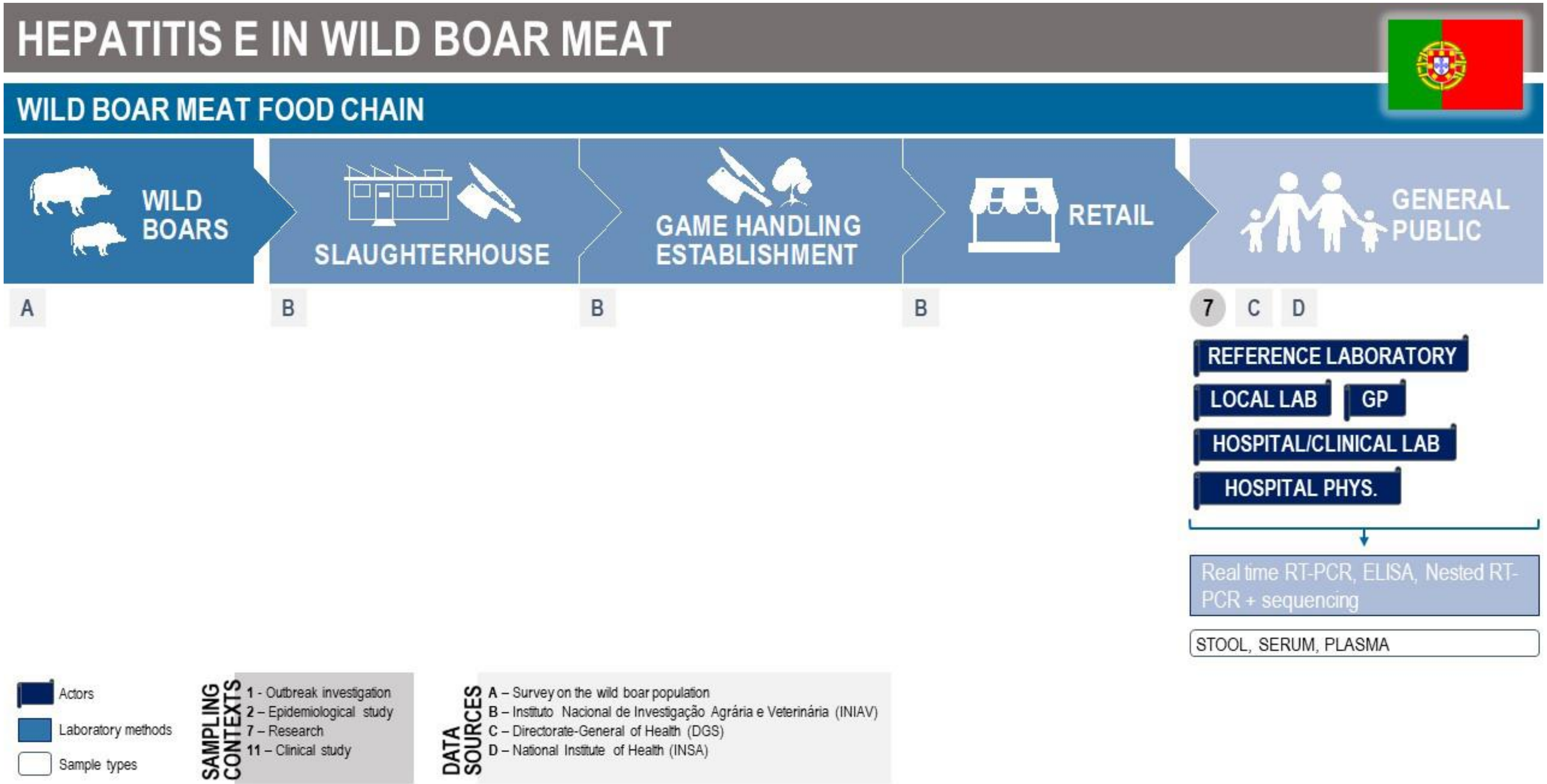

Figure A7 - Mapping of surveillance of HEV in wild boar meat food chain in Portugal

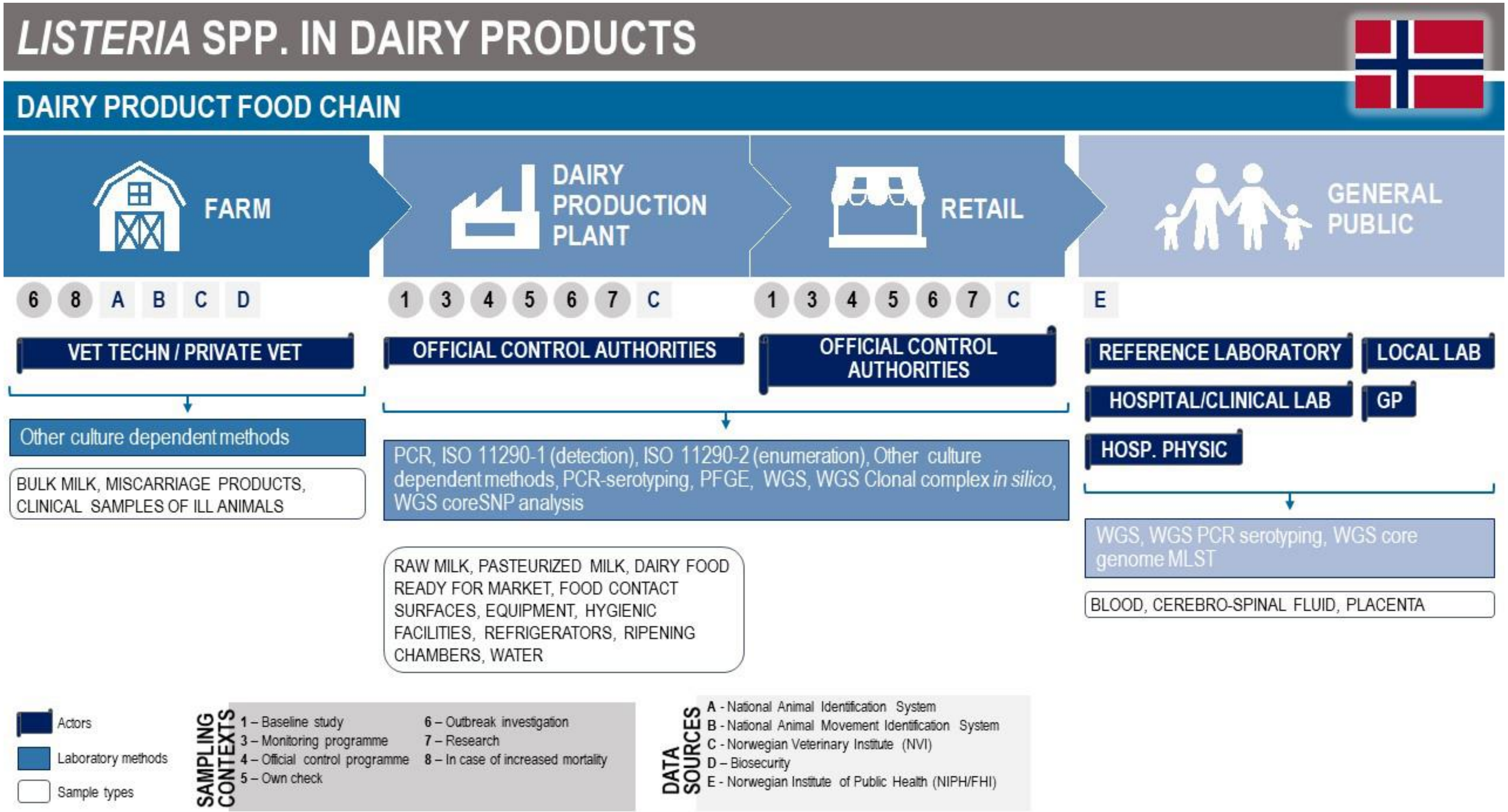

Figure A8 - Mapping of surveillance of Listeria spp. in dairy products food chain in Norway

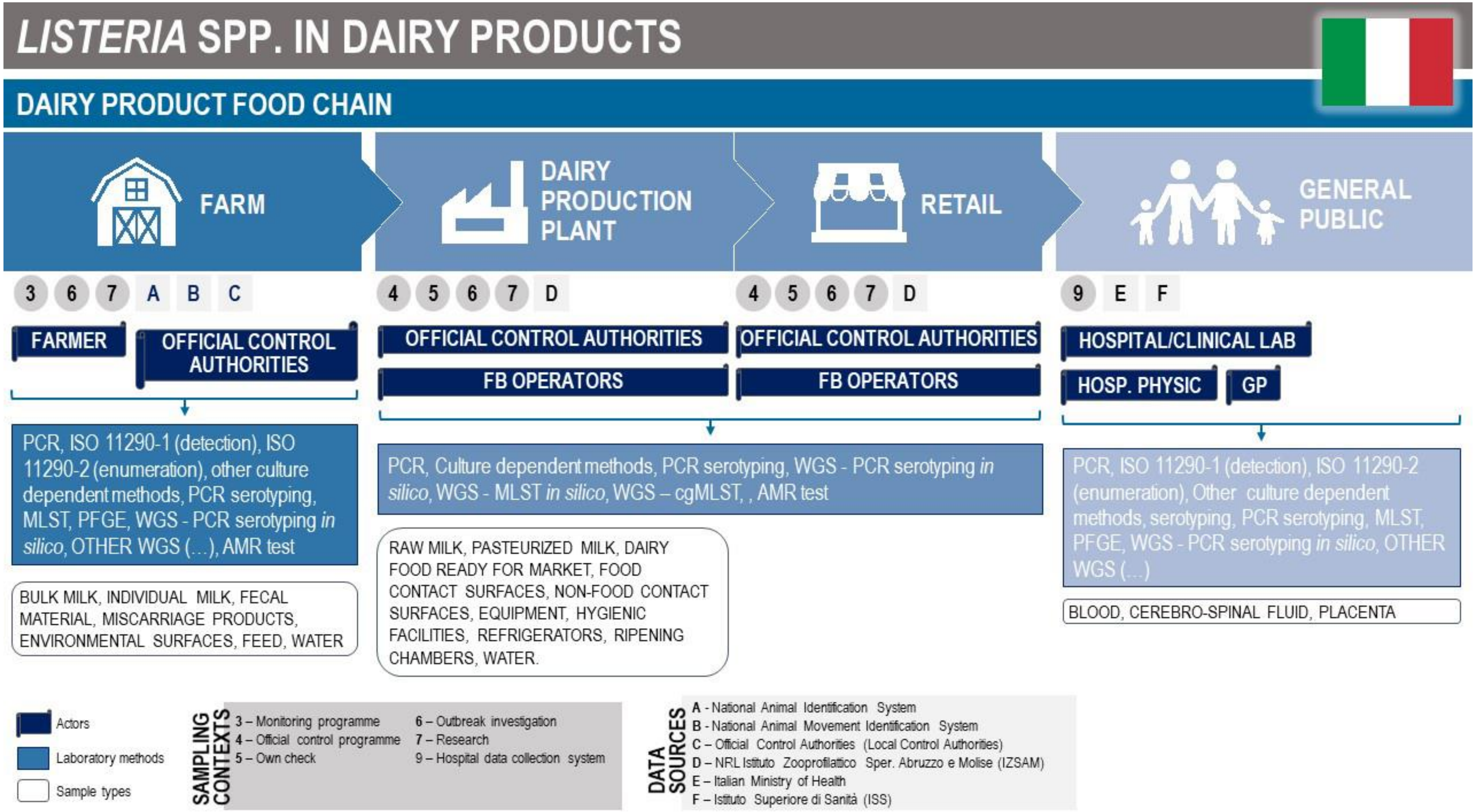

Figure A9 - Mapping of surveillance of Listeria spp. in dairy products food chain in Italy

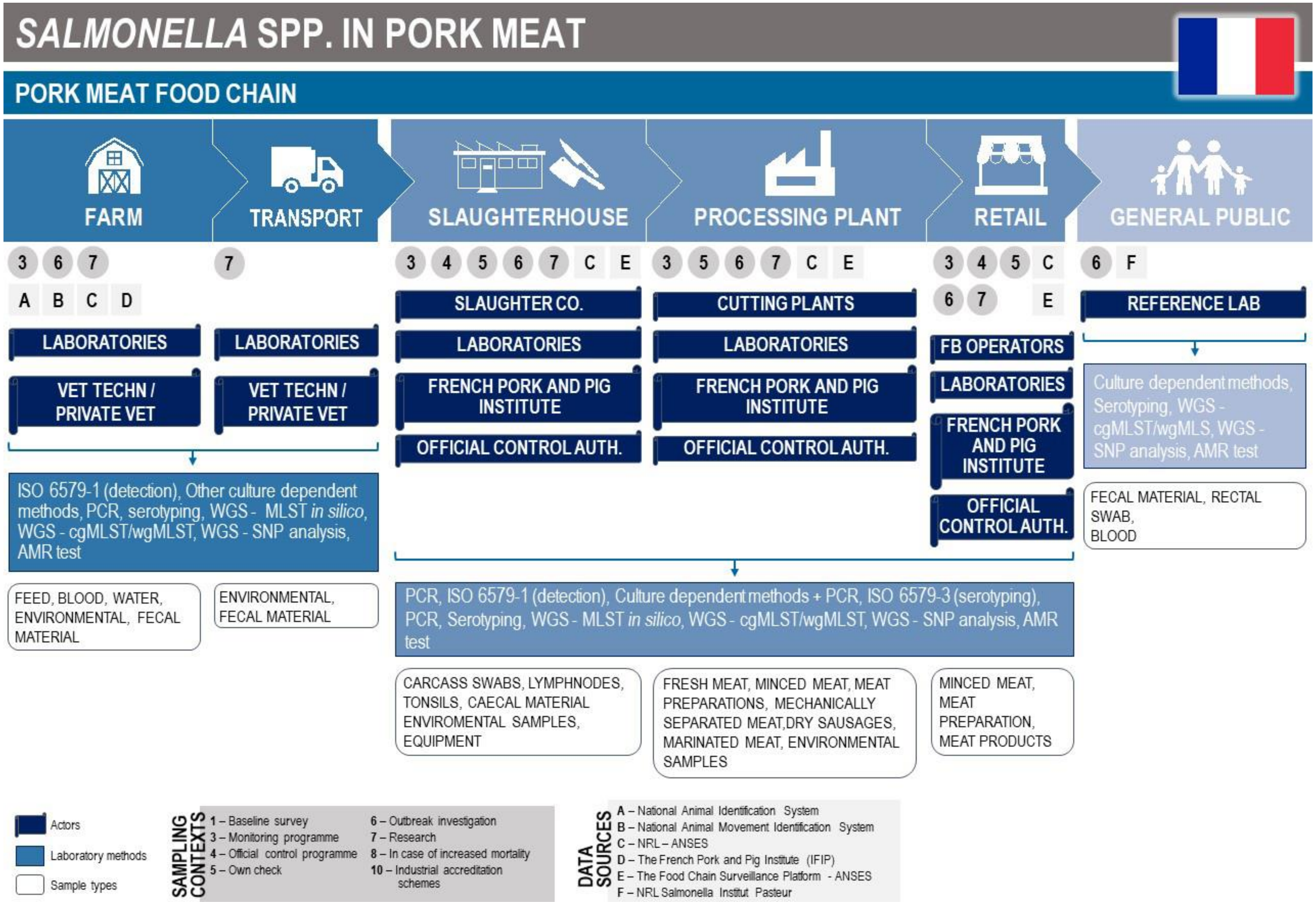

Figure A10 - Mapping of surveillance of Salmonella spp. in pork meat food chain in France

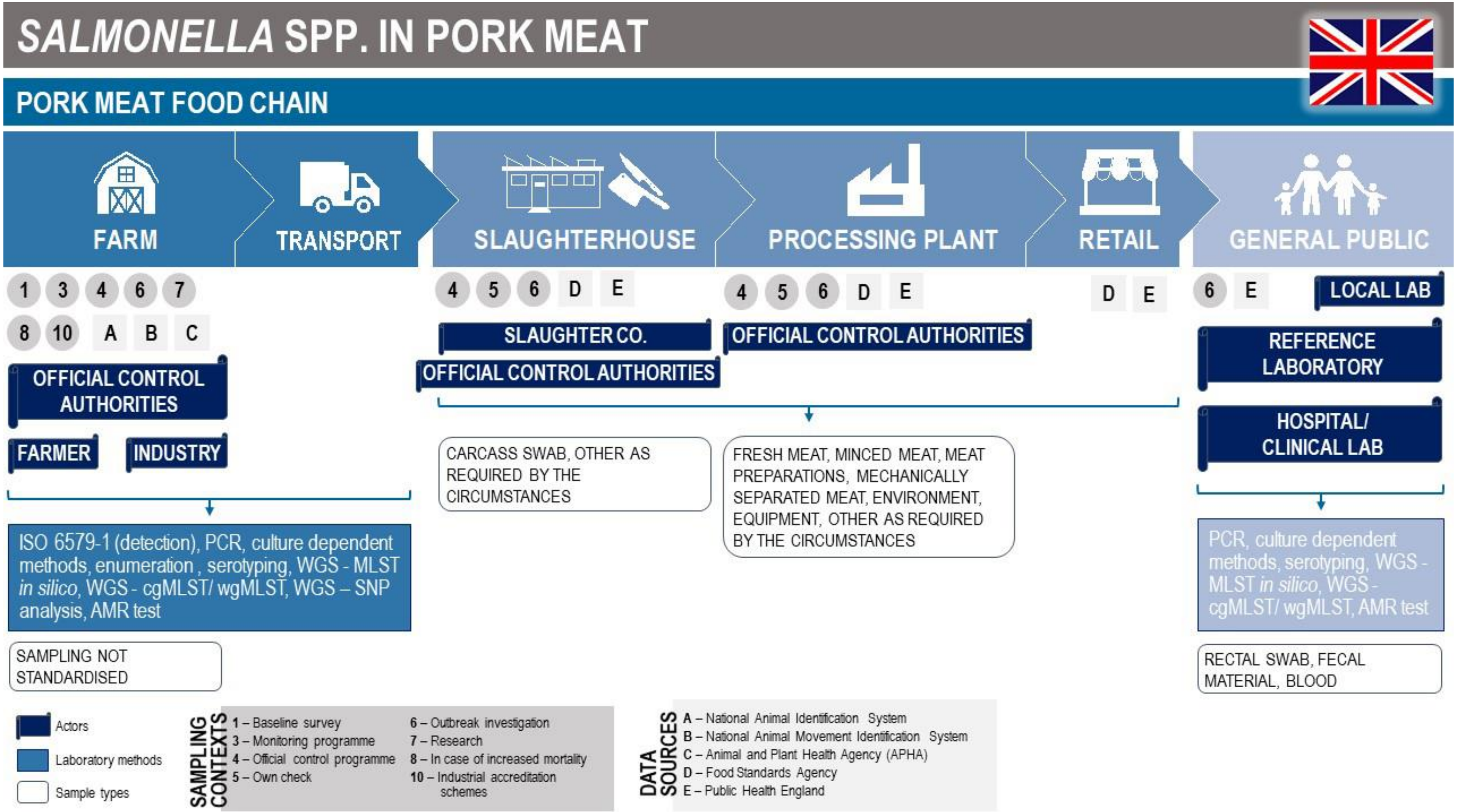

Figure A11 - Mapping of surveillance of Salmonella spp. in pork meat food chain in the UK

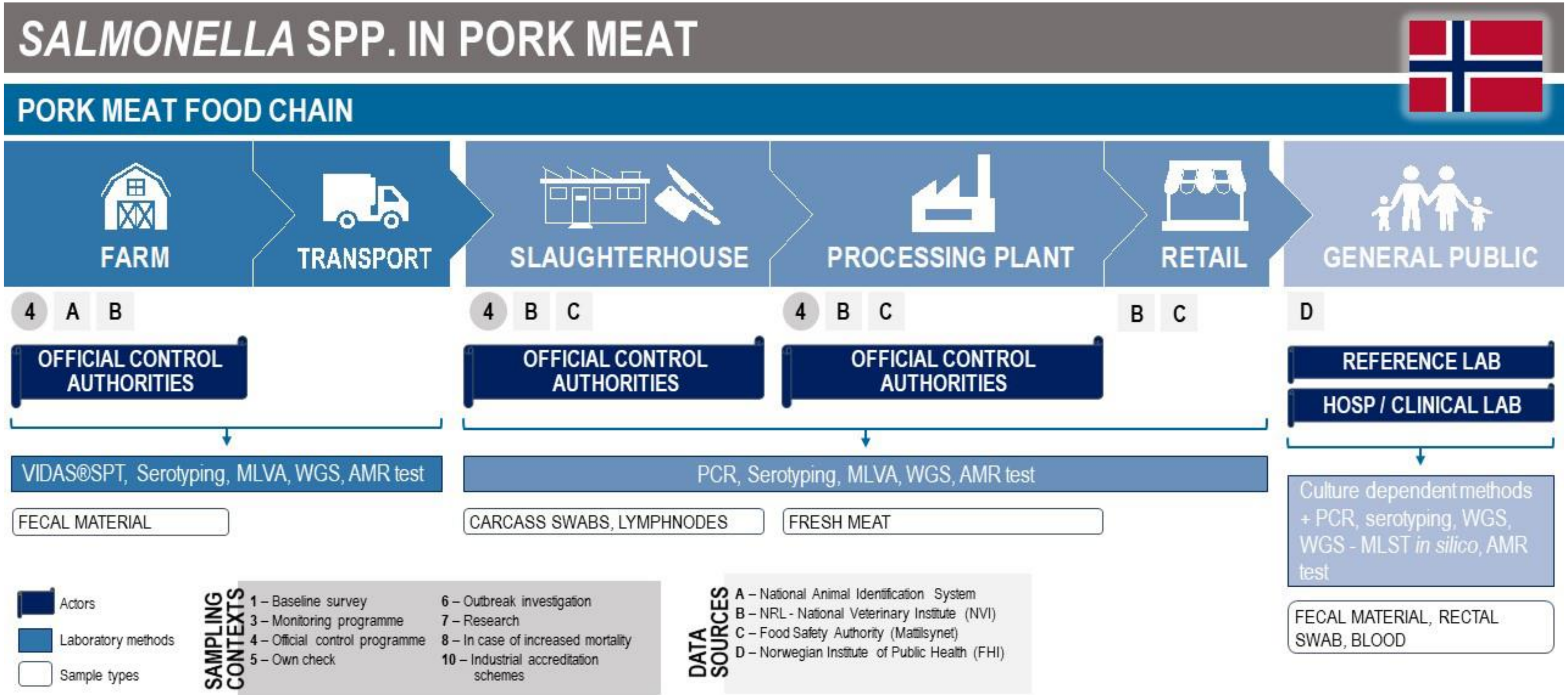

Figure A12 - Mapping of surveillance of Salmonella spp. in pork meat food chain in Norway

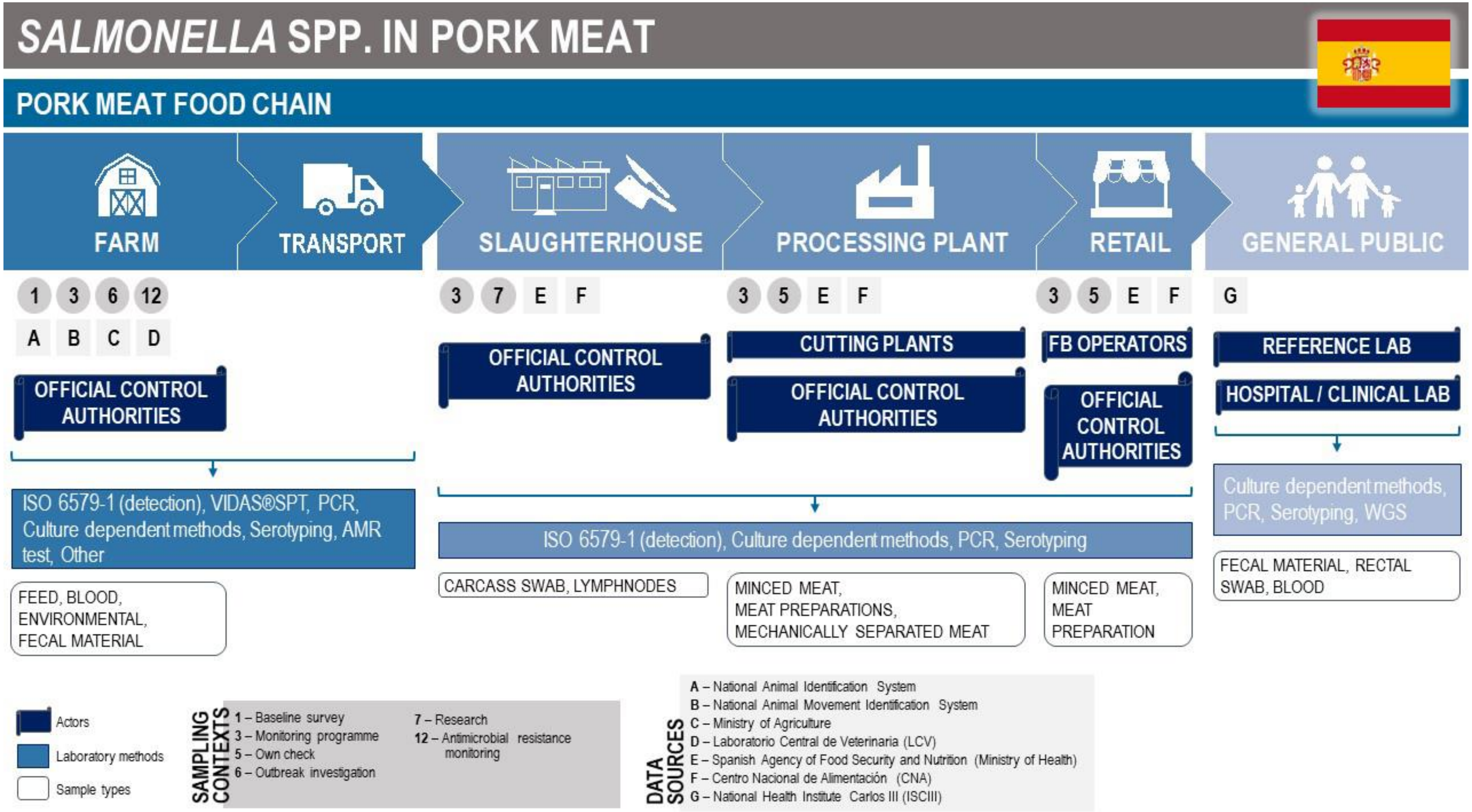

Figure A13 - Mapping of surveillance of Salmonella spp. in pork meat food chain in Spain

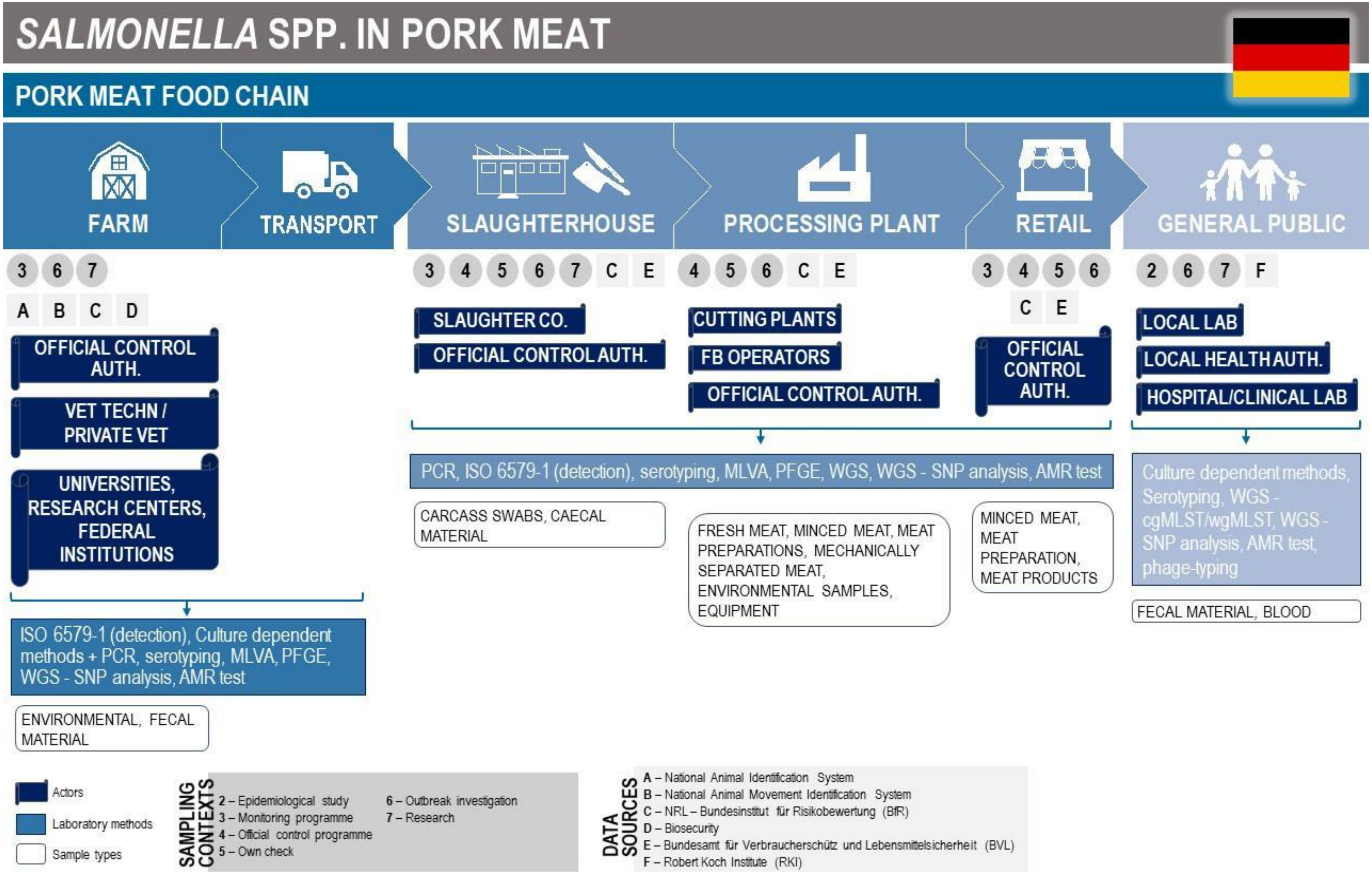

Figure A14 - Mapping of surveillance of Salmonella spp. in pork meat food chain in Germany