Deliverable – Suggested best-practices for multi-sectorial collaboration in order to achieve OHS[1]

OHEJP JIP MATRIX – WP2

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BEST PRACTICES FOR MULTI-SECTORAL OH COLLABORATION

Summary

Introduction

Health issues at the human-food-animal-environment interface cannot be effectively addressed by one sector alone. Collaboration across all sectors and disciplines responsible for health is required to address zoonotic diseases and other shared health threats at the human-food-animal-environment interface. This approach to collaboration is referred to as One Health[2] (OH).

Multisectoral means that two or more sectors are working together (e.g. on a joint program or in response to an event), but does not imply that this includes all relevant sectors. On the contrary, taking a OH approach means that all relevant sectors and disciplines are involved. The involved sectors correlate to which sectors are affected by the hazard. For hazards covered by the project MATRIX[3], mainly three sectors (animal health - AH, food safety - FS, and public health - PH) are involved but, depending on how the issue is approached, the scope of the collaborations tends to be narrowed to the issue of that particular sector, rather than a common issue across sectors. For example, in the case of a large number of hazards, there is a great source attribution caused by environmental factors, therefore it is worth considering including other relevant sectors, such as environmental, medical, social science, economics areas, and so forth, where appropriate to meet the OH objective.

Within the MATRIX project, Work-Package 2 (WP2) focuses on best practices and multi-sectoral collaboration, to implement the operationalization of OHS in Europe. In this context, WP2 firsts two tasks (WP2-T1 and WP2-T2) were implemented and the work performed has been reported in the first Deliverable of WP2, D-WP2.1 (1). 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.
Therefore, the development of best practices in the form of guidelines has the objective to facilitate the implementation of effective strategies for multi-sectoral collaborations, as expected for WP2-T3.

Most countries have inadequate mechanisms in place for administrative and technical collaboration among the animal health, food safety, public health, and environmental sectors, and with other sectors and disciplines. In zoonotic disease events and emergencies, the lack of joint preparation and established mechanisms for collaboration can result in confusion and delayed responses, and can lead to poorer health outcomes. For endemic zoonotic diseases, the lack of coordinated planning, information sharing, risk assessment, and control activities across all relevant sectors can obstruct and complicate the implementation of effective control programmes.

In some countries, a multisectoral OH approach has already been effectively implemented to address a current zoonotic disease threat, but then abandoned when the emergency was over. To ensure an effective implementation of zoonotic disease control activities, this approach must be made routine and sustainable.

Establishing and sustaining coordinated surveillance and information sharing mechanisms may not be equally perceived as beneficial by all sectors, for reasons such as differences in pathogenicity in animals and humans, or differences in the mandates of different government sectors and ministries.

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[2] One Health is an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes. The areas of work in which a One Health approach is particularly relevant include food safety, the control of zoonoses and combatting antibiotic resistance (24).

[3] MATRIX is a project of the One Health European Joint Programme (OHEJP), a partnership of 44 food, veterinary and medical laboratories and institutes across Europe and the Med-Vet-Net Association. MATRIX connects existing cross-sectorial One Health programmes in European countries. Today, 19 partner institutes representing the animal health, public health and food safety sectors from 12 countries continue a collaboration that started early in 2020 and will end in December 2022. More information can be found here.

Several relevant stakeholders[4] might be involved in the surveillance activities on different hazards; therefore, at an early stage of surveillance, it would be required to have a clear picture of the implicated actors. If we are dealing with a notifiable animal disease, important stakeholders are the government and animal health and public health agencies but also private veterinarians and breeders' associations. If the disease is not notifiable for animals, but it can be serious for humans and/or the hazard is food-borne, the food trade and/or the industry might be important stakeholders as well.

Since there may be legal, regulatory, cultural, or other constraints to sharing information, a clear identification of the different steps in which multisectorial collaboration could be a benefit should be performed. In addition, a clear subset of information that should be shared among the sectors should be identified (what, when, how). This may vary by country, by disease and by event.

The differentiation between sectors made above originated from the fact that the hazard can be notifiable in one or more sectors, in a specific context (e.g. species), and/or by serotype. For the majority of the diseases covered by the project MATRIX, there are regulations and legislation in place at the EU level that predefined minimum surveillance requirements. This is one of the most important aspects to take into consideration. All relevant legislation regarding the hazard should be consulted in order to make sure that no recommendations or best practices that do not comply with the corresponding EU regulation on the area are suggested.

Results from a coordinated surveillance system between all the relevant sectors can also be used for understanding disease burden, monitoring trends, as early warning system, and supporting outbreak investigation and response. To fulfil the objective of WP2-T3: "Propose best-practice guidelines and effective strategies for data collection, analysis and dissemination aimed at multi-sectorial OH collaboration, for each specific track", we choose to focus on three different surveillance purposes:

A. Measure the levels and temporal trends of exposure and burden of disease

Here we refer to understanding disease burden (for public health and animal health) and monitoring trends (for example, to detect an increase in the number of cases reported over a given period or determine the seasonality of the disease under surveillance).

B. Support early detection and response to outbreaks

To respond to zoonotic disease outbreaks, the surveillance activities should be coordinated and should use a multisectoral approach to reduce time and efforts in the outbreak response.

C. Identify risk factors to implement control measures

The context in which zoonotic diseases occur can influence their severity, impact, and/or speed of spread. Understanding the risk factors for transmission of zoonotic diseases to people and animals, and their presence in food sources, allows for informed decision-making. In some cases, transmission pathways and risk factors are unknown (as in the case of emerging threats), therefore, it is important to identify and analyze the risk factors that contribute to the likelihood and/or impact of the disease, to reduce their effect in each situation. Finally, this third purpose is referring to the identification of factors that increase the magnitude or frequency of zoonotic disease events to implement management and communication measures to prevent the disease agents from creating health risks or to lessen their frequency, distribution, intensity, or severity.

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[4] People or groups who have an involvement or interest in some system, including beneficiaries, providers and funders (24).

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Many publications and guidelines focusing on this topic have already been made available by international organizations i.e. the tripartite guide to addressing zoonoses jointly published by WHO, FAO, and WOAH (former OIE) (2). Therefore, "best practices" are here intended not as "solutions", but rather as "**suggestions**" **to operationalize One Health surveillance**. As a consequence, and using the OH-EpiCap tool (3) developed by the MATRIX consortium as a reference, the focus is only on the "operational dimension" of surveillance, while the other two dimensions evaluated by the OH-EpiCap tool (i.e. "organization" and "impact") are not considered.

The **four areas** deal with the aspects of OH in operational activities of the OH surveillance system. It comprises four subsections:

- **Data collection** and methods' sharing, which concern the level of multisectoral collaboration in the design of surveillance protocols, data collection, and harmonization of laboratory techniques and data warehousing.
- **Data sharing**, which addresses data sharing agreement, evaluation of data quality, and use of shared data.
- **Data analysis and interpretation**, which address multisectoral integration for data analysis, sharing of statistical analysis techniques, sharing of scientific expertise, and harmonization of indicators.
- **Results dissemination**, this subsection focuses on both internal and external communication processes, dissemination to decision-makers, and information sharing in case of suspicion.

The "best practices" apply to the four Hazard Tracks (HT) of the OHEJP MATRIX, namely *Listeria*, *Campylobacter*, *Salmonella*, and Emerging Threats. To set the background on which the best practices were implemented, a short paragraph will introduce each HT in the following pages, with particular attention to the importance of collaborations between sectors.

Hazard-tracks specific sections

I. *Listeria*

Listeria monocytogenes causes the illness listeriosis in animals and humans. The animal illness is notifiable in some countries, but it does not represent a serious disease. For humans, on the other hand, the disease is severe and can cause mortal illness and abortions (4). *Listeria* is considered among the top five most serious hazards according to risk rankings carried out and number of foodborne illness cases in Europe (5,6). Most human cases of listeriosis are food-borne.

The purposes of *Listeria* surveillance can vary for the AH, FS, and PH segments. For animals, *Listeria monocytogenes* contaminated feed is the main source of animal listeriosis, while contaminated food is for human listeriosis. *Listeria* is a ubiquitous bacterium, which means that attempts to eliminate the bacterium are not realistic, and further, that positive *Listeria* samples can be expected unless there have been processes or treatments that eliminate the bacterium. Therefore, *Listeria* is a hazard that society have to live with and manage to keep the number and seriousness of listeriosis cases as low as possible. The assumption made is that all human cases of listeriosis are food-borne, that all serotypes of *L. monocytogenes* can cause illness, that only some serotypes are likely to cause outbreaks of human illness, and finally, that the serotypes most related to human illness are not necessarily the same ones as those who cause animal illness. These characteristics are reflected in the design and strategies for surveillance chosen for the different segments and in the food legislation.

A typical pattern of listeriosis surveillance data and regimes for each sector is:

- Animals: passive sampling of suspected cases. In case of listeriosis on a farm, feed and environment samples will be taken as follow-up samples to identify the source and eliminate it.

- Food: the food business operators (FBOs) perform a number of sampling as part of their internal control plan. Typically, the focus is more on the production environment than on products, even though the microbial criteria are given for foods. To some extent, it is up to the FBOs to define how to deal with positive production environment samples. In some cases, arrangements on data sharing might be in place in business-to-business and authority-to-business relations. Data sharing of the results of official active surveillance programs could be made easier since the samples are owned by players within OH. For FBOs that export food, a certificate from the authorities is often needed, and in this way, the authorities get an overview of positive samples. If no active official surveillance program of food at retail or consumer level is present in a country, a passive sampling approach can be applied by sampling of products and production environment when products are recalled from the market. Monitoring of typical conditions that lead to recalls can also be used to investigate risk triggers.

- Human health: passive sampling of suspected cases. It differs between countries whether single cases are followed up to identify the food that caused it, but outbreaks are normally followed up with interviews and additional sampling.

For food, official surveillance programs are implemented carrying out active surveillance activities: sampling is performed on a wide range of foods, in particular ready-to-eat foods with growth potential, or a high likelihood of being contaminated. The growth potential of the food is relevant because the threshold level for increased likelihood of illness is relatively high, indicating that foods with lower concentrations are not risk factors for increased illness in themselves, but they could be for cross-contamination. In addition to official control programs, FBOs can carry out extensive sampling in their internal control system. Critical control points for temperature and other parameters that have an influence on survival and growth of *Listeria* are also included in their HACCP systems. Both the food production environment and the food products are included in the programs. The latter is an obligation with a basis in the Food Law (7), as it is the producers' responsibility to ensure that the food is safe and document compliance with the microbiological criteria in the food law. The samples of the food production environment are more related to the detection of contamination and troubleshooting.

Opinions on the relative importance of the different purposes for the sampling of *Listeria* in foods vary among stakeholders, both in trade and authorities. The stakeholders sometimes disagree about how the different sampling regimes can be used to assess risk and links between contamination, prevalence and illness. This is a source for conflicting interests in data sharing, data interpretation, data signalling, etc.

It is beyond doubt that the sampling done in internal control by the food-producing companies is very valuable. In terms of keeping listeriosis to a minimum level, keeping the levels of *Listeria* in food low has proved to be an effective way, as foods with the potential to cause illness are removed from the market and the trade develop production practices to limit growth and (re)contamination of the food during processing and storage. The interaction of sampling in the trade and official sampling programs represents a potential, but also a number of unsolved challenges, in terms of OH surveillance. In this document, the focus is on the official surveillance programs, but examples of uses of trade samples are included for illustration in some points.

However, food sampling by private actors is also a challenge in OH surveillance, to find and minimize the presence and concentrations of *Listeria* is considered an internal matter to companies, in particular as long as the concentration is below the limits in the legislation. In these cases, there is no duty to report positive samples to the authorities. On the other hand, the presence of *Listeria* in a factory has an influence on the ranking of the company in terms of being a preferred supplier or not, even if the concentrations are far below the threshold levels considered in the legislation. Therefore, in times with no outbreaks, the food trade has no interest in sharing data or samples with other OH activities, as it may hamper their business for "no reason". In cases of outbreaks, or other unfortunate situations, the trade may have an interest in rapid access to data from another OH segment, in order to document that they were not the source of the outbreak or contamination.

Taken together, *Listeria* OH surveillance is characterised by many dilemmas, such as the ubiquity of the bacterium and the different ownerships of data. If these aspects are not taken into account in the design and execution of the OH activities, there is a risk that the trade stops to take samples for troubleshooting, which in turn will increase the listeriosis risk. On the other hand, the official OH organisation also has an important job to do by preventing illness in the human and animal populations. The best practices, therefore, have to be built on a "give and take" approach, and find ways that optimize the benefits and minimize the drawbacks of OH surveillance.

II. Campylobacter

Campylobacter is a gram-negative bacterium that causes gastrointestinal disease in humans, often characterized by diarrhoea and general discomfort. *Campylobacter* is considered one of the most frequent causes of human illnesses in the developed world, caused by foodborne infections. The most common infection is with *Campylobacter jejuni* but also *Campylobacter coli*, among others, causes food-borne human infections.

Campylobacter further causes reproductive problems when infections occur with the strain *Campylobacter* fetus. As such, the infection is notifiable in animals under the disease name Bovine Genital campylobacteriosis, and is notifiable under the Animal Health Law. This is in contrast to infections with *C. jejuni* and *C coli*, which are regulated under the food law, and are hence relevant for the food safety sector, whereas *C. fetus* is relevant to the veterinary sector.

The European Member States (MSs) are required by regulation to monitor campylobacteriosis and agents thereof, and the foodborne outbreaks due to these agents are subject to epidemiological investigation. This is implemented on different levels and in different ways within each MS (8).

In food and animals, *Campylobacter* is monitored along the entire food chain. According to the Regulation (EC) No 2073/2005 in the EU, broiler carcasses at the slaughterhouses are checked to satisfy regulatory microbiological process hygiene criterion (PHC) (9).

Moreover, *Campylobacter* in animals is regulated under Animal Health Law (AHL), but limited to *Campylobacter fetus* and *veneralis*, and further limited to the species of bovine (bovine genital campylobacteriosis) (10). Moreover, it is also regulated under the WOAH terrestrial code (11).

Contaminated poultry meat is the biggest single source attribution to the human disease burden (12,13), but the estimates indicate that the total amount of the human disease burden from *Campylobacter* is multifactorial, and poultry meat does not account for the total disease burden in humans, even though it is the biggest single source attribution. Other attributions to the human disease burden include cattle, close contact with pets - especially dogs, contaminated water reservoirs, contaminated fruits and vegetables, and close contact with other infected humans. Moreover, for some countries, a large proportion of *Campylobacter* cases is represented by acquired infections abroad.

Surveillance is currently in place in most countries for *Campylobacter* in poultry, where the surveillance targets different areas of the supply chain, in order to mitigate the contamination of the poultry meat and hence mitigate the large disease attribution in humans.

Campylobacter has no apparent direct vertical transmission route in poultry, but eggs can be contaminated on the outside/ the shell, and infect the chicks in the hatching process. This in contrast to *Salmonella* spp., where the infection can be transmitted through infections of the ovaries of the layers, causing the vertical transmission to the actual egg and eventual offspring, as with vertical transmission that can be seen in mammals, where the fetus is infected with the causative agent through trans placental transmission of the agent.

This indicates that the infection of *Campylobacter* in poultry is to some extent caused by spill over from the surrounding environment and insufficient biosecurity measures. This is in line with studies and surveillance from Denmark that show that the prevalence of *Campylobacter* is significantly higher in free-range flocks than in conventional flocks (12), with less direct contact with the surrounding environment. On the other hand, studies from Sweden suggest a relevant number of human cases related to strains coming from conventional breeders flocks. These strains are considered industry-specific and their presence is possibly explained by suboptimal cleaning equipment and poor sanitization procedures (14,15).

A OH approach could be considered to mitigate a large attribution of human campylobacteriosis by tackling the infection in poultry. However, when looking at *Campylobacter* as a whole, the environment seems to be the major driver for re-infecting poultry and causing the variety of different source attributions.

In the context of OH surveillance, stakeholders and other competencies representing the environmental aspect of the system dynamics of *Campylobacter*, should therefore play a bigger role in understanding the complexities of the drivers behind *Campylobacter* infections in humans, and not just from the food safety sector, but also in the environment surrounding both humans and animals, and the interactions between these parameters.

III. Salmonella

Salmonella is a widely distributed bacterium, with many animal reservoirs including farmed livestock. Salmonellosis, the illness resulting from *Salmonella* infection, is the second most common cause of foodborne disease outbreaks in Europe (16). Consumption of contaminated food is the most common cause of salmonellosis in humans; however, the contaminated food consumed is not limited to meat products and can include salad and processed plant products (17). As salmonellosis does not always require medical treatment or hospitalisation, it is estimated to be significant under-reporting of the disease burden in humans. *Salmonella* is a priority disease in EFSA's extended control program for zoonotic diseases and all EU member states set up and implemented enhanced Salmonella control programs in poultry.

Being a widely distributed bacterium defining a single point of exposure in the farm to fork processing chain for pork meat is especially challenging with cross contamination of carcases and food products. There is added complexity in tracing *Salmonella* due to the movement of food and processed products within Europe, to support local monitoring activities EFSA and ECDC produce a joint publication monitoring trends across Europe (5,6), this includes human cases acquired during human travel within the EU. In conjunction with surveillance and monitoring for *Salmonella* in the farm to fork production chain, prophylactic measures are also aimed at safe food preparation in the kitchen to prevent human infection during food consumption (18). Due to the ubiquitous nature of the bacterium, there are many other sectors that may be involved in monitoring *Salmonella*, such as the environmental and companion animals' sectors.

For the reasons above, having a OH approach is essential to reduce human cases and to evaluate control measures in place in the different steps of the food chain, to mitigate human exposure. The main challenge could be the collaboration between the public and private sectors (industry), since the interests may be very different. Data originating from private sector, however, could greatly contribute to the evaluation of *Salmonella* surveillance and to meet the objectives of the research.

Improvements in the identification and characterisation of *Salmonella* by whole genome sequencing (WGS) is becoming more widespread through sampling across the complete farm to fork production chain. WGS analysis has the potential to give high-resolution tracing capability with the current challenge being harmonisation of analysis methodologies to allow direct comparison between analysis (19).

Following the implementation of the joint ECDC-EFSA molecular typing database, MSs can submit their typing data from human samples to ECDC Molecular Typing System and food, feed and animal samples to EFSA One Health WGS system, respectively. The two systems are interoperable, exchanging core genome Multi Locus Sequence Typing (cgMLST) profiles and minimum metadata. The technical guideline for reporting these data gives clear indications on the WGS analysis methodologies to be used to allow comparisons (20).

IV. Emerging threats

Within the MATRIX project, a number of emerging threats are being explicitly considered across the different activities (Work Packages).

These are:

- Antimicrobial Resistance (AMR) - which may relate to *Listeria*, *Campylobacter* and/or *Salmonella*;
- *Echinococcus multilocularis*;
- Hepatitis E;
- Psittacosis;
- SARS-CoV-2;
- West Nile Virus;
- Zoonotic Pathogens (broadly defined).

As can be seen, examples of viruses, bacteria and macro-parasites are included, and this section focuses on the general overarching themes.

The first point of relevance for OH surveillance is knowledge of the reservoir and routes of transmission. For most of the emerging threats considered within MATRIX, this is generally the case. However, when new threats arise, it can surprise different actors in a surveillance system. For example, the emergence of SARS-CoV-2 in 2019-2020 led to a large number of studies looking at possible transmission from pets, livestock and wildlife, with significant amounts of funding dedicated to this task. Within the MATRIX project, we have been actively engaged with COVRIN, another OHEJP project that works exclusively on SARS-CoV-2 emergence, risk assessment and preparedness (21).

Once the reservoirs and routes of transmission are known, evaluating risk factors also becomes important. This is another area that has seen a lot of research recently for SARS-CoV-2, but also historically for many of the emerging threats mentioned above (22).

With any surveillance programme where different sectors are involved, it is critical that different actors are aware of who else is involved in the surveillance activities. A good example of collaboration (in this case between the animal and human sector), is represented by the programmes that tackle the parasite *Echinococcus multilocularis*, where cooperation between sectors tends to be frequent and continuous. It is important to note that, specifically for emerging viruses, diverse serotypes might be present in different hosts, thus the relevance of different serotypes will vary for surveillance activities. Therefore, genome sequencing can add significant value for some of these emerging threats.

In general, analysis capacity is not a primary bottleneck issue. This is because many emerging threats can often be perceived as high risk and can then be prioritized. However, developing screening methods and guidance can be difficult. For some emerging threats, there is a lack of standardized diagnostics, which limits the information that can be gained and actions that can be done to prevent further spread. Similarly, when sectors need to cooperate, communication must include sharing data. This aspect can be challenging when different diagnostics are used, or when standards for database management are not agreed upon, with the result of hampering and delaying actions. Moreover, ownership of the successes and failures of a cross-sectoral programme have to be clear, which might be complicated further when certain threats are a priority for one sector but are better tackled through actions in another sector. An example is the deworming sheep/goats and dogs for parasites such as Echinococcosis to prevent diseases in humans.

One Health approaches ensure buy-in across sectors, which can lead to shared success and more action, particularly with conflicting priorities. Clear guidance and planning in terms of data collection, sharing and analysis, as well as dissemination of results, is thus key.

Best practices

As mentioned, a list of suggestions for each one of the following sections has been described:

1. Data collection (Annex I);
2. Data sharing (Annex II);
3. Data analysis and interpretation (Annex III);
4. Results dissemination (Annex IV).

Every section addresses the three different surveillance purposes:

A. Measure the levels and temporal trends of exposure and burden of disease;
B. Support early detection and response to outbreaks;
C. Identify risk factors to implement control measures.

Moreover, at the beginning of each section, the context is given by analyzing pre-existing:

- Facilitators;
- Barriers and challenges;
- Practices to overcome the challenges;
- Lessons learned, and recommendations.

As reported in Deliverable WP5.1– Report on requirement analysis for "OHS roadmap template" (23), facilitators are defined as the strengths (internal to the system) or opportunities (external to the system), of aspects that could facilitate the OH approach, while barriers are defined as the weaknesses (internal to the system) or threats (external to the system) that pose a challenge for the implementation of the approach (23). Both facilitators and barriers could be infrastructural, economic, or other natural aspects that influence the design, development, and implementation, including monitoring, of OHS along the entire surveillance pathway in European countries.

Additional findings of the work performed for Deliverable WP5.1 (23), but not included in it, have been used as starting point to describe the context of the sections. Moreover, at the end of each section, a list of questions to be raised when implementing multi sectoral collaboration is suggested.

Four table-type attachments, one per section (data collection, data sharing, data analysis and interpretation, results dissemination), represent the proposed list of suggestions for best practices. In each table, the analyzed section has been split into aspects, features, and steps, where relevant general and Hazard-specific annotations are gathered.

Annexes

- Annex I. Data collection;
- Annex II. Data sharing;
- Annex III. Data analysis and interpretation;
- Annex IV. Results dissemination.

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