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TECHNICAL REPORT OF THE FOOD STANDARDS AGENCY:

Thematic Workshop on Hepatitis E Virus 26/27 March 2018

CONTENTS

SUMMARY

Hepatitis E is caused by a virus that is found worldwide and can be transmitted by the faecal-oral route in the developing world. The disease is common in resource-limited countries with limited access to essential water, sanitation, hygiene and health services. In contrast, in the developed world the virus may spread from animals to humans through the consumption of undercooked or raw pig and game meat, processed pork and shellfish. Person to person transmission of the virus is exceptionally rare, but the virus can be passed between people through blood transfusion and solid organ transplantation.

Hepatitis E virus (HEV) is a zoonotic virus for which domestic pigs seem the most relevant reservoir for human infections. Pigs and humans normally do not show clinical signs of HEV infection, and HEV infection usually produces a mild disease but can be life-threatening in risk populations such as solid organ transplant recipients.

Since 2002, increasing numbers of infections have been reported across Europe in people who have never travelled to countries where the virus circulates actively. This received attention from food safety and public health authorities, scientists as well as the media and led to an increase in concern regarding safety of pork and pig products.

Following the 'joint UK FSA-EFSA workshop' on foodborne viruses (2016), recent scientific publications, thematic discussions and EFSA opinion (2017) assessing public health risks associated with HEV as a food-borne pathogen, it became evident that cooperation between European countries was paramount to further the understanding of HEV and options for control, ultimately ensuring consumer safety. To further the scientific understanding of HEV, including cooperation and enhance policy dialogue on HEV controls within Europe, we organised a thematic workshop on this topic to identify gaps in the fundamental understanding of HEV along with appropriate policy interventions, whilst considering different stages in the food chain (i.e. on-farm, at slaughter and processing and consumer exposure), accounting for interdependencies between these stages.

A questionnaire was circulated to all delegates in advance of the meeting. It was beneficial to use the workshop as an opportunity to support expert discussions on this timely and important issue of the public health impact of HEV. The results offered insight into the national situation, ongoing and future research, and policy considerations across most of the countries represented at the workshop. The workshop was organised in three parts: knowledge sharing and updates, discussion groups and prioritisation.

Measures that the group believed would have the greatest potential to address HEV were identified as:

- Effective on-farm interventions.
- Targeted inactivation HEV in high-risk products.
- Reducing human exposure.

The possible measures on 'Farm and in the Environment' level included: monitoring and surveillance, establishing HEV-free pig farms, prevent pig infection before they reach slaughterhouses, develop biosecurity measures and relevant guidance for different industry sectors.

The possible measures at 'processing' level included: risk profiling of pork products, develop guidance and training programmes for industry, HEV free material for non-heated products meant for consumption, influencing the regulators to accept suitable methods or set microbiological limit criteria.

The possible measures at 'consumer exposure' level included: selected immunisation of groups at risk of severe HEV disease, surveillance of patients at risk of severe HEV disease, targeted consumption and cooking advice for risk groups, statutory screening of blood donors.

All participants agreed on the importance of further work to develop the understanding of HEV, the use of these findings to identify risk intervention measures. The role of industry in preventing the spread of HEV and protecting consumer safety was highlighted.

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INTRODUCTION

Hepatitis E as a health concern

Hepatitis E virus (HEV) is a widespread viral infection of many animal species including humans and is divided into a number of genotypes. HEV genotypes 3 and 4 (G3 and G4) cause asymptomatic infection in animals, some of which are represented in the human food chain, for example pigs. Human HEV comprises genotypes 1 and 2 (G1 and G2). HEV G1 and G2 are spread from human to human by faecal oral contamination and can cause epidemics. Humans are also infected by diet principally by G3 as a zoonosis and sometimes by G4 through the consumption of flesh of viraemic animals. The majority of human G3 and G4 infections are self-limiting and do not pass from human to human except by transfusion and transplantation. Rarely acquisition of HEV in an immunosuppressed patient may lead to chronic infection with the potential for rapid progression to end-stage liver disease. The HEV in pork is recognised as an emerging problem and is of concern for public health and wellbeing. Reports from EFSA[1] and ECDC[2] indicate risks to consumer health associated with pork containing HEV, and uncertainty about the precise range of other commodities involved.

In the EU, foodborne transmission appears to be the major route for HEV transmission with pigs and wild boars identified as the main source of HEV G3. Other possible routes of transmission include consumption of contaminated food, such as shellfish. and possibly fruits and vegetables; contact with infected animals; or contaminated water may also lead to the acquisition of HEV.

Infection with HEV is important in humans and has led to 21,081 clinical cases reported between 2005-2015, along with 28 HEV-related fatalities[2] (ECDC). The majority of EU/EEA countries (20 countries) have HEV-specific surveillance for human cases in place. With the exception of the United Kingdom which has in place in both enhanced surveillance of clinical hepatitis E and most recently universal screening of blood donors (Ireland also has universal screening), data on disease and infection burden in the general populations are scarce. While pre-existing liver diseases are an important risk factor for severe acute hepatitis, immunosuppression is a major factor for chronic infection and disease developing from this (e.g. liver cirrhosis and liver failure).

Rosina Girones, chair of EFSA's working group on hepatitis E Virus, said: "Even if it is not as widespread as other foodborne diseases, hepatitis E is a growing concern in the EU. In the past, people thought the main source of infection was drinking contaminated water while travelling outside the EU. But now we know the main source of transmission of the disease in Europe is food[3]"

HEV G1/2 infections are acquired through faecal contamination of food and water in the face of poor hygiene and remain relatively uncommon and travel related in Europe. The dominant cause of human Hepatitis E in Europe are HEV G3 infections through the consumption of pig meat. It is not known with certainty which dietary components carry the highest risk though evidence in

1 https://www.efsa.europa.eu/en/efsajournal/pub/4886

2 https://ecdc.europa.eu/en/publications-data/hepatitis-e-eueea-2005-2015

3 www.efsa.europa.eu/en/press/news/170711

some countries supports processed pig meat, particularly when it is undercooked. Changes to animal husbandry practices (to increase biosecurity) can reduce the prevalence of infected pigs at slaughter. The thorough cooking of foods including pig meat to appropriate temperatures as advised by food safety authorities is recommended to inactivate the virus, if present. At present, this is seen as a very efficient control measure to prevent HEV infection from food. There continue to be fundamental gaps which need to be addressed in the understanding of HEV transmission (in pigs and to humans), epidemiology, pathogenicity, detection, control in animals and animal products, food, humans, and the environment.

European HEV workshop

Jointly organised by the FSA (UK), The Netherlands National Institute for Public Health and the Environment (RIVM) (Netherlands) and The German Federal Institute for Risk Assessment (BfR) (Germany) – core group

Rationale and aims

A number of publications are already available including the 'joint UK FSA-EFSA workshop' on foodborne viruses (2016), recent scientific publications, thematic discussions, EFSA opinion (2017) assessing public health risks associated with HEV as a food-borne pathogen, and ECDC report on assessing testing, diagnosis and surveillance for HEV in EU/EEA countries. These publications and follow-up discussions have made it evident that cooperation between European countries would greatly support improved understanding of HEV infection and options for control, ultimately improving consumer safety. As the UK national food safety regulatory body and in the spirit of EFSA focal point membership, we felt it was imperative that gaps in the fundamental understanding of HEV were identified, along with appropriate policy interventions. Different stages in the food chain (i.e. on-farm, at slaughter and processing, and consumer exposure) also needed to be considered in order to address and mitigate the root cause of pigs remaining infected at the time of slaughter.

We organised and led a thematic workshop on 26-27 March 2018 to address these aims of furthering the scientific understanding of HEV, including cooperation and enhanced policy dialogue on HEV controls within Europe and across the food supply chain.

The aims of the workshop were twofold:

1. Scientific areas for cooperation: to identify evidence gaps, cooperating in ongoing or future research activities within the theme.
2. Policy options and their implications: to identify interventions that would assist in mitigating risks to human health.

The workshop brought together scientists (clinicians, veterinarians, virologists and risk assessors) and policy advisors from different European countries with HEV expertise to facilitate cooperation amongst countries at the scientific as well as policy making level.

In addition to science and policy representatives from each EU/EEA country, EU authorities including EFSA and ECDC, and EU level industry representatives were invited. The inclusion of wider expertise and insights ensured informed discussions at this output driven workshop.

Questionnaire

The core group designed a questionnaire which was distributed to all delegates in advance of the workshop. Responses were analysed at national level and a summary was shared at the beginning of the event, informing discussions during the workshop and allowing us to make rapid progress and meet the aims of the workshop.

Representatives from 21 countries participated in the workshop, and questionnaire responses from 17 of these countries were received before the workshop. We would like to thank all delegates for taking the time to complete the survey.

The main topics covered in the questionnaire were: detection, policy approaches to providing advice to the general public and avenues for future research to refine policy in the area. The questionnaire included the following specific questions:

- Is HEV infection notifiable in your country?
- In your country is there a surveillance system in place to estimate incidence or measure frequency of HEV infection/disease in humans?
- In your country are there any ongoing screenings or surveys on the detection of HEV RNA in human blood products?
- In your country are there any typing data available on circulating HEV strains (e.g. from human, pigs or other)?
- In your country is there any indication (e.g. survey, scanning, monitoring and surveillance or research) of HEV RNA presence in pork products or in pig farms and wildlife?
- Are you aware of specific measures to address or mitigate risks associated with HEV?
- Please indicate if you have guidance or advisory documents specific to HEV in your country.
- Is HEV seen as a serious public health risk? You can use the relative scale from 1 (negligible) to 5 (very serious) or feel free to comment in the text box.
- Based on your understanding of the research area (including FSA-EFSA workshop 2016 and EFSA opinion 2017) please indicate your planned activities.

Workshop Structure

The workshop was organised in three parts: knowledge sharing and updates, discussion groups and prioritisation.

Knowledge sharing and update: Presentations were made on the state of play in the theme by ECDC and EFSA. Additional presentations covered options for control along the food chain; wider perspectives including the role of the environment, food and wildlife in HEV transmission; and an industry-led example of risk assessment at the stage of slaughter and processing. The presentations provided an opportunity for questions and answers followed by a panel discussion.

Discussion groups: Participants engaged in discussion groups of 6-7 participants each. They discussed the topics presented, survey results and points raised during the event. Views were also shared amongst all groups.

Prioritisation (including interactive online voting) of options for future co-operation: presentation of the key elements highlighted during the discussion groups with further discussion on priorities and expected outcomes.

SESSION 1: PRESENTATIONS ON PUBLISHED OPINIONS AND GENERAL DISCUSSION ON HEV RISK ALONG FOOD CHAIN

The session started with introductions from EFSA and ECDC regarding their recent analyses in the theme, key findings and information on the great potential for improvements to data collection and reporting in many more countries than at present.

ECDC activities on HEV – Situation overview on HEV in EU/EEA countries

(Cornelia Adlhoch, ECDC)

Evidence suggests that HEV is an under-recognised pathogen in high-income countries and not notifiable at the EU level. ECDC initiated several activities on HEV between 2015 and 2018. An expert group composed of nominated experts from the EU/EEA countries, external scientific experts and representatives of EFSA and world Health Organisation (WHO) has been established and supports ECDC. The purpose of an ECDC survey was to measure current testing, diagnosis, and surveillance for HEV in EU/EEA countries, and to conduct a baseline assessment of available epidemiological data. Of the 30 EU/EEA countries participating, 20 reported to having a specific national HEV surveillance system, case definitions and guidelines in place.[4] The incidence of HEV notifications has been steadily increasing across countries with 21 081 cases reported between 2005-2015, from 514 in 2005 to 5 617 cases in 2015, representing a ten-fold increase.[5] In total, 28 deaths associated with HEV infection were reported in five countries between 2005-2015. The data show that 98% of the infections are locally acquired with men and people over the age of fifty being most affected. More than 50% of the reported cases are diagnosed in hospital settings.

The number of reported cases of HEV is increasing and better surveillance practices alongside clinical awareness would support better understanding of the epidemiology of the disease and implementation of prevention measures. A technical report on national surveillance standards is planned for 2018/2019. In addition, ECDC also supported the development of a voluntary centralised sequence data repository called HEVnet that aims to facilitate molecular epidemiological investigations on circulating HEV subtypes and related clinical data across countries is hosted as well as operated at RIVM in the Netherlands.

4 ecdc.europa.eu/sites/portal/files/documents/HEV_Surveillance-report-2005-2015.pdf

5 ecdc.europa.eu/en/publications-data/hepatitis-e-eueea-2005-2015

EFSA opinion on HEV – Main findings of the 2017 Opinion on Public health risks associated with HEV as a food-borne pathogen

(Stef Bronzwaer, EFSA)

Hepatitis E virus (HEV) is an important infection in humans in EU/EEA countries, and over the last10 years more than 21,000 acute clinical cases with 28 fatalities have been notified with an overall 10-fold increase in reported HEV cases; the majority (80%) of cases were reported from France, Germany and the UK. However, as infection in humans is not notifiable in all EU/EEA countries, and surveillance differs between countries, the number of reported cases is not comparable and the true number of cases would probably be higher. Food-borne transmission of HEV appears to be a major route in Europe; pigs and wild boars are the main source of HEV. Outbreaks and sporadic cases have been identified in immune-competent persons as well as in recognised risk groups such as those with pre-existing liver damage, immunosuppressive illness or receiving immunosuppressive treatments. The opinion reviews current methods for the detection, identification, characterisation and tracing of HEV in food-producing animals and foods, reviews literature on HEV reservoirs and food-borne pathways, examines information on the epidemiology of HEV and its occurrence and persistence in foods, and investigates possible control measures along the food chain. Presently, the only efficient control option for HEV infection from consumption of meat, liver and products derived from animal reservoirs is sufficient heat treatment. The development of validated quantitative and qualitative detection methods, including infectivity assays and consensus molecular typing protocols, is required for the development of quantitative microbial risk assessments and efficient control measures. More research on the epidemiology and control of HEV in pig herds is required in order to minimise the proportion of pigs that remain viraemic withhigh levels of virus in the liver and intestinal contents at the time of slaughter. Consumption of raw pig, wild boar and deer meat products should be avoided.

Also, discussed were the key outcomes[6] of the Risk Assessment Research Assembly (RARA)[7] whereby EFSA and its Advisory Forum declared their shared commitment to supporting the European Research Area[8].

Discussion on the overview presented by EFSA and ECDC

Participants commented on the state of knowledge and understanding in the theme, recognising the need for proactive approaches. Various views were expressed on understanding of the distribution of cases (e.g. number of unrelated individual cases, which might be widely spread on the continent). Participants also identified issues with monitoring and reporting systems (e.g. underreporting of locally acquired cases and variation in the hospitalisation rates, and implications related to the fact that only the minority of all human infections are expected to develop clinical symptoms). The role of reservoirs and options for detection and interpretation of the results were discussed. The association with an increase in the prevalence of disease in the older person was explained by the increased clinical penetrance of the infection with age,

6 http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4886/epdf

7 www.efsa.europa.eu/en/events/event/180207

8 www.efsa.europa.eu/en/press/news/180206

data from both the UK and Holland indicated that in contrast younger donors were more likely to be found viraemic than older donors. There is some data to suggest that men that have sex with men[9],[10],[11] and HIV positive patients[12] may be associated with a higher prevalence of antibody to HEV.

A reference was made to HEVNet, which is a voluntary repository of HEV genetic data. HEVNet development was partially supported by ECDC funds, but the platform and associated network is solely hosted by RIVM. Further information can be obtained via hevnet@rivm.nl or https://www.rivm.nl/en/Topics/H/HEVNet

Employing methods from molecular epidemiology would enable linking of the sequences with metadata (e.g. host type, factors and clinical signs) and reveal underlying patterns. Participants noted the potential to seek greater collaboration in this area.

Interest and enthusiasm was expressed when exploring options for funding support on the topic of research and thematic cooperation. The understanding is that the Horizon Europe programme is still at a high-level discussion and other options can be explored. However, the established networks and professional partnerships would help widen the interest.

Key elements for HEV control along food chain and wider perspectives

Three presentations highlighted the importance of various elements along the food chain and in wider perspective when considering implications for the environment and wildlife.

Wider perspectives – food, environment and wildlife

(Saskia Rutjes, RIVM, Netherlands)

Non–travel-related HEV genotype 3 infections in persons in developed countries have a zoonotic origin. Because pigs and wild boar are considered the prime reservoirs, transmission through consumption of contaminated pork and wild boar products is suspected, this is supported by case-control studies of diet in the UK but there are indications that environmental transmission may contribute to human HEV cases as well. Based on different lines of the research in Netherlands, the most relevant identified risk factors for HEV infection and disease were: 1) the consumption of dry sausages containing raw pork, 2) contact with contaminated (waste) water, and 3) contact with pigs. Seropositivity was not associated with residential proximity to pig farms. The attribution of these different routes of transmission to exposure and infection of HEV is unknown although on balance of probability food products containing pork remained the most likely source. When more is known on the attribution, cost-effective preventive actions can be taken to reduce exposure to HEV through the transmission routes concerned. Preventive actions that may reduce transmission include: reducing the number of farms associated with a high prevalence of anti-HEV in their herds, preventing discharge of contaminated waste water, manure

9 https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciy596/5059684?redirectedFrom=fulltext

10 https://www.ncbi.nlm.nih.gov/pubmed/29103401

11 https://www.ncbi.nlm.nih.gov/pubmed/30557324

12 https://www.ncbi.nlm.nih.gov/pubmed/27998748

treatment, general food hygiene measures, and adjusting production processes of food products containing pig liver and meat. In addition, reduction of HEV exposure may be obtained by advising (vulnerable) populations to avoid consumption of food products that may contain HEV.

Slaughter age of animals and the presence of HEV in the liver

(Nicole Pavio, ANSES, France)

In the pig farm industry, growers (fatteners) constitute the main source of HEV positive animals that enter into the food chain. Weaners shed high quantity of HEV and are an important part of the epi-zoology within the herd. Given the faecal-oral route of transmission of HEV, the level of contamination is dependent on high pig-to-pig contacts and the accumulation of high viral loads in the environment. Hygiene factors such as cleaning, disinfection, emptying of pre-pits, and sub-floor areas, as well as husbandry practices including mixing animals with different infectious statuses during the farming period, are likely to have a significant impact on the spread and maintenance of the virus within farms. High seroprevalence within farms (>25%) is associated with a higher risk of HEV positive liver at slaughter. Experimental co-infection of pigs with HEV and Porcine reproductive and respiratory syndrome virus (PRRSV) leads to HEV chronic infection with prolonged viremia and muscle meat contamination. Although porcine liver is more likely to contain high levels of virus, consumption of any meat, especially when incorporated in a processed meat product, carries a risk of HEV infection.

Pig slaughtering depends on the live weight of the animal but not the age. On the basis of a model generated from published data, the prevalence of fecal shedding of HEV is highest at the age of 90 to 120 days and stops after a mean of 6 months. In infected pig farms, most infections occur in the first and second thirds of the fattening stage, but there is high individual variability. An interval between infection and slaughter of fewer than 20 days increases the risk of liver contamination. The probability of the virus being present in the liver and flesh cannot be directly inferred from the slaughter age since the exact infection date is not known.

Certification of HEV-free farms could be an option for the preparation of safe pork products. Serological certification could be performed on a regular basis in sows and/or on fattening pigs at the fattening stage or at the slaughterhouse. HEV RNA could be detected in faecal samples on farm or at the slaughterhouse, indicating the possible presence of the virus in the liver. These two strategies could potentially be combined. In addition to the improvement of husbandry practices and hygiene measures on farms to control zoonotic HEV, immunisation could be a useful tool when available.[13]

Policy context and options for reducing the risk of HEV in the food chain

(Milen Georgiev, FSA, Falko Steinbach, APHA, Richard Tedder, Imperial College London, UK)

The speakers described considerations in a recent risk analysis and appraisal of options for intervention in the UK.

13 www.anses.fr/en/content/opinion-anses-concerning-request-assess-risks-related-contamination-delicatessen-meats

The detection of clinical cases in humans has risen significantly in the last 10 years and while the vast majority of infection remains asymptomatic, HEV presents a significant risk to immunocompromised individuals. Human infections with HEV genotype 3 may have several sources, but the most likely one in Europe seems to be infection via meat and meat products from infected animals.

According to current models of the infection cycle in pigs this seemed counter-intuitive as the infection should have been cleared at slaughter age. The UK abattoir study, however, demonstrated that this was not the case and while the number of animals testing positive for HEV at slaughter was low overall some animals seemed to pose a particular risk. While it is best practice to cook pork meat thoroughly and in accordance with current advice, it must be investigated whether current industry standards post slaughter are sufficient to inactivate the virus. "*Regulations related to hygienic measures for foods of animal origin and control of products of animal origin for consumption are laid down in EU Regulation (EC) 853/2004 and 854/2004.*"[14] The focus of practical mitigation measures in the long run has to prevent viraemic pigs from entering the food chain at the time of slaughter.

Alternatively, HEV infection may be controlled at farm level – at least to prevent the spread of HEV infection at slaughter age, but potentially to avoid it completely. Available data indicate that HEV-free farms exist and that part of the problem is that HEV positive adult animals come into contact with the virus relatively late in life.

Data from blood donation analysis indicate that as many as 100,000 infections occur annually across England and Wales so the clinical attack rate is very low (at present). A majority of human cases presenting with clinical hepatitis are caused by viruses not present in the UK pig population. The same applies to the screening of blood donors.

Discussion: Key elements for HEV control along the food chain and wider perspectives

The audience appreciated the comprehensive presentations and expressed interest in various points. Queries were raised on the importance/relevance of different exposure routes, dietary preferences (e.g. vegetarians), and occupational exposure of farmers and vets. It was flagged that high exposure rates in the population are not always associated with health consequences, however some groups appear more affected. Opportunities for targeted advice to some groups were highlighted and opinions were raised that in addition to the high relative risk related to the consumption of pork and pork products, further investigation is needed on other transmission routes. Studying non-pork eating populations could contribute to identifying risk factors other than pork consumption. A recent study from Italy points towards travel as a risk in this group in particular, but in some other areas environmental contamination cannot be excluded. A case study in Croatia found an elevated risk along the Rijeka river possibly relating to environmental associations between animals, human, wildlife and HEV infections.

Furthermore, available data suggest that a substantial part of the average population has been exposed (approximately ⅓rd) without many health consequences. However, other figures of sero-prevalence indicate some exposure in communities that do not traditionally eat pork.

14 www.efsa.europa.eu/en/efsajournal/pub/4886

At animal population level, participants discussed what methods for sampling and detection are available to certify the status of animal population/farms and utilise serology and molecular methodologies. These two approaches were seen to be complementary to each other. The use of vaccines in pig production was discussed. However, there is a lack of options to distinguish vaccinated and not vaccinated animals and substantial work is necessary to secure development of a safe and effective vaccine for animals. In addition, concerns about the use of vaccines in pigs were raised due to economic considerations and the absence of disease in pigs. As is common for many diseases, the monitoring of herd status is possible when considering appropriate sampling frames. An attendee reported success of a similar monitoring scheme when sampling was organised to control herpes virus in bovine herds. It was also reported that an ongoing epidemiological study looking at the results from various farms to investigate associated factors such as animal husbandry and biosecurity. Some results indicate a long history of maintaining an infection-free status (e.g. in breeders) with promising possibilities for investigating common practices. Further comments were made on variations in pig production across different countries, including husbandry practices and the number of pigs in herds. Those variations may reflect on actual risks of exposure and potential for re-infection in different places.

Prioritisation of pork products for potential foodborne HEV transmission – An example of risk analysis

(Martijn Bouwknegt, Vion, Netherlands)

The presentation focused on a study that was initiated to prioritize groups of pork products in relation to their contribution to foodborne HEV transmission. To that end, all consumed pork products in the Netherlands according to the Dutch National Food Consumption Survey were grouped into one of seven groups based on the ingredients and processing steps: fresh meat, porcine liver (whole), liver sausage, raw meat products, cooked meat products, fermented products, and blood sausage. A quantitative microbiological risk assessment model was developed to compare estimated exposure doses among these food groups. As data scarcity made characterisation of all required parameter distributions and the generation of absolute risk estimates impossible, parameters were quantified as ordinal, order-of-magnitude levels. The results showed that of the two sources of HEV-introduction in meat, that is, blood and liver, the contribution of blood was negligible. The two food groups “fermented sausage” and “porcine liver (whole)” together were estimated to cause about 95% of pork-related HEV cases. Fermented sausages were most likely contaminated due to carry-over liver when using the diaphragm as an ingredient, and refraining from using diaphragm in fermented sausages reduced the estimated contribution by about 60%. Interventions such as effective heating of whole pig liver reduces the estimated risk by approximately 25%. The authors indicated a manuscript in preparation – *Bouwknegt M, Van’t Hooft BJ, Koppen K, Rietvelt H, Straatsma G, Heres L., Prioritisation of pork products for potential foodborne HEV transmission*.

Discussion: an example of risk analysis

Representatives of attending countries were interested in the methodology and decision taken when different parameters in the assessment were defined, including expected log reduction, time temperature combinations, knowledge of the production chain and consumption data, and

utilisation of various tissues. Other comments reflected on the specific option for improved meat safety if food is processed under high pressure processing (HPP).

Panel discussion

All participants discussed key elements and areas to be considered in future policy interventions or research activities.

There was wide recognition of the importance of knowledge sharing, good biosecurity practices and targeted advice in order to maintain good animal health and welfare as well as prevent HEV transmission. The difficulties and variations among primary producers and processors were acknowledged but options for elevating safety beyond current standards of production of food (i.e. by accounting for potential risks in the specific supply chain) were suggested. The option for risk profiling of products and associated costs and impact on traditional products was also highlighted.

It may be important to consider the source of meat (and included tissues) in products which are not cooked or intended to be consumed undercooked or raw. This also includes those processed pork products which are sold raw but are expected to be cooked by the purchaser. The regulatory advice concerning these must be informative and practical.

Reinforcing good hygiene practices and correct use of cooking instructions were indicated as a baseline to follow but critically dependent on compliance.

Many comments referred to innovative as well as standard technologies for virus inactivation in food (e.g. irradiation, high pressure, pH modifications, and salt). However, it was accepted that due to the nature of the product that is to be produced not all methods may be applicable. Development of models including virus characteristics and survivability of the virus in different matrices can offer important insights to refine the control/preventive measures.

There were different views on the best approach for establishing HEV-free status of pig herds and on practical options to achieve and maintain this status. It may be challenging to eradicate HEV from a farm although, freedom from viraemia at slaughter is a possible step forward in the process.

Further, HEV-specific knowledge on biosecurity measures could be obtained from epidemiological longitudinal studies. More information on the virus characteristics (e.g. adaptability, diversity) would help to identify virus dynamics and persistence of the virus in the environment and host. Some experts suggested the development of an infectivity assay and determining the infectious dose at least in an animal model would be necessary to fully understand the potential for HEV transmission.

Testing for HEV in blood donors offers solid monitoring and prevention of spread in human populations. Further analysis of genetic data though is needed to clarify the transmission chains.

SESSION 2: DISCUSSION OF THE RESPONSES TO THE PRE-WORKSHOP QUESTIONNAIRE

A questionnaire (see Annex) was circulated to all delegates in advance of the meeting. It was beneficial to use the workshop as an opportunity to support expert discussions on this timely and important issue of the public health impact of HEV. The results offered insight into the national situations across the EU, ongoing and future research, and policy considerations across most of the countries represented at the workshop.

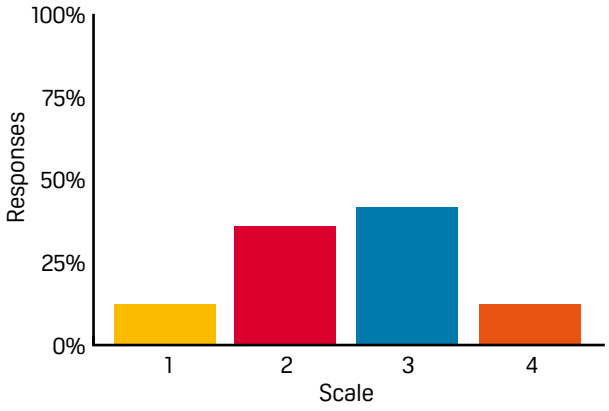
Indeed, of the 31 countries invited to participate in the workshop, 21 countries attended the workshop and representatives from 17 countries participated in the survey.

High level survey results were shared to provide an overall picture of the situation for HEV amongst the countries that responded to the survey. All delegates were then invited to discuss measures to address HEV control in smaller groups of 6 or 7.

We started with the question of whether HEV was seen as a serious public health risk.

The responses suggested that there is a general recognition amongst this group that HEV is a concern: Respondents could choose a value of 1 to 5 to represent how serious a health risk HEV is considered to be, with 1 being negligible and 5 being very serious. 40% of respondents chose 3, and 35% chose 2, placing concern about this issue in the lower middle of the range. No respondents rated the risk as a 5, which would suggest that it is not considered to be a very serious public health risk.

Figure 1: Perception of respondents regarding how serious HEV is considered to be as a public health risk. Responses were provided on a scale of 1 (negligible) to 5 (very serious). None of the participants considered HEV to be 'very serious' (5).

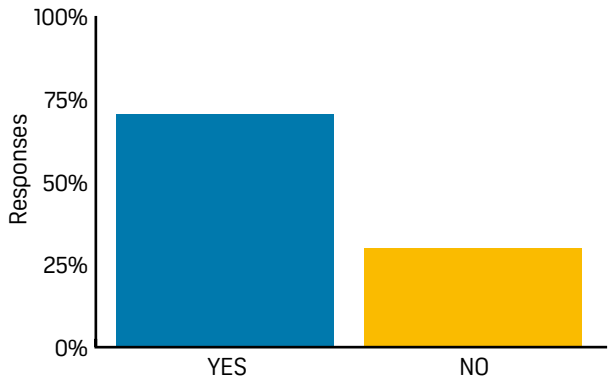


Responses to the question about HEV as a notifiable infection reflect the level of concern indicated in the answers to the aforementioned question. HEV is notifiable in 12 EU/EEA countries, but not notable in 5. And while its status as a notifiable infection in at least a third of EU/EEA countries reflects its importance as a priority disease, HEV is yet to be given a notifiable status at EU level.

Some of the comments in the survey responses indicated that HEV is not considered a serious public health issue as the majority of infections are self-limiting and asymptomatic.

However, some responses indicated that HEV could be an emerging concern, particularly due to the fact that there is limited information on the extent of the risk, both in terms of disease burden in the general population and sources of the infection, and research on this issue is at a relatively early stage.

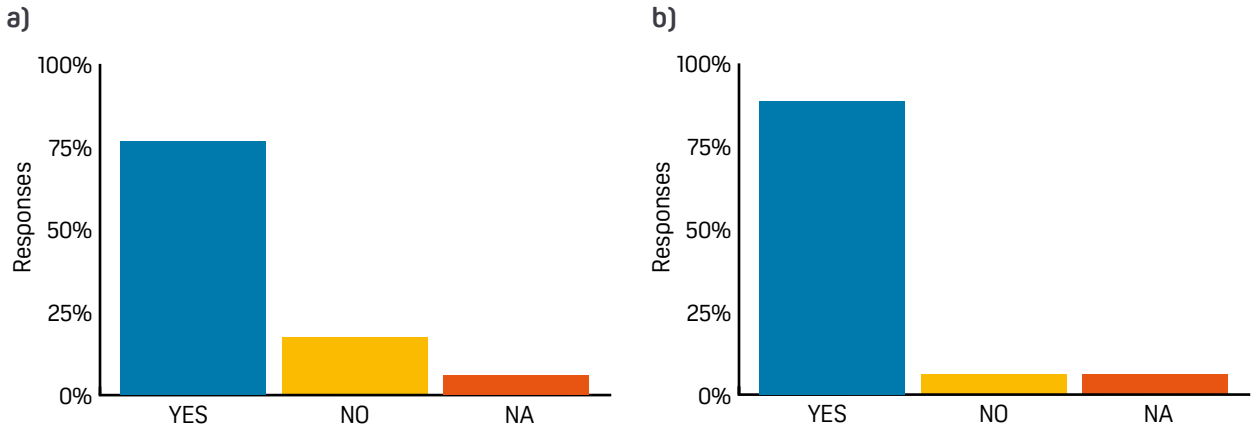
Figure 2: Responses to the question "is HEV infection notifiable in your country?"



Looking at the responses to the questions about ongoing and future research activities, two-thirds of respondents indicated that to date there have been research activities on HEV. Most respondents indicated that there are planned research activities to determine prevalence in pigs and pig products as well as molecular epidemiology and methods for rapid detection. There is also ongoing or planned work in risk exposure assessment and the findings are intended to be used to identify potential control points and risk mitigation measures for HEV and other viral foodborne pathogens, infectivity assays, potential risk factors for HEV exposure, research on animal reservoirs, and risk assessment on HEV in food and water. ECDC is also in the process of developing a technical guidance document for national testing and surveillance for HEV in the EU/EEA.

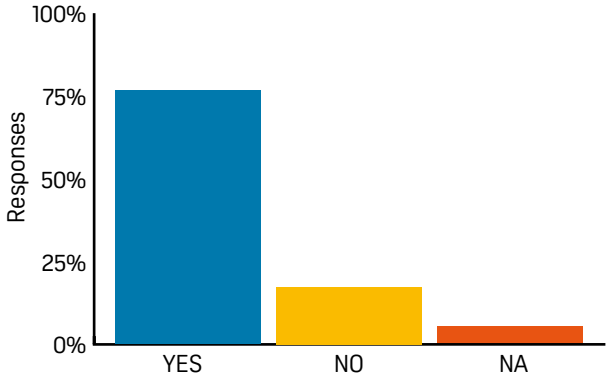
The responses to the survey questions clearly showed emerging evidence on the prevalence and molecular epidemiology of HEV in human and animal populations, and some previous or future planned research on detection of HEV in food products and reservoirs of infection. There has been less research on risk and mitigation approaches or on the stability and inactivation of HEV during food processing.

Figure 3: a) Ongoing and recently completed research activities, b) future research plans



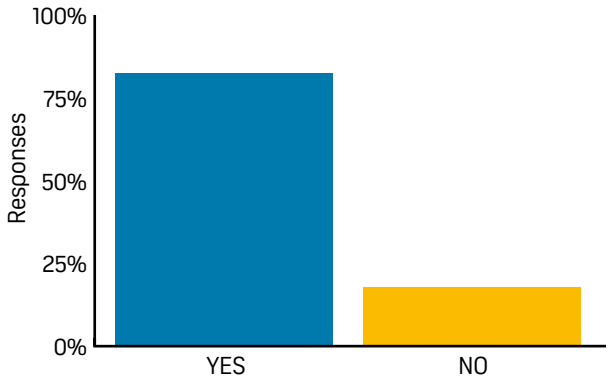
Most of the countries represented in this survey were also undertaking some form of surveillance to measure the frequency of HEV infection in humans. In some countries, individual cases are reported, in others only grouped cases are notifiable. Active and enhanced surveillance approaches are also being undertaken in some countries.

Figure 4: In your country is there a surveillance system in place to estimate incidence or measure frequency of HEV infection/disease in humans?



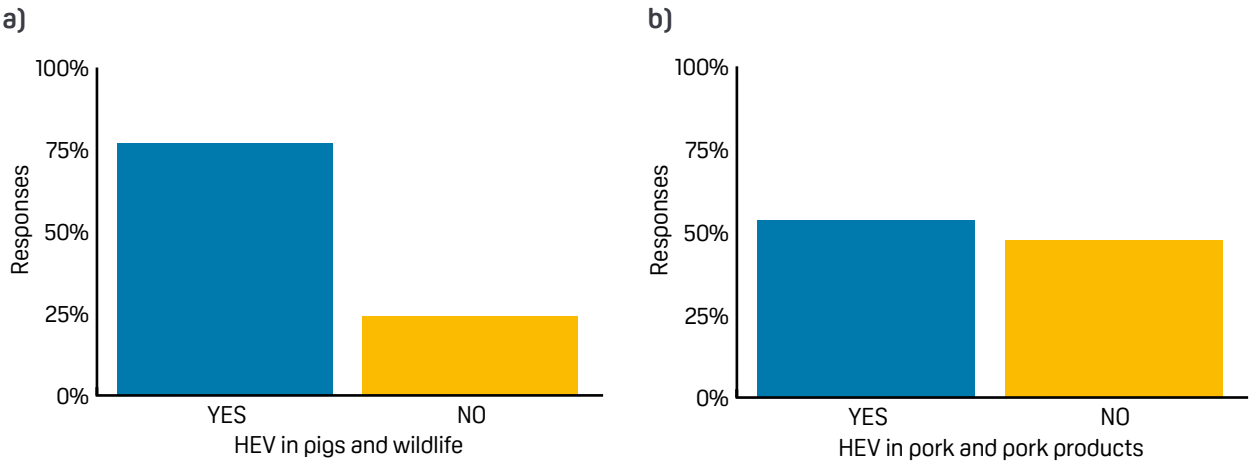
Most respondents indicated that typing data is being collected in their country on circulating HEV strains.

Figure 5: In your country are there any typing data available on circulating HEV strains (e.g. from humans, pigs or other)?



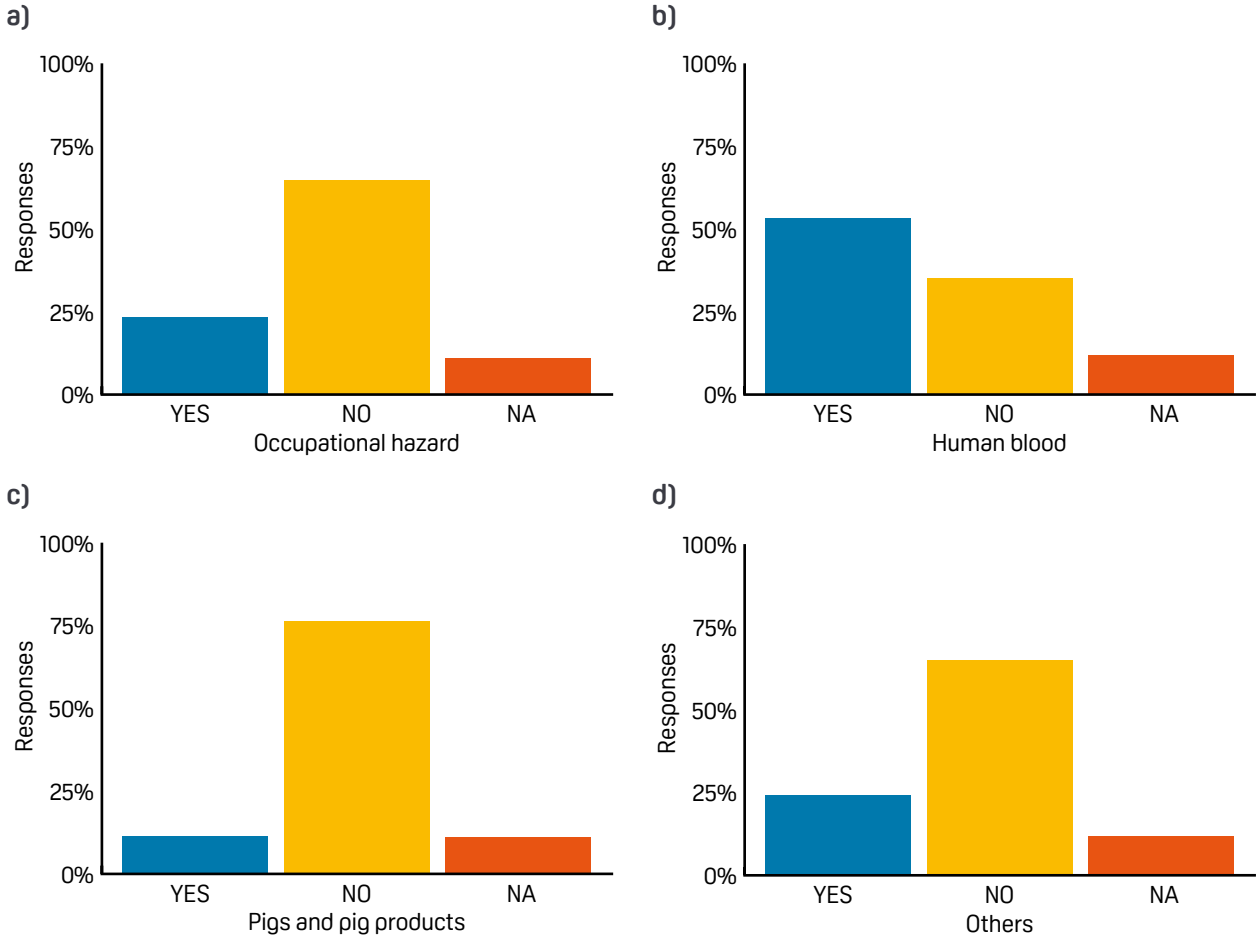
When it comes to screening or surveys to detect HEV RNA, detection in many countries seemed to be focused on animal populations, and less so on food products and the environment.

Figure 6: HEV incidence in a) pigs and wildlife, b) pork and pork products



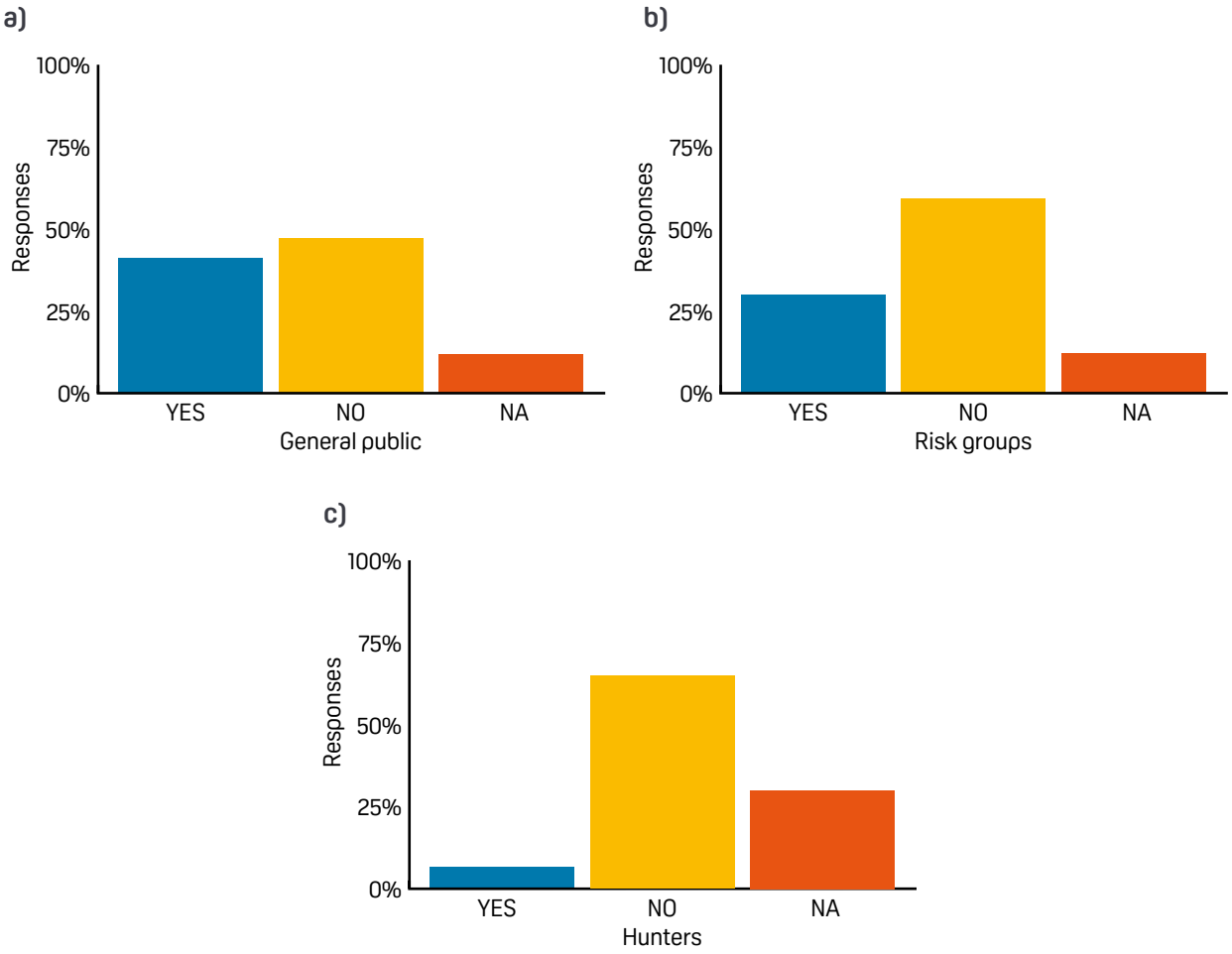
However, fewer countries have specific mitigation measures in place to address HEV.

Figure 7: Are you aware of specific measures to address or mitigate risks associated with HEV a) as occupational hazard, b) in human blood, c) in pigs and pig products, d) others?



The survey responses indicated that while some countries have guidance for the general public, there is limited guidance for risk groups such as blood recipients and renal transplant patients.

Figure 8: Indicate if you have guidance or advisory documents specific to HEV in your country for a) the general public, b) risk groups, c) hunters



More specifically, as can be seen in Figure 8, 41% of the responders indicated that advice for the general public is available in their countries. Advice for risk groups, however, is available in 29% of the countries that responded to the questionnaire.

The overall picture shows that most European countries consider HEV as a medium risk to public health with the vast majority reporting some level of past or planned research and surveillance activities. However, despite confirmed incidence of HEV in living animals and pork products, there are few mitigation measures in place. Targeted advice to risk groups appears to be largely missing as well.

The aim of the workshop was to build on previous discussions (see Introduction) with the intent to move towards action on this issue. The discussion group session that followed was therefore focused on policy measures and ways to address challenges in this area.

SESSION 3: IDENTIFYING AND PRIORITISING POLICY INTERVENTIONS

Participants were asked to consider measures to tackle HEV at three separate stages of the food chain, namely on farm and in the environment, at the processing stage and consumer exposure. Participants selected potential measures considering their effectiveness, benefits and drawbacks at each stage. The selected measures were identified with the aim to allow for a policy driven intervention rather than for the sole merit of acquiring further information without an expected outcome.

As a second step, participants were asked to rank the measures (per group) that they had identified and consider the knowledge gaps that may be preventing application of the measure and achievability of the three measures ranked as the most critical.

Consider measures to address HEV at 1) farm and in the environment 2) processing 3) human consumption level.

- Select **up to three measures per theme** for discussion in your group.
- Consider how **effective** you understand each measure to be addressing HEV.
- Consider the **benefits and drawbacks** of each measure.

Possible Measures on Farm and in the Environment

A. Monitoring and surveillance

The detection of HEV infected pigs based on clinical conditions alone would not be possible as no clinical disease is evident in pigs. Establishing standardised test protocols (e.g. frequency of sampling, number of animals, farming system effects) as well as standardised detection methods for the HEV genome in different matrices, and the determination of antibodies were identified as the main areas of uncertainty that would need to be addressed on the route to establishing HEV negative herds. Any sampling would need to aim for setting a baseline for detection of seroprevalence and/or genotype and quantifying the extent of HEV prevalence at a level that would allow to stop a further spread on farm. Accordingly, monitoring and surveillance on farm were identified requirements upon which other measures discussed could be implemented. Overall, farmers may have concerns to invest in intervention as no clinical disease is evident in HEV infected pigs but the option offers the market advantage to farmers that their pig herds do not represent a source of potential HEV transmission and less risky to have viraemic pigs at slaughter.

B. Establish HEV free pig farms by

a. Modulating the dynamics of the virus on farms, influencing risk and transmission factors.

b. Investigating the role of coinfection with porcine pathogens as well as the role of manure in HEV transmission.

c. Identifying introduction and prevention factors to reduce within farm transmission, including the role of wildlife and humans.

The participants acknowledged and discussed specifics within the three points but focused on the overarching idea rather than the specific implementation approaches. There was wide agreement amongst participants that this measure to stop spread would be highly effective overall in achieving food safety. Despite its effectiveness if achieved, it was thought that HEV free farms may be difficult, implicating some extra resources and costs and should involve good understanding of the associated risk factors.

C. Prevent viraemic pigs before they reach slaughterhouses by

a. Immunising pigs at an early stage (3 weeks – 3 months old).

b. Slaughtering pigs at a later stage.

Immunisation was suggested as a potential approach to achieve this measure. However, participants acknowledged vaccination was a long-term intervention. In addition, as stated previously, farmers may have concerns to invest in intervention if they do not see economic benefit of the measure. Vaccination was linked to several difficulties including the need for farmer cooperation, current unavailability of a suitable vaccine and the need to devise a vaccination strategy. In terms of effectiveness, participants believed that it could help reduce the circulation of the virus. Slaughtering pigs at a later stage was suggested as an intervention. This, however, requires further understanding of viral infection dynamics.

D. Target veterinarians for training

HEV does not affect the health of pigs and therefore it is unlikely that veterinarians consider HEV as a serious concern when devising measures to protect animals from infections. Raising the issue with professionals was thought to be of low effectiveness yet necessary to support other measures (and key to getting cooperation for any farm-level measures). Differences between farming systems between, as well as within countries were discussed and thought to present difficulties in developing training programmes at an EU/ international level.

E. Develop biosecurity measures and relevant guidance for different industry sectors

Biosecurity supported by relevant guidance was considered to be a general but challenging measure that could mitigate pathogen transmission, including HEV, and reduce the opportunities for the introduction of the virus onto the farm. There were points raised about the economic efficiency of biosecurity, but enhanced biosecurity may well bring additional benefits in the fight against other, economically more impacting diseases such as Porcine Circovirus Associated Disease (PCVAD) or Porcine Reproductive and Respiratory Syndrome Virus (PRRS).

Possible Measures at Processing

Some participants believed that the processing stage could be a more realistic option for interventions due to relatively well-defined gaps, that is, risk profiling of products, effectiveness of processing treatments on the virus and development of an infectivity assay. Within this context the following measures were discussed:

A. Risk profiling of pork products

For effective actions to be taken at the processing stage, the level of HEV contamination of different products needs to be determined. It was thought likely that the type of products to be surveyed would differ between countries due to differences in traditions and food consumption habits. Animal tissues and processing treatments (e.g. radiation, curing, fermentation) should be included in this data collection exercise. In addition, the infectivity of the virus in different matrices should be assessed while looking for methods to inactivate the virus without affecting the quality of the products and for this an infectivity assay is needed. Participants thought that identifying high and low risk products could lead to further interventions such as selecting less contaminated parts for non-heated/ cooked food products. Testing retail products could also increase awareness among manufacturers and, by extension, farmers. A prerequisite for these investigations would be the standardisation of extraction and rescue of HEV genome from food matrices, detection methods for the HEV genome in different food products as well as the development of reliable HEV viability assays to assess its infectivity and inactivation. These costs, however, were invariably higher (testing multiple products) than testing pigs at/before slaughter.

Identifying food processing parameters that inactivate the virus, including heat inactivation

The lack of knowledge on how process conditions may affect the viral load and infectivity was thought to be an important parameter that affects policy decisions. Therefore, this was identified as one of the first areas to focus on before taking any further measures at the processing stage, despite its potential high cost. Once this information is known it can have a high impact on health by making food safe from HEV. Heat inactivation could cause reduced consumer acceptance in some cases when it affects the quality of the product and changes the flavour. However, heat processing cannot always be applied (e.g. on fresh or cured meat). And again, a prerequisite for these investigations would be the development of reliable HEV viability assays to assess its infectivity and inactivation.

B. Develop guidance and training programmes

A training programme for the industry, including food processors, managers and food business operators would increase awareness and result in the incorporation of HEV in Hazard Analysis and Critical Control Point (HACCP) programmes. HACCP is an approach to managing food safety hazards. Food safety management procedures should be based on HACCP.

This step was identified as an opportunity to work collaboratively with industry. However, time and expenses required for such training must be thought through carefully so as to develop a practical and achievable programme.

C. Choose HEV free material for non-heated products

Some parts of the animals may be more contaminated than others, for example, the liver and diaphragm. On this basis, it may be possible to exclude potentially highly contaminated products such as the liver and diaphragm from the manufacturing of minimally-treated products, especially non-heated products. If applied across all European countries, this measure was seen to be of significant effectiveness. It has the advantage of reducing exposure at the source, beyond the farm level. However, it is recognised that if pig immunisation is not feasible, virus free or low contaminated herds, although not ultimately needed, are preferable for this measure to be applied effectively, which implies a strategy to reduce infected animals at slaughter.

D. Apply regulatory control by influencing the regulators to accept suitable methods or set legal limit microbiological criteria

It was thought that applying regulatory control by influencing the regulators to set suitable methods or set a legal limit on microbiological criteria will be challenging. This method is often seen as allowing the industry to relax vigilance so should be considered as a last resort. Setting a microbiological standard in the legislation could be helpful for control purposes and for raising awareness in the industry. However, it cannot be considered yet due to the absence of standard detection methods or sampling plans, and knowledge of effective processing parameters.

Possible Measures at consumer exposure

The diagnosis and monitoring for HEV infection and its outcome was considered important. A number of interventions were suggested for consideration, summarised below.

A. Selected immunisation of groups at risk of severe HEV disease

it is possible to identify persons who are at particular risk of severe hepatitis following acute HEV G3 infection and also identifying persons who are at risk of persistent HEV infection if infected. Acquisition of HEV infection during bone marrow transplantation may be associated with severe and fulminant and occasionally fatal hepatitis. In addition, patients who are immunosuppressed following transplantation are at serious risk of acquiring viral persistence should they become infected. Where HEV infected blood and organ/tissue donors are screened, the residual risk of diet remains there is no licensed vaccine available in Europe to immunise patients undergoing these procedures and we simply do not know seroconversion rate following immunisation in these patients nor the duration of protection following immunisation in such patients. What is more appropriate in the short term is to develop protocols that enable the identification of individuals in the risk groups who may have become infected through dietary exposure.

B. Surveillance of patients at risk of severe HEV disease

It remains difficult to define precisely who should be considered as ‘risk patients. In principle any patient who is immunosuppressed either through primary disease or through iatrogenic immunosuppression for therapeutic purposes is at risk of persistent infection. There are varying underlying factors such as age, susceptibility, eating habits, etc which make it challenging to clearly define the risk of acquisition within such groups. Once infected an immunosuppressed

host may clear spontaneously though in the seronegative patient this is unlikely and viral persistent infection is likely to follow. Persistence is defined as detectable HEV RNA over a three-month period. Progression to chronic liver disease may occur in a matter of a few years and therapy with ribavirin will lead to clearance in the majority of such individuals. However clearance, defined by an absence of detectable faecal RNA on two occasions does not necessarily mean termination of virus infection. Retesting in the apparently cleared patient reveals recrudescence in a significant number of patients and retreatment may be indicated. Selective screening of patients in these risk groups, triggered by any episode of transaminase elevation, is cost-effective for preventing the onward cost of progressive liver disease. The prevalence of persistent infection is around 0.5 to 1% of random solid organ transplant recipients. The prevalence of persistence in haemato-oncology patients is much lower though not negligible, spontaneous clearance may be more frequent in this patient group, probably as a result of improved immune function following successful treatment of the primary disease.

C. Targeted consumption and cooking advice for risk groups

Targeted consumption and cooking advice would increase awareness among patients considered to be at higher risk of developing chronic hepatitis E and their families. Information could be distributed to general practitioners and to those other clinical practitioners who look after transplant patients. Increasing awareness generally for clinicians who look after patients transiting into a state of "immunosuppression" may prove more challenging. This measure was seen to be effective, provided the dietary advice is followed by the patients involved and reinforced by their practitioners. The advice could cover general hygiene measures, cooking parameters to inactivate the virus, and suggestions to avoid high risk products. There is a need to consider groups to whom getting out such messaging is challenging for various reasons. Cooking advice could be extended to restaurants as well, especially when cooking pork thoroughly is not habitual in a given country or region. The potential disproportionate negative publicity and economic impact should be considered carefully.

D. Labelling of retail food products

Retail product labelling could be amended to suggest "thorough cooking", "HEV-free" products, unsuitability for certain high-risk groups, or "raw meat/ liver" containing products. This approach would help to raise awareness at all stages of the food chain and could be effective if followed by risk groups. However, it was thought that a similar result could be achieved with targeted advice as only certain groups are adversely affected by HEV. Therefore, labelling needs to be considered carefully to avoid disproportionate negative publicity or public perception.

E. Statutory screening of blood donors

Universal screening of blood donors is already implemented in the UK and other countries in the EU/EEA[15]. Despite being resource-intensive, blood donor screening is believed to be very effective at reducing the transfusion risk.. Based on modelling of the duration of viraemia in blood donors and the transmission rate of around 40% in recipients of components from an infected donor, one year of dietary exposure is equivalent to the risk of an exposure to 13 blood donors.

15 https://www.ncbi.nlm.nih.gov/pubmed/28449730

Although selective screening would enable the provision of screened blood to a minority of recipients, experience in the UK of this policy demonstrated that selective screening was not cost-effective and as a result a move to universal screening was instituted. An unexpected benefit of donor screening is that it provides added information on the incidence rate in the general, healthy public and also provides viral sequences for phylogenetic analysis studies of HEV phylotypes in the population at large.

SESSION 4: PRIORITISATION EXERCISE

Ranking of interventions

During the group sessions, participants identified possible interventions and considered benefits and drawbacks for each, and then were asked to select up to three measures that they believed would have the greatest potential to address HEV. When doing so they were prompted to discuss the following questions:

- What are the gaps in our understanding of HEV that pose challenges for ongoing or future effectiveness of each measure?
- What are the cost and feasibility limitations?
- Is the measure achievable in the short-term or long-term?
- What is the estimated timeframe over which this measure could be introduced in your view?

After active discussions and interactive voting, the identified priorities were:

1. Effective on-farm interventions.
2. Achieve inactivation in high-risk products.
3. Reduce human exposure.

The interactive online voting summarised and visualised participant views on the relative priority of point discussed during the session.

Figure 9: Where would you advise focusing if we are aiming for effective intervention on farm?

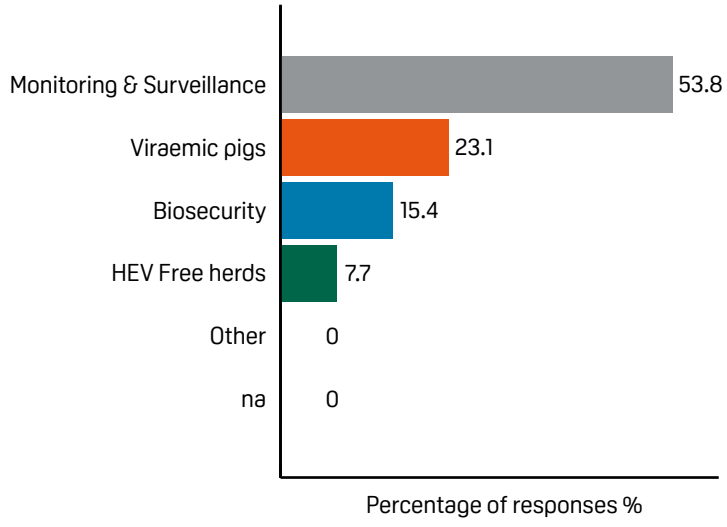


Figure 10: Where would you advise focusing if we are aiming for inactivation of HEV at processing?

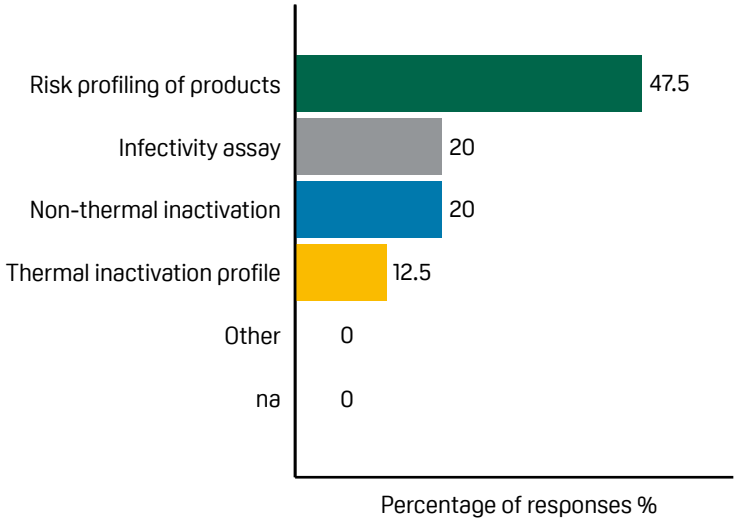


Figure 11: Where would you advise to focus if we are aiming for risk reduction at human foodborne exposure?

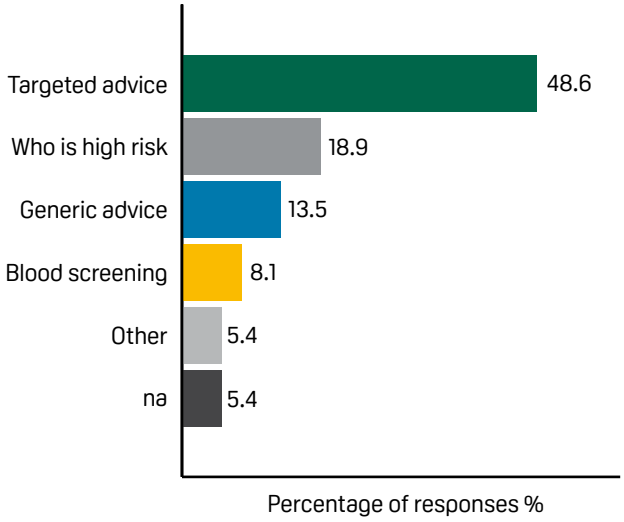


Figure 12: Do you believe it is likely that you can support and collaborate in these areas?

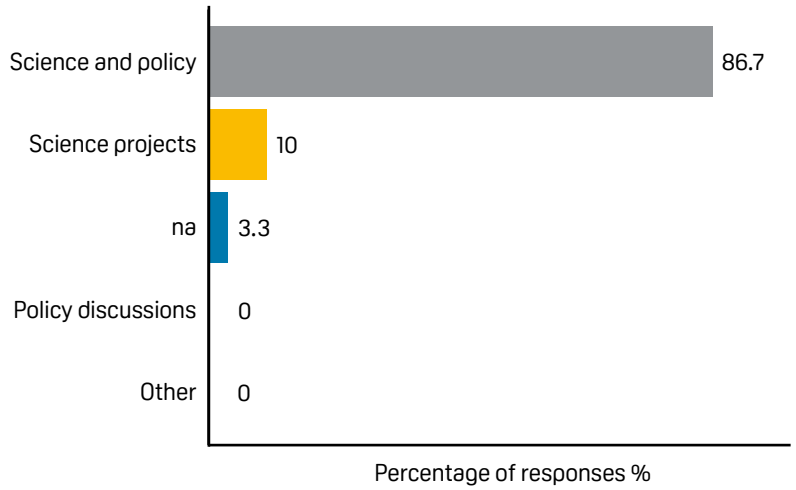


Figure 13: Have you identified potential co-worker or partners to collaborate with?

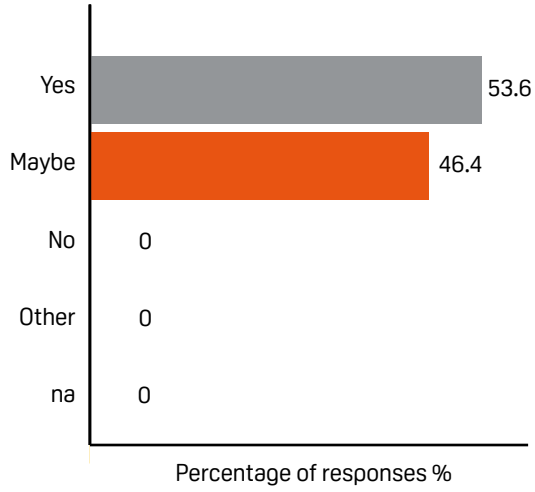


Figure 14: Would you endorse in-principle agreement on science, cooperation and risk management

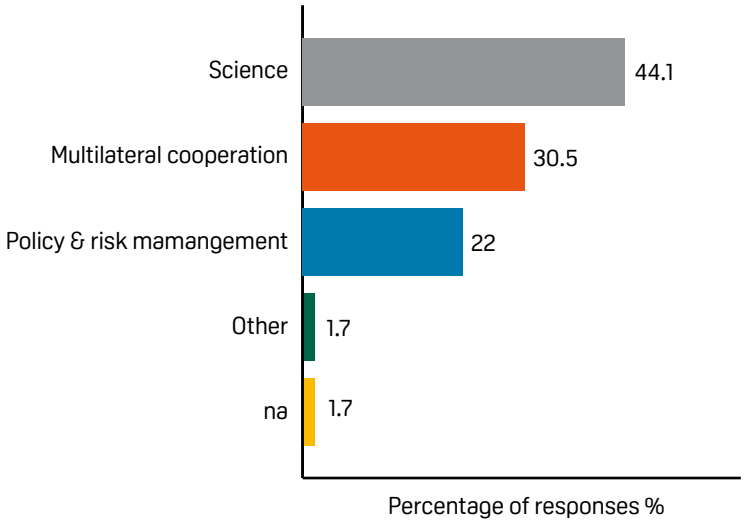
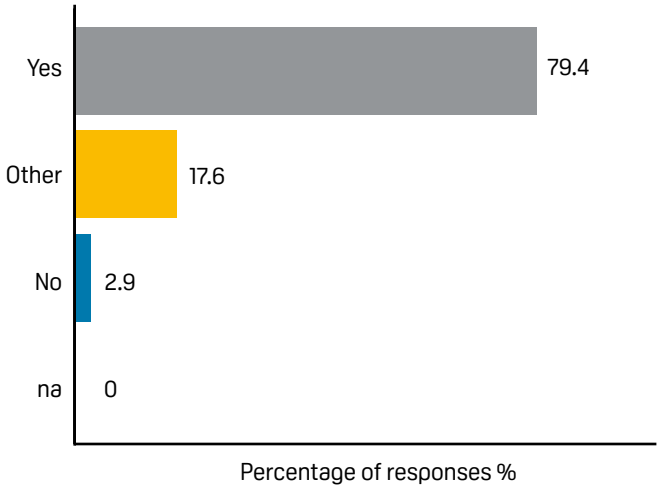


Figure 15: Would you support and participate in future discussions or exchange of views on HEV in a similar format?



SESSION 5: PRIORITISATION OF POLICY INTERVENTIONS

Delegates were asked to consider the following for each of the identified priorities:

- What **actions** are required to implement this measure?
- What **resources** are required to achieve this?
- **Who needs to be involved**? (consider national, regional and international levels)

Discussions on how to address the identified issues

Based on the number of options along the food chain, an elicitation exercise was carried out and participants voted on the options interactively and discussed the priorities identified in order to shortlist one measure per theme (on farm, processing, consumer exposure). The discussion focused on the 3 shortlisted measures with the aim to elaborate on what actions and resources are required to implement the measure and who needs to get involved.

The three shortlisted measures were:

1. Monitoring and surveillance (to determine the epi-zoology of HEV in infected herds, understand herd status, effect of immunisation or increase in susceptibility and adjust time/logistics of slaughter if possible, to achieve and maintain freedom).
2. Risk profiling of products (to better inform the use and exclusion of virus-containing tissues for appropriate products and thermal treatment.
3. Targeted advice (to inform more precisely the groups at risk according to the national/local situation).

1.1.1. A summary of the discussion on shortlisted measures.

The measures were described and discussed, along with the actions and expected resources before further discussion on practical considerations.

I. Monitoring and surveillance on farm

Measure: developing and establishing methods to undertake surveillance according to the set Monitoring and surveillance objectives (e.g. to estimate prevalence)

- Where are we looking for it (type of sample)?
- Which stage of production?
- How management practices may be affecting reproductive capacity of the virus, timing of infection and prevalence of viraemia and antibody?

Actions:

1. Experts to discuss protocols, e.g. number of animals, age, stage, etc.
2. Funding.
3. Pilot to check if standardised protocol works in all countries and redefine if needed.

Resources

We agreed that resources need to be secured for funding studies addressing the gaps identified and for experts, regulators, veterinarians and farmers, working in partnership with the food production line (processors and retailers).

Practical considerations (discussion)

The participants indicated inter-dependences between different options and the importance of cost efficiency in the model for intervention.

Exchanging knowledge, expertise and experience will facilitate more accurate analyses (e.g. translating apparent vs. estimated prevalence), design of harmonised sampling protocols and the use of standardised detection methods (to allow comparison and inferences across a wider population). Involvement of a range of stakeholders (e.g. scientists, managers, farmers, retailers etc.) would facilitate implementation of measures. The importance of communication at a local level was highlighted.

Data from epidemiological studies in humans (e.g. repeated cross sectional) can be combined with animal movement and food production data in national risk analyses. It was noted that monitoring and surveillance itself has no effect on prevalence although it is a pre-requisite and information source for management decisions.

Sampling can be aligned with other ongoing programmes to achieve better cost efficiency. A well-designed Europe-wide baseline study of HEV in pigs at production stage may help in better understanding of the situation, particularly in non-studied places. Further commitments from interested countries will be needed if aim to investigate the distribution of HEV in pork in different countries. National plans supported by a wide range of stakeholders can also support progress.

The variation in the prevalence, genetic diversity and applied practices on farm or at the processing level should inform local/national adjustments. We could also consider consumption data available at EFSA in addition to country specific data.

Participants called for in principle agreement on progress in the theme, sharing contacts as well as collaboration on future projects.

II. Risk profiling of food products

Measure: to identify which pork products present a high risk to health

Actions:

1. Research to identify viral load in different pig parts.
2. Establish which processed products are to be cooked by consumers or are non-thermally treated ready-to-eat foods.
3. Infectivity needs to be determined for processed products.
4. Determine infectious dose.

Resources

There is an expectation that coverage of all action points will involve a substantial amount of money and may need investment and partnership between slaughterhouses, manufacturers, retailers, laboratories and competent authorities.

A case study can be developed as an international exercise analysing trade of pig parts. On the other hand, analyses at national or regional areas may be more efficient to clarify processed products that are consumed in specific areas or phylogenetic mapping in both humans and pigs in given countries would be instructive.

Practical considerations (discussion)

Risk profiling activities could be steered centrally by a scientific advisory board/Group or through the national Competent Authority (CA).

Further research is needed, particularly in the development of accurate detection methods for infectious virus (viability assay to be used in various food matrixes). More information on non-thermal inactivation of the virus (e.g. by salts, pH) may be useful and practical.

Analyses on potential risk and efficiency of the measures should inform the production/processing stage (e.g. informing HACCP). Education of people on appropriate hygiene and cooking practices will benefit people also in the prevention of risks from other microbiological hazards such as pathogenic bacteria.

Details real-time analysis of food and diet in blood donors comparing and contrasting the infected donor versus the uninfected donor would provide immensely valuable data. For example, why are 17 to 24-year-old donors more likely to be viraemic than older donors, what is the dietary reasoning behind this?

Options for funding research can be explored in cooperation between stakeholders, public authorities and researchers.

Risk profiling and channelling production may offer practical solutions, particularly if supported by assessment of 'mitigating options'.

Carrying out research on specific areas (e.g. development of infectivity models) between different countries is an area that can be supported as scientific cooperation by public bodies such as EFSA.

CAs can advise on the situation, consider implementing measures and introduce regulatory activities if and where necessary.

III. Targeted advice to high risk groups

Measure: offering well-defined advice to high-risk groups according to the national/local situation

Actions:

1. Define high risk: those who are most likely to have serious consequences form infection.
2. Educate the medical professions to advise patients and carers of risks.
3. Issue general hygiene advice such as 'do not eat raw pork', 'cook thoroughly', 'wash vegetables'.
4. Advise hunters who may be at risk as well as farmers, vets, and slaughterhouse workers.

Resources

The participants identified the importance of bringing together medical professionals, planning funds for training, designing topic leaflets, and organising discussion groups and meetings.

Practical considerations (discussion)

There is potential for more targeted advice to various groups (e.g. those at risk because of immunosuppression, age, and occupational exposure). Raising the awareness of physicians may be needed but veterinarians may also act as advisers on prevention of occupational exposure in discussions with farmers. Blood donor studies can be undertaken to determine whether occupational exposure is a significant risk for clinical disease, compared to being immunosuppressed, or being in one of the high risk groups.

Targeted surveillance of chronic persistence and follow up of patients may offer an extra degree of understanding during the course of the infection/disease and associated risk factors.

Coordination at national level by appropriate responsible officers is important, and CAs and stakeholders can discuss and prepare communication on various scenarios. As responsibilities related to occupational health, guidance, awareness of medicals, food hygiene and consumption habits are distributed between different CAs within a given country, coordination at a national level is essential. The involvement of CAs and relevant stakeholders in discussions to prepare communication on various scenarios would be required.

Generic hygiene measures, including appropriate cooking methods are valid and expected to be quite effective. However, some information/ training or a targeted campaign may be needed for specific groups such as hunters who may eat undercooked liver. Identification of risk groups at national level is important as exposure may be based on dietary preferences which limit /favour some choices.

Some participants considered this measure redundant as it is currently known which groups are at risk of infection. Instead it was considered that we would need to identify who may be persistently infected as this may go undiagnosed but still have a high cost, for example, losing a transplant. The option of vaccination was also discussed but was thought to be a non-viable option for immunosuppressed individuals.

SESSION 6: OVERARCHING DISCUSSION

Final remarks and views

ECDC and EFSA provided a summary of the two-day discussions by reiterating that knowledge gaps were identified and that there was a wide interest in sharing information, harmonising methods and procedures and collaborating using a 'one-health' approach. Understanding the molecular basis and attribution of the virus, as well as targeted advice as a cost-effective measure were mentioned.

An industry representative (Vion) considered cooperation and communication critical and cautioned against a public scare.

There is often a lack of information and it is characteristic that an increase in notified cases has been seen across Europe. An underestimation of infected cases is likely as the infection is frequently asymptomatic both in acute infection and in chronicity. The development of an EU-wide case definition was considered critical. ECDC is currently working with country experts on the development of optimum guidelines for national surveillance and case definition.

Some countries indicated that this workshop motivated them to undertake activities and further discussion at national level.

The UK thanked everyone for their participation in the discussions about the wider policy perspectives and interventions. It also welcomed ideas for further collaboration on research and international support.

Participants were positive about the prospect of holding similar workshops in the future but they thought that the format may need to change in order to become more specialised and will only be meaningful when funding is granted and research has commenced.

Future perspectives – next steps (recommendations by the participants)

All countries agreed in-principle to support wider policy intervention and scientific cooperation in the theme.

Participants called for professional co-operation on understanding wider perspectives (food, environment and wildlife), efficacy of biosecurity measures, the epidemiological situation, and diversity in applied practices in animal production.

All representatives called for funding for research followed by further workshops and a professional network for the exchange of ideas and practices, including on policy interventions and research cooperation.

CONCLUSIONS

Most participants agreed that HEV is considered to be of medium risk and acute viral hepatitis in humans is notifiable in their respective countries, including HepE. However, notification is not harmonized, thus HEV can also be regarded as an emerging concern, particularly due to the limited information on the infection and disease burden in the general population, in the immunosuppressed population and also regarding the sources of infections. Research on these issues is at a relatively early stage in many countries. Surveillance of HEV infection in humans, animals or pork products is in place in some participating countries, however, mitigation measures are rare and not harmonised.

Policy interventions were discussed at three distinct stages of the food chain, namely, on farm, food processing and consumer exposure. After prioritisation, participants ranked the following three activities as the most critical for tackling health risks associated with foodborne HEV infections in Europe:

- Monitoring and surveillance on farm.
- Risk profiling of food products.
- Issuing targeted consumer advice to high risk groups.

Practical considerations for the implementation of interventions were discussed and it was evident that further enhanced research activities would be essential in achieving the policy objectives. The lack of information on prevalence, viability, infectivity and dynamics of the virus in pig herds was thought to be one of the main obstacles in managing the risk. Both researchers and policy makers agreed that close collaboration is necessary. In some cases, participants identified potential collaborators with whom to form future partnerships and agreed to continue the discussion outside the workshop.

There are methods for sampling and detection of HEV, which can be used to certify the status of animal populations/farms. Serological and molecular methods can complement each other. Standardization of the detection methods should be attempted in order to enable better comparison of the retrieved data.

Some results indicate a sustained free from infection status (e.g. in breeders) which is promising for achieving a HEV free status across the sector. The importance of knowledge sharing, robust biosecurity practices and targeted advice, which can maintain the HEV-free status of animals or prevent transmissions was widely recognised.

Monitoring and surveillance activities themselves have no effect on prevalence in any population but are pre-requisites and information sources for management decisions. A Europe-wide analysis seemed warranted to identify the transfer of HEV along a free market. Further commitments from the EU to support the investigation of the biology of HEV in animals and humans, including support for thematic research was identified as a priority. National plans supported by a wide range of stakeholders can facilitate progress as well.

Risk profiling including identification of high risk pork products and directing those for safer production may offer short term practical solutions, particularly if supported by an assessment of 'mitigating options'.

There are two components to this mitigation, working on the assumption that the root cause of viraemic pigs at slaughter will continue for some time. Decreasing the exposure of the population to dietary-acquired infection by adopting appropriate cooking is a step which is anticipated to be quite effective. However, in targeting the advice is important as the exposure may be based on dietary preferences or social status which may impact on some choices. Direct transmission from animal husbandry to humans is likely to be rare.

Another issue is protection of those at risk of severe HEV disease in the "risk" population of the immunosuppressed person. Attention to culinary care to ensure adequate cooking of potentially infective dietary components is doubly important. However, development of policies to identify those who have been infected, whether by diet or medical treatment, and to bring them into treatment is nationally important. Surveillance of chronic infections and follow up of infected patients may offer an additional level of understanding on the course of the infection/disease and associated risk factors.

Communication and mutual understanding on research results, risk assessment or monitoring and surveillance data at national level is important. CAs and stakeholders can discuss further activities and prepare mutually understandable communication related to the findings.

While further research is needed, such as optimising detection methods in food matrices and understanding the transmission chains on farms and in the pork production sector across Europe, it seems feasible to design measures to reduce the HEV burden in the food chain and control HEV on farms.

While studies at a national level are valuable and should be encouraged, HEV is a pan-European problem, where cooperation between different countries should be supported by supranational organisations such as the EU, EFSA, ECDC, or even the FAO. This activity will be of added value in bringing expertise together.

LIST OF ATTENDEES

Attendees	*Organisation*	Country
Anna Rita Ciccaglione	Istituto Superiore di Sanità	Italy
Ilaria Di Bartolo	Istituto Superiore di Sanità	Italy
Audrey Giraudo	INAPORC – Leporc.com, Interprofession nationale porcine – France	France
Ingeborg Boxman	Netherlands Food and Consumer Product Safety Authority – NVWA	Netherlands
Friedrich Schmoll	AGES – Austrian Agency for Health and Food Safety Ltd	Austria
Vratislav Nemecek	National Institute of Public Health (Czech Republic)	Czech Republic
Apostolos Vantarakis	University of Patras (Greece)/ Department of Public Health	Greece
Martin Schrott	Swiss Federal Food Safety and Veterinary Office	Switzerland
Tiiu Saar	Estonian University of Life Science	Estonia
Martijn Bouwknegt	Vion Food	Netherlands
Petra Vasickova	Veterinary Research Institute (Czech Republic)	Czech Republic
Sigita Taurina	Ministry of Agriculture of the Republic of Latvia	Latvia
Zsuzsanna Sréterné Lancz	NEBIH (National Food Chain Safety Office of Hungary)	Hungary
Jana Kerlik	RUVZ – Regionalny urad verejneho zdravotnictva (Slovakia)	Slovakia
Pirkko Tuominen	Finnish Food Safety Authority – Evira	Finland
Tuija Gadd	Finnish Food Safety Authority – Evira	Finland
Yanko Ivanov	National Centre of Food Safety (Bulgaria)	Bulgaria
Anne Thebault	ANSES-French Agency for Food, Environmental and Occupational Health & Safety	France
Zanete Steingolde	Institute of Food Safety, Animal Health and Environment "BIOR" – Latvia	Latvia
Gemma López Orozco	Ministry of Agriculture, Fishing, Food and Environment – Spain	Spain
Ana Canals	Ministry of Health, Social Services and Equality – Spain	Spain
Hristo Daskalov	Head of National Centre of Food Safety – Bulgaria	Bulgaria
Lorena Jemersic	Croatian Veterinary Institute	Croatia

Attendees	*Organisation*	Country
Magnus Simonsson	National Food Agency – Sweden	Sweden
Jakob Ottoson	National Food Agency – Sweden	Sweden
Suzie Coughlan	University College Dublin – National Virus Reference Laboratory	Republic of Ireland
Lisa O'Connor	Food Safety Authority of Ireland	Republic of Ireland
Steff Bronzwaer	European Food Safety Authority	EU
Cornelia Adlhoch	European Centre for Disease Prevention and Control (ECDC)	EU
Elli Amanatidou	Food Standards Agency	UK
Dirk Dobbelaere	Secretary general-CLITRAVI (Liaison Centre for the Meat Processing Industry in the EU)	EU
Alex Mauroy	Staff direction for risk assessment of the Belgian Food Safety Agency	Belgium
Ria Nouwen	"Contract Research" of the Federal Public Service for Health – Belgium	Belgium
Richard Tedder	Public Health England	UK
Martin Eiden	"Laborleiter – Institut für neue und neuartige Tierseuchenerreger (Friedrich-Loeffler-Institut)"	Germany
Professor Artur Rzeżutka	National Veterinary Research Institue in Pulawy	Poland
Professor Adam Fronczak	Head of the Department of Public Health, Warsaw Medical University	Poland
Wim H. M. van der Poel DVM, PhD	"European Joint Programme-One Health"	EU
Richard van der Kruijk	Vereniging voor de Nederlandse Vleeswarenindustrie/ Dutch Meat Products Association	Netherlands
Marjolein Baart	Dutch Safety Board	Netherlands

PRESENTERS

Attendees	*Organisation*	Country	*Role*
Anusha Panjwani	*Food Standards Agency*	UK	***Organiser***
Milen Georgiev	*Food Standards Agency*	UK	***Organiser***
Saskia Rutjes	*National Institute for Public Health and Environment-Netherlands*	Netherlands	***Speaker***
Reimar Johne	*German Federal Institute for Risk Assessment*	Germany	***Speaker***
Nicole Pavio	*French Agency for Food, Environment and Occupational Health and Safety*	France	***Speaker***
Michael Wight	*Food Standards Agency*	UK	***Speaker***
Falko Steinbach	*Animal and Plant Health Agency*	UK	***Speaker***
Christianne Bruschke	*Chief Veterinary Officer-Netherlands*	Netherlands	***Speaker***
Elta Smith	*RAND corporation*	Europe	***Facilitator***

QUESTIONNAIRE

HEV WORKSHOP QUESTIONNAIRE-AMSTERDAM 26/27 MARCH 2018

GENERIC SECTION

1. Please provide your details

Name:

Organization:

Country:

2. Is HEV infection notifiable in your country?

Yes/No:

Please provide details:

3. In your country is there a surveillance system in place to estimate incidence or measure frequency of HEV infection/disease in humans?

Yes/No:

Please provide details:

Please add information on precise estimations on disease burden or data from specific surveys:

4. In your country are there any ongoing screenings or surveys on the detection of HEV RNA in human blood products?

Yes/No:

Please provide details:

5. In your country are there any typing data available on circulating HEV strains (e.g. from human, pigs or other)?

Yes/No:

Please provide details:

6. In your country is there any indication (e.g. survey, scanning, monitoring and surveillance or research) of HEV RNA presence in pork products or in pig farms and wildlife?

a) Indication of HEV RNA presence in pork products (e.g. sausage, salami, liver sausage etc.)

Yes/No:

Please provide details:

b) Indication of HEV incidence in pig farms and wildlife (e.g. wild boar, deer, etc.)

Yes/No:

Please provide details:

POLICY CONSIDERATIONS

7. Are you aware of specific measures to address or mitigate risks associated with HEV?

a) Measures to address/mitigate risks associated with HEV **for employees in food and food related industries?**

Yes/No:

Please provide details:

b) Measures to address/mitigate risks associated with HEV **in pig and pig products?**

Yes/No:

Please provide details:

c) Measures to address/mitigate risks associated with HEV **in others?**

Yes/No:

Please provide details:

d) Are any recent or planned screening or surveys on the detection of HEV RNA in human blood products?

Yes/No:

Please provide details:

8. Please indicate if you have Guidance or Advisory documents specific to HEV in your country.

a) Please indicate if you have Guidance or Advisory documents specific to HEV in your country **for the general public**

Yes/No:

If yes, please provide details:

b) Please indicate if you have Guidance or Advisory documents specific to HEV in your country **for risk groups.**

Yes/No:

If yes, please provide details:

c) Please indicate if you have Guidance or Advisory documents specific to HEV in your country **for hunters.**

Yes/No:

If yes, please provide details:

d) Please indicate any additional advice or guidance not covered above:

e) Please indicate, if applicable, the risk components and characteristics identified in your risk analyses:

f) Please provide details of the most effective points in your Guidance (you can divide interventions at farm level, production process (including meat industry, shellfish, fruits and vegetables production processes) and human exposure (e.g. dietary advice, vaccination, etc.):

9. Is HEV seen as a serious public health risk? You can use the relative scale from 1 (negligible) to 5 (very serious) or feel free to comment in the text box.

Relative scale of 1 to 5:

Comment:

RESEARCH AREAS

10. Based on your understanding of the research area (including FSA-EFSA workshop 2016 and EFSA opinion 2017, references included below) please indicate your planned activities.

References:
FSA-EFSA workshop 2016 (www.food.gov.uk/news-updates/news/2016/15612/key-priorities-established-for-research-on-foodborne-viruses).

EFSA opinion (onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4886/epdf) page 68.

a) Ongoing (or recently completed) research areas and activities

Yes/No:

Please provide details:

b) Future plans for research and activities

Yes/No:

Please provide details of key areas of the above:

ACRONYMS AND ABBREVIATIONS

ANSES	Agency for Food, Environmental and Occupational Health & Safety (France)
APHA	Animal and Plant Health Agency
BfR	The German Federal Institute for Risk Assessment
CA	Competent authorities
ECDC	European Centre for Disease Prevention and Control
EU	European Union
EFSA	European Food Safety Authority
FSA	Food Standards Agency
HACCP	Hazard Analysis and Critical Control Point
HEV	Hepatitis E Virus
HPP	High Pressure Processing
PCVAD	Porcine circovirus associated disease
PRRSV	Porcine Reproductive and Respiratory Syndrome Virus
RARA	Risk Assessment Research Assembly
RIVM	Netherlands National Institute for Public Health and the Environment
RNA	Ribonucleic Acid
WHO	World Health Organization
UCL	University College London