Network on Microbiological Risk Assessment Minutes of the 16th meeting

Held on 4/5 April 2017, Parma

(Agreed on 29 May 2017)

Participants

- **Network Representatives of Member States (including EFTA Countries):**

Country	Name
Austria	Monika Matt
Belgium	Lieven De Zutter
Bulgaria	Hristo Najdenski
Croatia	Brigita Hengl
Cyprus	Georgios Papageorgiou
Czech Republic	Barbora Macková
Denmark	Maarten Nauta
Estonia	Mati Roasto
Finland	Jukka Ranta
France	Pauline Kooh
Germany	Anja Buschulte
Greece	Vassilis Xanthopoulos
Hungary	Adrienn Berkics
Ireland	Lisa O'Connor
Italy	Dario De Medici
Lithuania	Indre Stoskuviene
Netherlands	Aarieke de Jong
Poland	Elzbieta Mackiw
Portugal	Luisa Peixe
Romania	Isabela Nicorescu
Slovakia	Lubomir Valík
Slovenia	Pavel Pollak
Spain	Elena Carrasco Jimenez
Sweden	Jakob Ottoson
United Kingdom	Joanne Edge
Norway	Danica Grahek-Ogden
Switzerland	Francoise Fridez

- **Hearing Experts**
  - Marie-Benedicte Peyrat (agenda item 4.6)
- **EFSA:**
  - BIOCONTAM Unit: Pierre-Alexandre Beloeil, Teresa Da Silva Felicio, Beatriz Guerra, Michaela Hempen (secretariat), Ernesto Liebana Criado (chair), Winy Messens, Valentina Rizzi, Pietro Stella.

1. Welcome and apologies for absence

The Chair welcomed the participants and invited them to introduce themselves.

Apologies were received from Mati Roasto (Estonia), Vassilis Xanthopoulos (Greece) and Luisa Peixe (Portugal).

2. Adoption of agenda

The agenda was adopted without changes.

3. Agreement of the minutes of the 15th meeting of the Network on Microbiological Risk Assessment held on 11/12 October 2016, Parma[1].

The minutes were agreed by written procedure and published on the EFSA website on 11 October 2016.

4. Topics for discussion

4.1. EMA and EFSA Joint Scientific Opinion, RONAFA

In January 2017, EFSA and EMA published their Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA).[2] The opinion reviewed possible reduction strategies, including measures that have been already implemented successfully in some Member States. The latter include national reduction targets, benchmarking of antimicrobial use, controls on prescribing and restrictions on use of specific critically important antimicrobials, together with improvements to animal husbandry and disease prevention and control measures. The opinion recommends that, to minimise antimicrobial use, a multifaceted integrated approach should be implemented, adapted to local circumstances. Recommended options include: development of national strategies; harmonised systems for monitoring antimicrobial use and AMR development; establishing national targets for antimicrobial use reduction; use of on-farm health plans; increasing the responsibility of veterinarians for antimicrobial prescribing; training, education and raising public awareness; increasing the availability of rapid and reliable diagnostics; improving husbandry and management procedures for disease prevention and control; rethinking livestock production systems to reduce inherent disease risk. Possible alternatives to antimicrobials include probiotics and prebiotics, competitive exclusion, bacteriophages, immunomodulators, organic acids and teat sealants. Animals suffering from bacterial infections should only be treated with antimicrobials based on veterinary diagnosis and prescription. Options should be

[1] https://www.efsa.europa.eu/en/events/event/161011

[2] https://www.efsa.europa.eu/en/efsajournal/pub/4666

reviewed to phase out most preventive use of antimicrobials and to reduce and refine metaphylaxis by applying recognised alternative measures.

4.2. Risk for the development of Antimicrobial Resistance (AMR) due to feeding of calves with milk containing residues of antibiotics

The BIOHAZ opinion on Risk for the development of Antimicrobial Resistance (AMR) due to feeding of calves with milk containing residues of antibiotics was published in January 2017.[3] EFSA was requested to: 1) assess the risk for the development of antimicrobial resistance (AMR) due to feeding on farm of calves with colostrum potentially containing residues of antibiotics; 2) assess the risk for the development of AMR due to feeding on farm of calves with milk of cows treated during lactation with an antibiotic and milked during the withdrawal period, and 3) propose possible options to mitigate the risk for the development of AMR derived from such practices. Treatment of dairy cows during the dry period and during lactation is common in the EU Member States. Penicillins, alone or in combination with aminoglycosides, and cephalosporins are most commonly used. Residue levels of antimicrobials decrease with the length of the dry period. When the interval from the start of the drying-off treatment until calving is as long as or longer than the minimum specified in the Summary of Product Characteristics of the antimicrobial, faecal shedding of antimicrobial-resistant bacteria will not increase when calves are fed colostrum from treated cows. Milk from cows receiving antimicrobial treatment during lactation contains substantial residues during the treatment and withdrawal period. Consumption of such milk will lead to increased faecal shedding of antimicrobial-resistant bacteria by calves. A range of possible options exist for restricting the feeding of such milk to calves, which could be targeting the highest priority critically important antimicrobials. β-Lactamases can reduce the concentration of β-lactams which are the most frequently used antimicrobials in milking cows. Options to mitigate the presence of resistant bacteria in raw milk or colostrum are mainly based on thermal inactivation.

4.3. Risk Assessment on Meticillin-Resistant *Staphylococcus aureus* (MRSA), with a focus on Livestock-associated MRSA, in the UK Food Chain

FSA published a risk assessment on livestock-associated *Staphylococcus aureus* (LA-MRSA) in February 2017.[4] Surveillance data has been collated on carriage and infection of LA-MRSA in humans and animals in the UK to assess the risk to UK consumers. Data on the presence of LA-MRSA in UK foodstuffs, such as raw meat and milk has also been collated.

There have been no reported foodborne outbreaks of LA-MRSA in humans in the UK or worldwide. The prevalence of MRSA in people in contact with livestock is higher than that of the general population.

The prevalence of LA-MRSA in animals in European countries appears to be higher compared to animals in the UK. Current data suggests that LA-MRSA CC398 is the most predominant lineage in animals in the UK and other European countries.

[3] https://www.efsa.europa.eu/it/efsajournal/pub/4665

[4] https://www.food.gov.uk/sites/default/files/mrsa_risk_assessment_feb17.pdf

The prevalence of LA-MRSA contaminated food is low in the UK, there are no reported cases of LA-MRSA being contracted through ingestion of contaminated meat or milk. Thorough heat treatment of raw meat is sufficient to destroy the presence of bacteria, including LA-MRSA.

In conclusion the risk to human health from the preparation, handling and/or consumption of LA-MRSA/MRSA contaminated foodstuffs in the UK is very low.

4.4. Risk profile - Foodborne antibiotic resistance in Sweden

The Swedish National Food Agency published a risk profile on foodborne antibiotic resistance.[5] This risk profile describes the state of knowledge about food as a dissemination route for antibiotic resistance in humans. The report includes seven types of hazards linked to resistance to particularly important clinical antibiotics: third/fourth-generation cephalosporins (ESBL/pAmpC-producing bacteria), carbapenems (carbapenamase-producing bacteria), penicillinase-stable penicillins (MRSA), fluoroquinolones, macrolides, glycopeptides (VRE) and polymyxins. The occurrence of ESBL/pAmpC-producing bacteria, fluoroquinolone-resistant bacteria and VRE in food, especially chicken, seems to have a limited impact on the prevalence of these resistant bacteria within the healthcare sector in Sweden. Resistance plasmids belonging to these bacteria can be transferred between bacteria isolated from foods and humans, but the extent is unclear. Intestinal bacteria may also constitute a reservoir of transferable macrolide resistance. However, the relatively low occurrence of macrolide-resistant pathogenic bacteria implies that the probability of exposure to these resistant bacteria via food is low. Emerging hazards such as intestinal bacteria producing carbapenemases or harbouring transferable resistance to colistin have been found in a few samples from various foods. There is no direct evidence today that these types of resistance are spread to humans via food, but there is a potential risk. MRSA bacteria, also occurring on meat, are not spread by faecal-oral exposure and there is currently insufficient evidence that consumption of meat contaminated with MRSA leads to higher incidence of MRSA in humans.

4.5. Implementation of the Swiss National Strategy against Antibiotic Resistance (StAR)

The Swiss National Strategy against Antibiotic Resistance (StAR)[6] was developed through close cooperation among the bodies involved: the Federal Office of Public Health (FOPH), the Federal Food Safety and Veterinary Office (FSVO), the Federal Office for Agriculture (FOAG), the Federal Office for the Environment (FOEN) and the Swiss Conference of Cantonal Ministers of Public Health (CMPH). The main objective is to ensure that antibiotics remain effective for human and animal use in the long term. Eight strategic objectives have been defined with these stakeholders in the light of the need for action. They all have the same validity for the areas affected (humans, animals, agriculture and the environment) and are directed towards achieving the primary objective. 35 measures have been grouped together in eight fields of activity to reflect the

[5] https://www.livsmedelsverket.se/globalassets/rapporter/2016/riskprofil-livsmedel-som-spridningsvag-for-antibiotikaresistens.pdf

[6] https://www.bundespublikationen.admin.ch/cshop_mimes_bbl/2C/2C59E545D7371EE5A7B100F51A6EBB0E.pdf

strategic objectives: monitoring, prevention, appropriate use of antibiotics, resistance control, research and development, cooperation, information and education, and general conditions.

4.6. Risk assessment of *Trichinella* in raw deli meats

The guest speaker from France, Marie-Bénédicte Peyrat, presented the Anses opinion on the contamination of raw delicatessen meat products with *Trichinella* spp.[7] The terms of reference were: updating of knowledge on *Trichinella* spp. in pigs and consumer risks, estimating the probability of detecting *Trichinella* in pork and evaluating the adequacy of the current surveillance system in relation to consumer health risks. The scope of the opinions was limited to free-range pig farms in Corsica.

The results of the dose-response relationship strengthen the conclusions of Teunis et al. (2012): cases of trichinellosis can be observed in humans at doses below 10 larvae per serving (corresponding to larval loads below 1 LPG).

The probability of detection associated with current screening conditions depends on the mass of the individual sample, the larval load, and the performance of the laboratory technique. Current practices in Corsica generally ensure that analyses are undertaken with a mass of at least four grams per pig. If all animals are tested with a mass of four grams, the probability of detection is 96.4% (for animals with a parasite load of 1 LPG). The probability of detection calculated with variable masses, in accordance with the current practices of the departmental laboratory, is 98%. With larval loads below 1 LPG, for example 0.1 or 0.5 larva per gram, the probability of detection is lower, at 37% and 85% respectively.

Anses recommends that pigs raised in Corsica should be slaughtered in approved facilities suited to *post-mortem* inspection, including screening for *Trichinella* larvae. Raw delicatessen meat products intended to be consumed cooked, such as figatelli, should be labelled appropriately.

4.7. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2015

The data on antimicrobial resistance in zoonotic and indicator bacteria in 2015, submitted by 28 EU Member States (MSs), were jointly analysed by EFSA and ECDC and published in February 2017.[8] Resistance in zoonotic *Salmonella* and *Campylobacter* from humans, animals and food, and resistance in indicator *Escherichia coli* as well as meticillin-resistant *Staphylococcus aureus* in animals and food were addressed. 'Microbiological' resistance was assessed using epidemiological cut-off (ECOFF) values; for some countries, qualitative data on human isolates were interpreted in a way which corresponds closely to the ECOFF-defined 'microbiological' resistance. In *Salmonella* from humans, high proportions of isolates were resistant to ampicillin, sulfonamides and tetracyclines, whereas resistance to third-generation cephalosporins was low. In *Salmonella* and *Escherichia coli* isolates from fattening pigs and calves under one year of age, resistance to ampicillin, tetracyclines and sulfonamides was frequently detected, whereas resistance to third-generation cephalosporins was

[7] https://www.anses.fr/fr/system/files/BIORISK2016SA0040.pdf

[8] https://www.efsa.europa.eu/it/efsajournal/pub/4694

uncommon. For the first time, presumptive extended-spectrum beta-lactamase (ESBL)-/AmpC-/carbapenemase-production in *Salmonella* and *Escherichia coli* was monitored in humans (*Salmonella*), meat (pork and beef), fattening pigs and calves. Varying occurrence/prevalence rates of ESBL-/AmpC-producers were observed between countries, and carbapenemase-producing *Escherichia coli* were detected in single samples of pig meat and from fattening pigs from two MSs. Resistance to colistin was observed at low levels in *Salmonella* and *Escherichia coli* from fattening pigs and calves under one year of age and meat thereof. In *Campylobacter* from humans, high to extremely high proportions of isolates were resistant to ciprofloxacin and tetracyclines, particularly in *C. coli*. In a few countries, a third to half of *C. coli* in humans were resistant also to erythromycin, leaving few options for treatment of severe *Campylobacter* infections. High resistance to ciprofloxacin and tetracyclines was observed in *C. coli* isolates from fattening pigs, whereas much lower levels were recorded for erythromycin. Co-resistance to critically important antimicrobials in both human and animal isolates was generally uncommon.

4.8. EFSA activities on Whole Genome Sequencing

EFSA is interested in using Whole Genome Sequencing (WGS) for: source attribution, outbreak detection and investigation, common source trace back investigations, detection and surveillance of emerging pathogens, and monitoring of antimicrobial resistance. In June 2014, EFSA organised a Scientific Colloquium on the use of WGS of food-borne pathogens for public health protection.[9] Activity 3 of a procurement on L. monocytogenes in Ready-to-Eat Foods focussed on the molecular characterisation employing WGS of strains from different compartments along the food chain and from humans (agenda item 4.10). EFSA has also launched a thematic grant on molecular approaches for identifying and characterising microbial foodborne pathogens, specifically using WGS analysis.[10],[11] The aim of these projects is to provide proofs of principle (genetic diversity, epidemiological relationships, putative markers conferring advantages), to establish transnational collaboration/scientist coordination (One Health Approach), develop new analysis tools and to translation of results into language that can be understood by a lay person. Further, there is a grant agreement between EFSA and DTU on Comparative genomics of quinolone-resistant *Campylobacter jejuni* of poultry origin from major poultry producing European countries (GENCAMP). WGS was used for case definition of an EFSA-ECDC rapid outbreak assessment on *S.* Enteritidis.[12,13] More activities are already planned under the "WGS Umbrella project".

4.9. Source attribution using MLST data

The representative from Finland presented a Nordic joint project (Denmark, Finland, Norway and Sweden; coordinated by DTU) on source attribution using Campylobacter MLST data. The project aim was to develop a typing-based

[9] https://www.efsa.europa.eu/de/supporting/pub/743e

[10] http://www.innuendoweb.org/

[11] http://www.engage-europe.eu/

[12] https://www.efsa.europa.eu/it/supporting/pub/1188e

[13] http://ecdc.europa.eu/en/publications/Publications/rapid-outbreak-assessment-Salmonella-Enteritidis-7-mar-2017.pdf

source attribution model which is applicable to a situation with sparse data and small sample size, and with modifiable code for further QRA needs.

4.10. Closing gaps for performing a risk assessment on *Listeria monocytogenes* in ready-to-eat (RTE) foods: activity 3, the comparison of isolates from different compartments along the food chain, and from humans using whole genome sequencing (WGS) analysis

EFSA carried out a number of activities on *Listeria monocytogenes* in ready-to-eat foods. This report results from an outsourcing project and was published as an external scientific report in February 2017.[14] The main objective of this tender was to compare *L. monocytogenes* isolates collected in the EU from ready-to-eat (RTE) foods, compartments along the food chain and from human listerioisis cases by the use of whole genome sequencing (WGS). A total of 1,143 *L. monocytogenes* isolates were selected for this study, including 333 human clinical isolates and 810 isolates from the food chain. The isolates were whole genome sequenced. The phylogeny showed a clear delineation between *L. monocytogenes* lineages and between clonal complexes within lineages. A range of typing methods were applied to the sequence data, providing the framework to answer questions on genetic diversity and epidemiological relationships. Retrospective analysis of nine outbreaks showed that WGS is a powerful tool in national and international outbreak investigations as WGS can accurately rule isolates in or out of outbreaks. Source attribution models showed bovine reservoir to be the main source of human disease although other sources also contributed and generally confidence intervals were high. Numerous consistent genetic linkages between *a priori* unlinked strains were identified, some of which involved isolates from multiple countries. The presence of putative markers conferring the potential to survive/multiply in the food chain and/or cause disease in humans was explored by detecting the presence of putative virulence genes, AMR genes and factors conferring the ability to persist in the food processing chain. This study has demonstrated one of the major benefits of WGS, which is the ability to address a wide range of questions including those on virulence, antimicrobial resistance, source attribution, surveillance and outbreak detection and investigation, in a single experiment.

4.11. Risk assessment related to *Listeria* and how the process is structured in an agency responsible for risk assessment as well as risk management and communication

The representative from the Swedish National food agency explains the process of an integrated approach to risk assessment, risk management and risk communication using the example of *Listeria monoctogenes* in ready-to-eat foods.

4.12. New and recent activities of the BIOHAZ Panel

The BIOHAZ secretariat informed the MRA network on the recently adopted mandate of the BIOHAZ Panel on Hazard analysis approaches for certain small retail establishments in view of the application of their food safety management

[14] https://www.efsa.europa.eu/en/supporting/pub/1151e

systems (EFSA-Q-2015-00819)[15] and the new mandates on: Request for scientific and technical assistance on proposed of EU minimum quality requirements for water reuse in agricultural irrigation and aquifer recharge[16] and Request for a joint ECDC, EFSA and EMA scientific opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals (EFSA-Q-2016-00638)[17].

5. Any Other Business

The presentations of the meeting are made available on DMS. Suggestions for 2018 meeting dates will be circulated via email.

6. Date for next meeting

The next meetings of the MRA network will be held on 10/11 October 2017 in Parma.

7. Closure of the meeting

The chair thanked the participants and closed the meeting.

[15] https://www.efsa.europa.eu/de/efsajournal/pub/4697

[16] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2016-00819

[17] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2016-00638