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SUMMARY REPORT

EFSA SCIENTIFIC COLLOQUIUM No. 12

Assessing health benefits of controlling *Campylobacter* in the food chain

4 – 5 December 2008, Rome, Italy

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I INTRODUCTION

The 12th meeting in the EFSA Scientific Colloquium Series on “Assessing the Health Benefits of Controlling *Campylobacter* in the Food Chain” was held in Rome 4-5th December 2008.

Enteric infections caused by *Campylobacter* are the most frequently reported zoonoses in humans in the EU with an incidence rate of approximately 50 confirmed cases per 100.000 population over 17 countries (EFSA, 2009).

The majority of cases of campylobacteriosis are self-limiting with 3-5 days of acute diarrhoea, abdominal pain and fever. However, disease in the very young and elderly can be serious and sequelae of infection, such as polyneuropathies, may result in the need for hospitalisation. Thus the public health and social consequences of campylobacteriosis are significant for the EU.

Some cases require antimicrobial treatment and the increasing incidence of antimicrobial resistance is seen as a potential public health issue.

Epidemiological studies worldwide indicate that campylobacteriosis is largely food-borne and that poultry meat is a major source. However, the proportion of illness due to poultry meat and the contribution of other potential sources remain unclear.

Campylobacter can colonise the intestinal tracts of birds at high levels and faecal contamination of poultry carcasses can occur during processing. One of the principle routes of human exposure is considered to be cross-contamination from poultry meat during food preparation in kitchens. Control of *Campylobacter* in poultry meat is a major public health strategy for the prevention of campylobacteriosis.

A substantial proportion of the broiler flocks in the EU is colonised with *Campylobacter* and this prevalence appears to vary between member states and according to seasons. An accurate comparison of prevalence has been difficult because of variations in sampling and testing methodologies. A harmonised and standardised baseline survey of the prevalence and antimicrobial resistance of *Campylobacter* broiler flocks and broiler carcasses in the EU was carried out during 2008 in compliance with the provisions laid down by the Commission Decision 2007/516/EC. This survey will provide information on the prevalence of *Campylobacter* in caecal samples and quantitative data on *Campylobacter* contamination on broiler carcasses at slaughter. These data are anticipated to be available by April 2010.

In 2008 the European Commission sent a request to EFSA for a scientific opinion to “Quantitatively update the 2005 Opinion related to *Campylobacter* in animals and foodstuffs as regards broiler meat production *Gallus gallus*” (EFSA, 2008a). EFSA assigned the mandate (EFSA-Q-2008-469) to the BIOHAZ Panel to deliver a risk assessment by 2010.

Specifically, the Panel was asked to:

- Assess the extent to which meat derived from broilers contributed to human campylobacteriosis at the EU level
- Identify and rank the possible control options within the broiler meat production chain
- Propose potential performance objectives and/or targets at different stages of the food chain to reduce the prevalence of human campylobacteriosis in the EU caused by broiler meat consumption or cross-contamination.

EFSA decided to organize this Scientific Colloquium and aimed to bring together international expertise, including risk assessors, stakeholders and risk managers, to:

- Discuss in an open scientific debate the current issues and future challenges concerning the risk assessment of *Campylobacter* in the food chain in the EU. Focus on best approaches for data collection and quantitative risk assessment within the EU, determine its impact on human health, fluoroquinolone resistance, and assess what are likely to be the most effective control measures.
- Identify what data are needed in order to assess the benefits of controlling *Campylobacter* (*e.g.* impact on human health, disease burden and costs).
- Discuss the risk to human health of fluoroquinolone resistant *Campylobacter* and its relation to antimicrobial usage in animal husbandry.
- Identify options to control the prevalence, concentration and distribution of *Campylobacter* infections and contamination throughout the food chain, and evaluate the current information on the effectiveness of these control options.

The Colloquium was attended by about 90 scientists and stakeholders, from 30 countries, including the USA and New Zealand, and including representatives from the EC (European Commission), ECDC (European Centre for Disease Prevention and Control), EMEA (the European Medicines Agency) and Member States. The meeting focused on four inter-relating topics. Each topic was introduced by a keynote speaker, in the opening plenary session, presenting the state of knowledge in that area. These presentations included:

- The source attribution and health impact of *Campylobacter* (speaker Prof. N. French, New Zealand),
- Quantitative risk assessment in broiler meat (speaker Dr. M. Nauta, The Netherlands),
- Resistance to fluoroquinolones (speaker Prof. A. Aarestrup, Denmark) and
- Effective control measures in broiler meat production from farm to fork (speaker Dr. H. Rosenquist, Denmark).

A briefing note had been circulated to all participants before the Colloquium addressing discussion points on these four topics. At the meeting participants divided into four discussion groups to deliver expert summaries, addressing the discussion points, and reporting back to the plenary in a final discussion session.

II REPORTS FROM DISCUSSION GROUPS

DG1: Health impact and attribution of *Campylobacter*

1. ***Assess the epidemiological evidence on human campylobacteriosis in the EU with a view to identifying the extent of the contribution of foodborne infection.***

The results of epidemiological investigations conducted both in sporadic cases of gastrointestinal illness and during outbreaks, indicate the important contribution of *Campylobacter* to the burden of bacterial zoonotic illness. In particular, in those countries where a comprehensive and extensive public health surveillance system is in place, *Campylobacter* is recognised as the leading cause of bacterial zoonotic gastrointestinal illness (EFSA, 2007; ECDC, 2008). Furthermore, in many countries, the incidence of reported cases has increased since the early 1990s.

The high level of incidence of campylobacteriosis in humans is also confirmed by population-based studies of gastrointestinal illness, for example in the UK and The Netherlands (Wheeler *et al*., 1999; De Wit *et al*., 2001). More recently, sero-surveillance studies have confirmed the high exposure rate to *Campylobacter* by humans (Ang *et al*. 2007).

Although human campylobacteriosis has been mainly characterised by the occurrence of sporadic cases, a substantial number of foodborne outbreaks caused by *Campylobacter* in the last years is observed in the Community Zoonoses Report (EFSA, 2007).

2. ***Consider the applicability of different approaches to source attribution for human campylobacteriosis in the EU (as described in the BIOHAZ opinion "Overview of methods for source attribution for human illness from food borne microbiological hazard").***

Different approaches exist for source attribution (EFSA, 2008b) including:

(a) Microbial sub-typing The *Campylobacter* population is highly variable and there are many sub-typing methods described. The selection of strains may bias the data available for source attribution due to the selectivity of bacterial culture techniques and sampling procedures in food animals, food, the environment and patients. Nonetheless, some typing methods [(*e.g*., multilocus sequence typing (MLST)], when applied to carefully selected but comprehensive strain collections, coupled with modelling techniques, have recently shown promising results for *Campylobacter* source attribution (Dingle *et al*. 2008; Wilson *et al*. 2008). Further activities are needed to refine and combine different typing methods (*e.g*. MLST with PFGE and antimicrobial resistance patterns) to identify the most proper "markers" for source attribution purposes, and to refine and evaluate statistical models able to properly assess the contribution of different sources. In particular, the general applicability of this approach needs to be evaluated. Attention should be given to the interpretation of *Campylobacter* strains isolated from the environment (*e.g*. water pools, lakes, rivers, soil, *etc*.), but probably originating from animal reservoirs. A distinction, in fact, should be made between vehicles of infection, like for example recreational waters, and the animal reservoirs as primary (host) sources, which amplify the bacterial population.

(b) Outbreak investigations. The outcomes of investigations of *Campylobacter*-outbreaks can give useful information on vehicles and pathways. However, they cannot be directly used for source attribution studies, because the distribution of sources and vehicles for sporadic and outbreak cases are unlikely to be the same (Olson *et al*., 2008). The results of these investigations may give valuable information to better interpret the results of attribution studies and provide essential information on the contribution of risk factors, such as cross-contamination pathways. Often outbreak investigations are hampered by the difficulties in obtaining microbiological evidence or evidence from an analytical epidemiologic study of the responsible vehicle(s).

(c) Epidemiological studies. In many situations case-control studies of sporadic cases have provided useful information (Whittemore, 1983; Coughlin *et al*., 1994; Stafford *et al*., 2007). However, they have serious limitations. In addition to well known biases such as recall bias and selection bias, a high degree of exposure and illness may also limit their applicability to address very common exposures, such as handling or eating poultry, as potential risk factors. Furthermore, the interpretation of results of several studies has been a challenge (*e.g*. interpreting exposure variables as “protective” factors when an odds ratio below 1 is obtained). In some cases the use of spatial analysis methodologies for exploring associate risk factors (*e.g*. age distribution of human cases) may be of benefit (FDI/236/2005). In general the combination of epidemiological studies with microbial sub-typing and modelling techniques is recommended.

(d) Comparative exposure assessment. This approach addresses pathways taking into account the level of contamination in potential sources (Evers *et al*., 2008). It has not been applied broadly to *Campylobacter*. It has serious limitations in predicting the contribution of each source to the burden of human campylobacteriosis due to the uncertainty of the events in the different possible pathways (*e.g*., cross-contamination in the kitchen) and the dose-response relationship. At present it can be used primarily to stimulate the generation of hypotheses.

(e) Expert opinions. Risk managers often base decisions on expert opinions. It can be particularly useful when a rapid opinion or assessment is needed for risk management purposes or when data for other source attribution methods is lacking. However, the opinions should be based on evidence and be updated as knowledge evolves (Havelaar *et al*., 2008). Since one of the main limitations of using expert opinions is the difficulty in merging different opinions, specific techniques to “*weight*” the expert opinions exist but have not yet been applied to source attribution.

(f) Intervention assessment. The assessment of management interventions should ideally be carried out in the framework of controlled studies. However, when applied to national control measures, the main problem is related to the fact that interventions are often not planned in a way that enables a systematic assessment of the effects, for example with relevant process measurements or more importantly the measurement of public health outcomes. However, even with “unplanned” interventions (and “natural experiments”), it is important to carefully analyse the effects. Intervention studies should ideally be carried out in pilot areas and with proper controls before the extension to a broader scale (*e.g*., at the national level). If this is feasible, it will permit to properly assess the impact of possible mitigation actions on a small scale, before their more general application.

3. ***Consider data availability and propose additional data collection (special studies, surveillance) in humans and in the food chain needed for source attribution, taking into account differences between Member States.***

The strengthening of public health surveillance systems (case-based reporting of human data, travel history, storage of randomly collected samples) should represent the first option for increasing the quantity and the quality of information available. In addition, it is fundamental to strengthen the surveillance and sampling designs to generate comparable data on human disease and food contamination, particularly at the retail level (EFSA, 2008c), for their use in exposure assessment studies. Such studies may not necessarily be implemented in the whole EU, but “sentinel” representative sites may be selected around Europe. It would be important to develop a joint protocol for such in-depth studies with a combination of strain collection at various sources, information on exposures, and collection of clinical isolates at the same geographical sites.

In relation to data available at the food chain level, the main source of data on prevalence of contamination in chickens is represented by the 2008 EU baseline study (EC, 2007). Prevalence data reported in the Community Zoonoses Report may represent useful background information, but their use in source attribution studies is limited. These data, in fact, derive mainly from (multi)annual plans performed in the EU Member States and, often, the availability of quantitative data is scarce. In addition, the comparability of values among Member States is difficult to ascertain.

Isolates from foods and animals are available from some laboratories and they can be the source of important additional information. However, the methods and criteria of sample collection and related information are not always known or recorded in a standard fashion.

Food production and sales data, as well as data on import-export and intra-community trade are also available. Nevertheless, the degree of accessibility of these data, and the completeness of information, especially regarding products having a local market, should be explored. EFSA has initiated some activities to gather data on food consumption at the EU level (EFSA, 2008d; EFSA, 2008e).

Regarding the availability of data at the human level, information on reported cases is available in most EU Member States, but often as aggregated data. Data generated by case-control studies and outbreak investigation are only available in some Member States. *Campylobacter* isolates from humans are also available, but a systematic collection of samples is in place in only a few countries.

In relation to promoting additional actions to collect further data, the first priority should be to improve the accessibility to the existing data sources, (isolates and samples taken during *e.g.* case-control studies). An overview of the studies and data suited for source attribution might be of benefit.

Finally, a consensus should be reached in the EU on the methods for *Campylobacter* sub-typing and for the registration of these data in a global typing database.

4. ***Identify possible approaches for establishing the degree of under-reporting of human cases and discuss their applicability at national and EU level.***

First of all, a difference between under-reporting and under-ascertainment should be made. Under-reporting can be determined by a systematic inventory of reporting practices of existing diagnostic laboratories that examine stools samples for *Campylobacter* spp. Under-ascertainment is more difficult to determine. An estimation of the degree of under-ascertainment may be conducted at each level of the surveillance pyramid (% of persons with acute gastroenteritis referring to physicians, % of stool samples taken, % of false negative laboratory results, *etc*.).

Targeted retrospective or prospective studies (by questionnaires, phone interview, *etc*.) may be conducted, to estimate the burden of diarrhoeal illness and multiplication factors by which to multiply incidences as reported through the notification system and to obtain a more accurate estimate of the true disease incidence. More recent developments in communication technology (SMS, web, *etc*.) may offer further opportunities for accessing a larger population sample.

Sero-epidemiological studies may be of benefit, in particular because some of the methodological problems related to information bias affecting or influencing the above mentioned studies, may be overcome. Furthermore, sero-epidemiology is a cost-effective tool. The main critical point is the knowledge of the disease/infection rate and the nature of this relationship. In addition, host factors (immunity, medical history, genetic factors and interaction with heterologous strains) may be taken into consideration in the further refinement of this approach.

DG2: Quantitative risk assessment of *Campylobacter* in broiler meat in the EU

This discussion group considered the following 4 discussion points:

1. ***Consider the state-of-the-art of risk assessment of Campylobacter in the broiler meat chain. Discuss to what degree different models have come to the same conclusions or appear to be contradictory. Propose recommendations for further development of risk assessment models.***
2. ***Evaluate current available quantitative data on Campylobacter in the broiler meat chain as well as on the cross contamination between broiler meat and other foods. Identify critical data gaps to support risk assessment modelling and validation.***
3. ***Consider quantitative insights from current risk assessment models on the effectiveness of interventions (such as the importance of reducing numbers rather than prevalence, the degree of effectiveness of logistic slaughtering, etc.) and evaluate the availability of data to validate such models. Identify areas where model results are disputable or at odds with available data (e.g. the impact of partial depopulation) and ways forward to address these issues.***
4. ***Consider the applicability of current models to support decision making on control options at the European level. Assess in particular the effectiveness of interventions across the EU so as to support the setting of targets and/or performance objectives.***

In the last decade, several countries have developed risk assessment models for *Campylobacter* in the broiler meat chain. Overall, the models come to similar conclusions. The risk assessment approach has emphasized that both the prevalence and the concentration of bacteria are important to the risk to public health impact and in assessment of the effectiveness of interventions. However, the relative importance of these two factors will be dependant on the stage of the food chain under consideration. For example the relationship between risk and prevalence in the flocks are less direct than the relationship between prevalence of *Campylobacter* and risk later in the food chain (*e.g.* drumsticks at retail level), and may also be dependent on which processes have been considered (*e.g.* cross-contamination, drip fluids).

Consumer risks appear to be particularly associated with (relatively rare) exposures to high numbers of bacteria. Although it is a simplification, it might be said that high prevalence carcass contamination with low numbers of organisms would be preferred over low prevalence contamination with high numbers of organisms. However, the importance of high and low bacterial numbers is dependent on the shape of the dose-response model.

The risk assessment models indicate cross-contamination as an important factor in the transmission of *Campylobacter* from broiler meat. However, the module on consumer behaviour may require further revision. Incorporating expertise on social sciences on consumer behaviour should be used to fine-tune this important module and link contamination in the food chain to the public health outcome. In some of the models this module is limited by only considering cross-contamination and not undercooking. This will need to be adapted when considering emerging food items brought to the market, such as minced meat and meat preparations of broiler meat.

In addition, all the risk assessment models utilise the same dose-response model that is based upon a limited data set and fail to take into account the known variability of *Campylobacter* at strain level. Although this is not an easy task, further effort should be focussed on the development of better dose-response models *e.g.* based on acquiring more information from outbreak data or establishment of the dose response curves for various strain types (defined by MLST or other typing method) with variable epidemiological associations in human illness versus attributable sources. Other difficulties relate to inclusion of multiple exposure, *i.e.* immunity due to repeated challenge, in risk characterisation (Havelaar *et al.,* 2009).

Further developments are expected with regard to the methodology of risk assessment. Bayesian modelling, with the ability to update the model estimates and to include prior knowledge (to combine observation and expert opinion), might be used as an integrated approach with Monte Carlo simulation, in order to use all the information available. If data are available it is recommended to include variability on processing practices in the models. Although it is difficult especially if many assumptions are made, the risk assessment models should include uncertainty as an important feature in any communication to risk managers.

As the input or basis of *Campylobacter* risk assessments, models often refer to the same available quantitative data sets that were derived from one specific situation in one specific country. There is a need to know the variability in the broiler meat chain among Member States but also among food business operators (slaughter and further processing) within a country. In addition, awareness of consumer behaviour differences occur between and among Member States' populations. Cultural differences, for example, affect the consumption patterns of the main types of fresh broiler meat and meat preparation; knowledge that is needed to compare the risk derived from various types of broiler meat within Europe.

At present, more quantitative data is becoming available on the occurrence and dynamics of *Campylobacter* in the broiler meat chain as well as on cross-contamination between broiler meat and other foods. Nevertheless, data gaps are still identified, which relate to the quantitative effect of technological interventions, and the variability depending upon the exact conditions of implementation of such interventions. Of importance is the quality of the available data sets in order for them to be a sound basis for risk assessment. For example, (i) the need for appropriate detection methods enabling resuscitation of sub-lethally injured cells, in acquiring presence/absence data or enumeration data of *Campylobacter* in the food chain; especially if evaluating interventions that stress these bacteria, and (ii) acquiring data for transfer rates of *Campylobacter* from naturally-contaminated samples or acquiring data on consumer behaviour, using observational studies. The integration of new data in risk assessment models and the comparison of model predictions with field measurements has not yet been extensively done. There is a need for a set of "Good Practices" on how to treat the quantitative data, to take into account measurement uncertainty and to turn such data into distributions, especially with regard to handling data below the detection limit.

Current risk assessment models were predominantly developed within individual Member States to compare intervention measures or to identify critical data gaps by systematic analysis of the broiler meat chain. Occasionally it was also the purpose to link the contamination and control of *Campylobacter* in broiler meat to a public health outcome.

Risk assessment contributes added value to observational studies because it is multidisciplinary, brings together available data, integrates knowledge in a systematic manner and is prognostic in nature. Validation of these models establishes whether these models are fit for purpose. If the purpose is to put forward the most promising options for interventions, or identify lack of supporting data, the models succeed in providing quantitative insights on the effectiveness of interventions and/or the availability of data for science-based decision making. Nevertheless, the feasibility of a promising intervention measure will subsequently need further pilot studies in selected food business operators in the broiler meat supply chain, to establish cost/benefit, efficacy and variability of implementation in the field. Quantitative risk assessment by scenario analysis enables a targeted approach for data gathering and further testing of intervention measures in field trials. The use of (repeated) baseline surveys might be an indirect measure of implemented control measures but many (risk) factors interact in the supply chain. Underlying changes/new trends in production practices and consumer behaviour might intermingle and confuse the effect of such intervention measures.

If the purpose of the risk assessment is to estimate the risk to public health due to *Campylobacter* contamination in the broiler meat, validation might be particularly difficult as it is necessary to know the contribution of a particular food item (*i.e.* fresh broiler meat) to the burden of disease. Routine surveillance for campylobacteriosis might not be able to do this. Validation might only be feasible by setting up targeted epidemiological studies.

Because of increased awareness about the issue of *Campylobacter* in broiler meat and its effect on public health, the food industry needs guidelines or targets in, or at the end of, the production chain. It is important that these targets are well communicated, and are valid and acceptable for both EU and international food business operators in order to assure and improve public health of the European consumer.

Current risk assessment models concur that reducing the numbers of *Campylobacter* on broiler meat will effectively reduce campylobacteriosis. There are many target setting options. One target might be that "X% of birds (caecal samples) or Y% of fresh meat (broiler carcass or neck skin or broiler meat at the end of production line) cannot have more than Z cfu/g or cm^2 (defined by the method) at a certain stage of the food chain".

If the target is set in the supply chain at a stage close to the consumer, the link to public health outcome, as assessed by the models, will be less prone to variability and uncertainty. But from a point of view of the food business operator, it is less practical for targets close to the consumer as there is little room for corrective action, especially taking into account broiler meat being a raw and perishable food item. If the target is set closer to the beginning of the supply chain, the implementation of effective interventions and control measures might be more feasible but the confidence level in improved public health might be less because of the variability in processes further along the food chain. Nevertheless, this variability becomes less important for *Campylobacter* than most other bacterial foodborne pathogens as *Campylobacter* does not grow on food during storage and handling.

It should be noted that, even with the same target, outcomes on public health (human cases) will vary between countries depending on consumer behaviour and consumption patterns.

Models available today are constructed at the national level and do not necessarily cover the full "farm" to "fork" supply chain. It is debatable if some assumptions or data sets used within these models are valid at an EU level. Quantitative data throughout the broiler meat production chain, and throughout Europe, will help to fine-tune the models for risk assessment, provide more accurate estimates and contribute to establishing quantitative targets. Particular research attention is needed on i) the acquisition of microbiological data *i.e*. enumeration of *Campylobacter* with robust methods and ii) consumer behaviour *i.e*. in relation to food handling and consumption patterns. The next challenge will be to integrate variation throughout Europe and to develop a generic model to support decision-making on control options at the European level or, in particular to, assess the effectiveness of interventions across the EU. Such information will support the setting of targets and/or performance objectives.

The applicability of current models to support decision-making on control options at the European level is restricted, thus a pragmatic approach is recommended. The opportunity should be taken using the availability of the quantitative data from each Member State, from the 2008 EU-wide baseline survey on *Campylobacter* in broiler flocks and broiler carcasses, to initiate setting targets for *Campylobacter* in the broiler meat chain. The food industry must be able to achieve these targets by implementing appropriate Food Safety Management Systems. However, it is clear that such strategies, will not lead to zero risk of campylobacteriosis due to consumption of broiler meat.

DG3: Fluoroquinolone resistance (FQ) in *Campylobacter*

1. Consider the prevalence of FQ-resistance in poultry flocks, on carcasses and on poultry meat and its relationship to antimicrobial usage in animal production.

There are some country reports on the prevalences of FQ resistance in *Campylobacter* from poultry, poultry meat, humans (EFSA, 2007). In order to be able to relate the prevalence of FQ resistance to drug usage, monitoring of both resistance and drug use at the national levels is essential. Monitoring of drug usage will enable to follow trends, perform relevant risk assessments, suggest interventions, and monitor effects of interventions. Several countries have national drug use monitoring systems in place, while in many other countries drug use data are known, but not easily accessible. Furthermore, data collection systems differ considerably between countries (*e.g*. based upon prescriptions, sales at species level, or just total sale).

Scientific evidence shows that the use of FQ has led to the emergence of FQ resistance in *Campylobacter* in poultry flocks. However, the exact nature of the relationship, *i.e*. influence of high level or low level usage, is not known. Furthermore, it is unknown whether strategic use (*e.g*. only within the first week of life) would lead to less emergence of resistance. It is not known what the differences are between the different quinolones in their ability to select for resistance. There appears to be a correlation between resistance levels of bacteria in broilers, on carcasses and on meat. However, the latter is more difficult to determine because of the effect of cross-contamination and also because meat at retail comes from different sources (*e.g.* imported meat).

The effect of withdrawal of FQ is poorly understood. However, expert opinion indicates that major interventions (*e.g.* ban, stringent compliance) on drug usage are necessary to halt further increase in resistance, but it is unknown if resistance levels will decrease or disappear. The importance is emphasised in assessing the effects of any interventions, such as the ban of enrofloxacin in poultry production in the US. The missed opportunity in monitoring effects on antimicrobial resistance in relation with the recent ban on growth promoters was noted.

2. Evaluate the significance of FQ-resistant Campylobacter on broiler meat from a public health perspective. Consider the available evidence and risk assessment models to quantify the proportion of FQ-resistant human cases attributable to broiler meat.

The evidence for a significant or added risk on public health of FQ-resistance in *Campylobacter* is debatable. Different studies/reviews/analyses have reached different conclusions as to whether FQ-resistant strains are more hazardous in regard to prolonged symptoms (diarrhoea), severity and hospitalization rate. Studies in DK and US have found increased risks (Helms *et al*., 2005; Nelson *et al*., 2007), whereas a study in the UK (*Campylobacter* Sentinel Surveillance Scheme Collaborators, 2002) did not. A meta-analysis of all such studies (Wassenaar *et al*., 2007) found no association. There are different risks for different patient populations, as mild cases do not require antimicrobial therapy anyway, and as severe cases of diarrhoea of unknown origin are normally treated empirically with antimicrobials (generally a FQ if suspicious of *e.g. Salmonella*). If FQ-resistant organisms, including *Campylobacter*, are present there is increased risk of treatment failure and adverse outcome. Furthermore, there are indications of increased infection rates with FQ-resistant *Campylobacter* strains in humans that are receiving FQ treatment (Helms *et al*., 2005).

It is considered that the majority of *Campylobacter* infections are acquired from broiler meat. It therefore seems reasonable to assume that the same is true for infections with FQ-resistant *Campylobacter*. However, sources for *Campylobacter* (including FQ resistant strains) other than broiler meat, should be taken into consideration. For instance, the environment and water can be contaminated with *Campylobacter* due to indirect (faecal) contamination from animals (including broilers) and possibly humans.

3. Consider the possibilities for, and impact of, reducing antimicrobial usage in broiler production on the occurrence of resistant Campylobacter on broiler meat and the public health impact of such control.

It is assumed that there will be a positive public health impact from reducing FQ use in broiler production. It is a fact that FQ-resistance is increasing in *Campylobacter* isolates from both humans and poultry. Studies show that resistance in humans follows the usage of FQ in food animals and the build up of resistance among *Campylobacter* in food animals (Endtz *et al*., 1991; Thwaites and Frost, 1999; Nachamkin *et al*., 2002). Danish and Norwegian studies showed that the proportion of FQ-resistant *Campylobacter* among domestic poultry (low usage of FQ in poultry) and domestically-acquired cases was low, as opposed to travel related cases where the proportion of FQ-resistant *Campylobacter* was very high (Helms *et al*., 2005; Norström *et al*., 2006).

It appears possible to reduce FQ use in broiler production. A prerequisite is that antibiotics, including FQ, are only available by prescription. Prescription for antibiotic use in animal production is a requirement in the EU, and such a policy would be commendable in the rest of the world. However, there is also the issue of non-compliance and illegal use. Thus, enforcement is critical. Some countries have shown that it is possible to produce poultry with limited or without FQ use, *e.g.* Australia, New Zealand and the Nordic countries. Moreover, the US banned FQ in poultry in 2006 in light of public health risks associated with such use. There is, however, lack of knowledge of what will be the impact on different management options (ban; use only for certain indications; off-label use; use only after susceptibility testing, *etc*.). FQ are slowly degraded in the environment and there is a carry-over of small quantities of FQ in the poultry environment (especially for FQ used in water).

4. Identify critical data gaps and recommend further studies to address these data gaps.

The importance is noted of establishing national monitoring programmes for usage of antimicrobial agents in animal production, including poultry production. Currently, there is good progress in this field in some countries. However, monitoring programmes need to be harmonized for comparability between countries. The introduction of an EU database on drug usage in food animals would contribute to such monitoring. Further discussion, including a work-shop on best and feasible practices for monitoring drug usage, should be held, to recommend a common system for EU countries.

The exact relationship between antimicrobial use, including FQ, and resistance require further investigation. Experiences from different countries, *e.g.* the US and Australia, regarding policies and interventions on FQ use, need to be studied. For example, what is the public health impact and what are the effects on the poultry industry, including animal health? A careful re-analysis of previous work regarding the public health risks of FQ-resistant versus FQ-susceptible *Campylobacter* strains should be considered. There is a need for more studies to assess the risk factors for FQ resistant *Campylobacter* infection. Also, the impact of the importation of FQ-resistant *Campylobacter* through food from third countries should be assessed. One approach could be to conduct longitudinal studies in human volunteers (travel, type of foods (broiler meat, imported foods), patients' previous antimicrobial exposure, *etc*.), including susceptibility profiles and typing of the isolates, with regular samples from environmental sources and samples from locally-produced and imported foods from the same period. Such risk factor studies should not focus on broiler meat only, but include all poultry meats (*e.g.* there is usually higher antibiotic use in turkey production). There is also a lack of knowledge regarding whether FQ-resistant isolates belong to specific clones and/or have particular properties (*e.g.* increased fitness or virulence).

The discussion group agreed the following main conclusions to be reported back to the final plenary session:

- There is scientific evidence that the use of FQ in poultry has led to the emergence of FQ-resistance in *Campylobacter* in poultry and that such strains have further spread to humans.
- There is a public health benefit from reducing FQ use in food animals, including poultry. However, is it not yet possible to quantify the effect in case of *Campylobacter*.
- Different studies/reviews/analyses have reached different conclusions as to whether FQ-resistant strains are more hazardous to public health than FQ-susceptible strains.

- Severe cases of diarrhoea of unknown origin are normally treated empirically with antimicrobials and if FQ resistant *Campylobacter* are present there may be an increased risk of treatment failure and adverse outcome.
- There are recent indications of increased infection rates with FQ-resistant *Campylobacter* strains in humans that are receiving FQ treatment.
- It is possible to produce poultry with limited, or even without, FQ use. However, there is a need for more data on the public health benefit and the impact on the poultry industry including animal health.
- FQ is a critically important drug in humans and should therefore be a drug of last resort for therapeutic use in food animals.
- Prudent antimicrobial use policy in all sectors should be promoted and adhered to.

DG4: Assessment of effectiveness of control measures in the food chain

Assessment of effectiveness of control measures in the food chain has to be made on the basis of evidence-based science rather than the socio-economic constraints related to the food industry or consumer/political premise. Before addressing the four questions raised to the group, a number of presumptions were discussed, including: (i) pre-harvest is defined as before animals are killed and all steps in the production chain after killing are defined as post-harvest, (ii) it must be assumed that GHP and HACCP are fully implemented management systems (iii) pre- and post-harvest measures may be complementary in their effect but need to be considered separately and (iv) conventional systems are the norm for broiler production, and although organic/free range systems must be considered, chickens produced by such management systems are in the minority.

1. From the European perspective, consider the effectiveness of current and proposed pre- and at-harvest controls for Campylobacter in broiler chicken flocks and propose further studies to develop more effective controls. State the strong and weak points of the control measures identified, considering explicitly the perspective of industry and consumers, and identify possible barriers to their introduction.

<u>Pre-harvest control options</u>

Some aspects of increasing biosecurity can be done at relatively low costs and could be implemented without the need for further research. However, to maintain biosecurity, every single opening in a poultry house needs to be closed or protected, which is largely impractical.

Recently, a critical review of risk factors for *Campylobacter* on farm has been completed (FSA, 2009). This highlighted that some risk factors are common between countries but others are more country or region specific (*e.g.* drinking water in Nordic countries). Additionally, the risk factors may vary over the year. In particular the major risk factors during the peak months appear to be different than in the rest of the year and the timing, extent and importance of seasonality can vary between countries. Consequently, the assessment of the efficacy of different biosecurity measures is complex and cost/effectiveness should be estimated separately for each country.

Intervention studies on biosecurity measures have been performed with different levels of success in different countries. Such variation may be explained by differences in the *Campylobacter* ‘loads’ in the environment. Thus the effectiveness of biosecurity-related intervention strategies in primary production, might be strongly dependent on regional conditions.

Data collected over the years in Europe suggests much lower prevalence in flocks in Nordic countries compared to countries in more median latitudes like United Kingdom or the Netherlands and a very high prevalence in southern countries such as Spain and Italy. This may be a result of climatic factors (*e.g*. temperature, humidity) but may also reflect management differences in poultry production, like the popular free-range systems in France. The current EU baseline study using standardised methods will show whether these presumed differences in prevalence are true.

In conclusion, although a general level of biosecurity should be established, regional and/or seasonal modifications must be added and even so effectiveness cannot be guaranteed.

Thinning, which is partial depopulation, is identified as a significant risk factor in many studies. The explanation is that the maintenance of reasonable levels of biosecurity by thinning crews and their equipment is impractical. The risk of detectable colonization of a substantial part of the remaining flock is related to the number of days the birds stay on the farm. This reflects the 5-7 days before the flock is detectably colonized with *Campylobacter* after initial introduction. One country with an effective *Campylobacter* control plan (Iceland) does not apply thinning as part of its biosecurity measures.

Age of birds is also a major risk factor and has been well described in many prevalence studies world wide. Iceland, and some other Nordic countries, slaughter birds at younger ages (about 33 days, particularly in summer). In other countries, birds are larger and older (*i.e.* in Denmark, birds are on average 45 days of age at slaughter). The prevalence of *Campylobacter*-positive flocks increase with the age of the birds.

Drinking water may be a risk factor but there are reported regional differences on the relative importance of this risk factor and this may relate to the water source (*i.e.* mains or bore hole). Simple measures are available for the treatment of drinking water (UV-treatment).

There are several options for feed and or water additives (*e.g.* organic acids). The effectiveness is variable for different products and the claims are sometimes hard to reproduce in slightly different settings.

Additional measures that are under development to be considered in the longer term are vaccination, phage therapy and bacteriocins. Such approaches are needed to complement biosecurity and for implementation in non/less-biosecure production systems (*e.g.* free range systems). However, considerable additional research on these strategies is needed. Some (*i.e.* bacteriophages and bacteriocins) are ready to test under field conditions but appropriate field conditions (*e.g.* contained poultry houses) are lacking and the current EU legislation precludes the controlled studies that are needed.

Transportation from the farm to the processing plant is not seen as a major risk factor for contamination of the final product, but might be an issue to the farmer if a negative flock becomes contaminated during transport and this affects payment of incentive bonuses.

Logistic slaughter, which is the separate processing of negative and positive flocks, will not necessarily have an impact on the reduction of human campylobacteriosis, in terms of preventing cross-contamination in the processing line, as the numbers of *Campylobacter* tend to be low on any cross-contaminated carcasses from negative flocks. However, scheduled slaughter could be effective when combined with the diversion of the products from positive flocks towards freezing or other treatment such as cooking. Nevertheless, scheduled slaughter is logistically impractical when the prevalence of positive flocks is high. Consequently, the implementation of such a strategy would be country- and season- dependent. A rapid test to show the *Campylobacter* status of the flocks, preferably on farm at the day before slaughter, would facilitate effective implementation of such an intervention.

An overview of the possible control options, indicating effectiveness, strong and weak points, barriers to introduction and an indication of the further research needed, is listed in Table 1 (pre-harvest).

Table 1: Potential pre-harvest control options

Measure	Effectiveness	Strength	Weaknesses	Barrier to introduction	Further research needed
Biosecurity	Geographically dependent	Reasonable costs; Available	Effect unpredictable	Doubts regarding effectiveness	Regional/seasonal effectiveness
No-thinning	High	effective	Economic constraints	Economics	None
Younger age at slaughter	High	effective	Economic constraints	Economics, consumer/ demands, imbalance of trade, traditional products….	Scarce data on birds >45 days of age
Uncontaminated Water	Local	If needed, techniques are available	None	None	None
Feed composition/additives*	Many options available; not all are effective	Available	Reproducible effects; economic constraints	No guaranteed effect	Available data should be collected and evaluated independently
Vaccination*	Unclear	Wide application; usable in addition to other measures	Cost	Not yet available	Required on vaccine candidates, and delivery systems
Phage therapy*	Unclear	Wide application; addition to other measures	Costs	Not yet available	Required on effectiveness in the field and production
Bacteriocins*	Unclear	Wide application; addition to other measures	Costs	Not yet available	Required on safety, effectiveness in the field and production
Feed withdrawal	Yes	Available		Welfare issues	None
Hygienic transport	Not effective to improve public health	-	-	Farmers loses bonuses for neg. flocks and incorrect feed back	-
Importation	Unclear risk factor				More data needed

* regulatory issues

Post-harvest

Table 2 contains a list of possible post-harvest strategies with detailed comments. Carcasses with the highest *Campylobacter* contamination levels are considered to contribute most to the number of human campylobacteriosis cases (though this assumption has been questioned by DG1). However, the within-batch contamination levels are not homogeneous. More research is needed to generate reliable methods and strategies to detect the most highly contaminated carcasses in order to identify such products.

The detection of faecally-contaminated carcasses is theoretically one way to enable the removal or decontamination of highly contaminated carcasses. USDA, ARS has developed and validated an on-line sensing technology system for wholesomeness inspection of freshly slaughtered chickens. The FSIS Risk Management Division approved the technology for commercial implementation to pre-sort chicken carcasses online. However, it is not yet clear how this system will perform in a fully operational processing plant.

Although *Campylobacter* blood infection may occur in chickens, and poultry meat/offal may be internally contaminated, the highest level of the contamination is expected to be at carcass surface.

Physical decontamination, such as freezing and crust freezing will reduce the *Campylobacter* levels by a few logs but crust freezing has to be combined with additional methods (*e.g.* ultrasound) to have any real impact. The feasibility of introduction of such processes in fully operational production lines is questionable.

Based on an extensive surveillance programme at production, one country (Iceland) has legal requirements on freezing (or heat treating) the whole flock of broilers, which are *Campylobacter*-positive prior to slaughter. As it is important for the poultry industry to market fresh poultry meat, the farmers have placed their effort in producing *Campylobacter*-negative flocks. Concurrent with this strategy, the incidence of human campylobacteriosis of domestic origin has been reduced from 117 cases in 1999 to about 10 – 15 cases per 100.000 inhabitants in the last three years.

Processing technologies that could reduce *Campylobacter* viable numbers on carcasses, such as air chilling, should be considered.

At the end of the slaughter line the poultry end-product should be placed in leak proof packaging. Fluid absorbing packaging or edible films may help in preventing cross-contamination in the kitchen. Modified atmosphere packaging (MAP) is under development and may reduce the numbers of viable *Campylobacter*. However, it should be recognised that modern processing, which generates very short production chains, and retailing using protective plastics and dark, moist and cool storage, all contribute to *Campylobacter* survival on the end product.

With reference to product labelling there are conflicting opinions. The labelling of meat as *Campylobacter*-negative may result in less careful handling by consumers and this would undesirable.

Table 2: Potential post-harvest control options

Measure	Effectiveness	Strengths	Weaknesses	Barrier to introduction	Further research needed
Logistic slaughter	Poor	-	For burden no effect	-	-
Scheduled slaughter (redirection of colonized flocks)	Medium-High	Effective	Dependant on prevalence, costs, market imbalance	Economic barrier, high prevalence in some countries, rapid testing requirement	Development of rapid test assay
Prevention / detection of faecal contamination	Medium-High	In particular to eliminate high level contaminated carcasses	Practicality questionable FSIS approved system is available not tested in field	Cost unknown	Further data required on quantitative effects in processing plants & ease of implementation.
Detecting high/low level contamination	Discussion point as there are large differences in viable counts on carcasses within flocks so what kind of sample should be tested and what would be representative of a batch?				
Physical treatments (crust freezing, steam, ultrasound, ...)	Medium-High but a combination of strategies needed for effectiveness	Fairly effective.	Practical constraints of implementation in production lines	Cost-effectiveness	Collaboration with industry to investigate practicality and efficacy
Chemical decontamination*	High; already used in some countries outside Europe	Some treatments are effective	Regulation constraints	Regulation constraints	Safety issues
Leak proof packaging	Medium to prevent cross contamination			Cost	Efficacy data needed
Modified atmosphere packaging	Medium to reduce bacterial viability			Cost	Efficacy data needed
Labelling (i) to indicate *Campylobacter* status (ii) with safe handling & cooking instructions	Poor	Cheap	(i) Possibly misleading as other pathogens might be present (ii) often not read or followed		
Contribution of imported products	Unknown	-	Regulation constraints	-	Need data on contribution

* regulatory issues

2. List and rank the possible post-harvest controls in terms of effectiveness from a European perspective.

A list of potential measures for consideration are given in Table 2. As the effectiveness of most of the potential control measures is hard to quantify, it was considered infeasible at this stage to rank these measures.

3. Consider the evidence on the effectiveness of producer, processor and consumer education to reduce the risk of human campylobacteriosis. Consider the need for new studies aimed at the identification, collection and evaluation of new data on the effectiveness of education and awareness programmes.

The effect of education was briefly discussed for 3 groups in the food chain:

Producers
For producers educational messages tend to be short lived, incentive- and cost-related. However, some countries have invested in educational programmes particularly related to biosecurity on farms, and targeted towards the farm staff and catching crews. Such programmes have included the distribution of printed booklets, posters and talks. There is no evidence of the effectiveness of such measures largely because they are rarely implemented in isolation from other strategies and because monitoring of the effect on flock-positivity over time is not undertaken.
Processor
The message for producers is also short lived. HACCP compliance is already high and it is difficult to see how this helps with an organism that does not grow under natural conditions outside the host. This may change if effective post-harvest interventions become available.
Consumer
The message for the consumer is also short lived; the evidence suggests that people do not listen to educational messages. The best approach may be through school children, who can educate their parents.

4. Consider at which points along the food chain, monitoring, targets, microbiological criteria, and/or performance objectives would be most effective and recommend how best this would be implemented.

There are multiple points along the food chain at which monitoring can take place. Each has its own advantages and disadvantages.

On-farm monitoring gives the option for the separation of positive from negative flocks and could monitor the effectiveness of biosecurity but is remote from the consumer. There is also the issue of late flock-positivity, which might reduce the sensitivity of monitoring particularly after thinning. The monitoring of faecal material only also has problems of sensitivity.

Monitoring of birds at slaughter using culture of caecal contents is closer to the consumer and likely to give a more reliable positive or negative result. Caecal contents tend to have very high bacterial numbers, which ensures effective bacterial recovery. This strategy has been used for the EU baseline survey and is considered effective.

Monitoring at the end of the slaughterline can take into account the effectiveness of any post-harvest interventions during processing. Moreover, this stage can provide quantitative indicators of bacterial load on the carcass, which would give the most valuable information to incorporate into risk assessment models and assess the effectiveness of interventions.

Retail monitoring is the closest to the consumer but does not provide information on the effectiveness of, or give options for, interventions. Importantly, the distinction between imported and domestically produced products would be unclear, so domestic interventions would not necessarily be assessible. In addition, the time that the product was on the retail shelf would be variable and this could have a big effect on bacterial numbers.

It seems likely that a combination of monitoring points will be needed to provide the most appropriate information.

The discussion group finally discussed some concluding remarks at the end of the session:

- In the current economic climate there is an increasing demand for cheaper products and consequently imports may increase with unknown effects on risk.
- Alternative systems with reduced biosecurity are a challenge for the balance between welfare and product safety.
- There are clear *Campylobacter* strain differences, for example with regard to survival along the food chain and (probably) virulence traits. This field needs more research to come to a differentiated risk assessment.
- Incentives for farmers would increase the farmers’ motivation to produce *Campylobacter* free flocks.
- There should be a fully integrated farm-to-consumer approach.
- Focus should be on decontamination/elimination of highly contaminated carcasses.

III FINAL PLENARY DISCUSSION: CONCLUSIONS & RECOMMENDATIONS

Health impact and attribution of *Campylobacter*

Even though *Campylobacter* is recognized as the leading cause of acute bacterial enteritis in Europe, the true incidence of campylobacteriosis is considerably higher than reported, and the under-ascertainment is likely to vary considerably between countries. Public health surveillance systems need to be further strengthened, and focussed studies to calibrate the "surveillance pyramid" should be encouraged. To better understand the full disease burden, case-based reporting in the Member States needs further promotion. Collaboration between the medical profession and experts in the food and veterinary sectors, and other specialists, is key to improving the data collection needed to provide baseline information on campylobacteriosis and to monitor the effectiveness of interventions. New tools for source attribution of campylobacteriosis are emerging, and standardised data collection across the EU to inform such studies should be encouraged.

Specific research needs and recommendations identified in this area include:

- The importance of poultry meat as a vehicle, and poultry as a reservoir for human campylobacteriosis, should be established in order to better determine where interventions would be most effective.
- Passive surveillance is not capable of demonstrating the impact of interventions in the food chain on public health. Active surveillance is needed to demonstrate that a specific intervention has delivered a public health effect.
- New and innovative chicken products coming onto the market have to be considered in any risk assessment or source attribution exercise, as experience in some countries has already shown them to have a significant effect on human exposure.
- An international strain-typing database, including data on *Campylobacter*, using unbiased and appropriately structured sampling methods, from all sources (animals, food, humans and environmental) is a priority. Strains in such databases need to be made readily available for research.
- It has been difficult to harmonise typing methodology against a background of rapidly improving methodology. Ideally, a decision would be made to focus on one or a few methods.

Quantitative risk assessment of *Campylobacter* in broiler meat in the EU

Even though there are many reservoirs and transmission routes for the bacterium, contaminated poultry meat is considered a major source of human exposure. Quantitative risk assessment models have provided new insights to support risk management strategies particularly applied to the poultry food chain. Further development of these models, including application at the EU-level rather than country level, should be encouraged to support decision-making. Access to reliable quantitative data at each stage of the production chain throughout Europe will help to fine-tune models for risk assessment and will contribute to our understanding of those interventions that are likely to be most successful. There are many data gaps, in particular with reference to field data. However, it will be a time-consuming process to address this and risk management action may be considered while these data gaps are being filled.

Specific research needs and recommendations identified in this area include:

- The currently available risk assessment models are good enough for scenario analysis, but are incapable of predicting real numbers of human cases.
- The currently available QMRA models are often based on assumptions, or are tailored to farming, processing or consumption patterns, that may be Member State specific and will thus need adapting before application in risk assessments at an EU level.
- A pragmatic approach to QMRA is important in order to give a timely output. Current limitations on data availability should not delay efforts to model the European situation.
- Field studies (pilot then full scale), to validate promising interventions strategies identified by QMRA studies, are needed. Currently, field trials are using *ad hoc* experimental set-ups. The elaboration of harmonized protocols, with minimum requirements for conducting field trials, is recommended.

Fluoroquinolone resistance in *Campylobacter*

There is evidence that the use of fluoroquinolones in poultry has led to the emergence of fluoroquinolone (FQ) resistance in *Campylobacter* in poultry and contributes to the occurrence of antibiotic-resistant *Campylobacter* infection in humans. It is to be expected that there would be public health benefit in reducing fluoroquinolone use in animals, although it is not yet possible to quantify this in the case of *Campylobacter*. There is a need to monitor usage of antimicrobial substances overall in animals. In particular, monitoring, preceded by appropriate modelling, should be considered as a preliminary step when planning any intervention.

Few data exist on the establishment of reservoirs of FQ resistant *Campylobacter* in the environment [exceptions include (Leatherbarrow *et al*., 2004; Waldenstrom *et al*., 2005; Fallacara *et al*., 2001)]. Such data would help to establish the potential for control measures to reverse the upward trend of prevalence of FQ resistant *Campylobacter*. Nevertheless, control measures may at least ensure that further emergence could be prevented. Existing research suggests that the prevalence of FQ resistant *Campylobacter* remains constant following withdrawal of FQ, implying that it is “fit” and established in the environment (Luangtongkum et al., 2009).

Specific research needs and recommendations identified in this area include:

- In future, in order to better assess the effectiveness of control measures, it is strongly recommended that monitoring studies are undertaken parallel to interventions.
- As a first step towards managing the increasing prevalence of antimicrobial resistance, better reporting of all antimicrobial use, by sector, is essential, and should be coordinated and harmonised at a European level.

Assessment of effectiveness of control measures in the food chain

Several possibilities for intervention at various stages in the broiler meat food chain have already been identified. Prevention of flock colonisation would be ideal but reducing numbers of *Campylobacter* on a carcass, rather than complete elimination, may also have important public health benefits. Experts noted that it is unlikely that there will be a single effective measure applicable across all Member States. Currently available interventions are apparently limited in their effectiveness or difficult to sustain. Well-designed field trials, informed by quantitative risk assessments, to test the most promising strategies, are needed. Novel control strategies are also required but will need advanced planning for the evaluation of efficacy and safety.

Specific research needs and recommendations identified in this area include:

- Control should aim at reducing the numbers of *Campylobacter* on carcasses as well as prevalence of contaminated carcasses, although these are two sides of the same coin. This in turn could lead to a definition of appropriate sensitivity of detection methodologies, which would be useful.

- Education is very important, and should start with children – there is currently in the EU much work on nutritional education which could be extended to include food hygiene. There are ongoing opportunities to reinforce food safety education (*e.g*. E-Bug project).

- The labelling of poultry meat products as part of an education campaign might be worth considering. However, labelling on how to safely handle and cook the product, has very different implications from labelling the product as "free from *Campylobacter*". Multi-disciplinary studies on *Campylobacter* interventions should in future include social scientists to understand the impact of human behaviour.

- There is a need for a harmonized protocol for assessing control measures with fixed numbers of farms/flocks, to allow for rapid validation of intervention strategies. Criteria need to be defined for assessing safety and efficacy of novel intervention methods like phage therapy.

- Many barriers to introducing control measures are economic. The European Commission may need to consider what incentives are necessary, as industry margins are very low.

- Interaction between the leading European agencies, EMEA, ECDC, EFSA and the European Commission will be important to successfully address the problem.

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