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EFSA Scientific Colloquium
Summary Report

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ASSESSING HEALTH BENEFITS OF CONTROLLING *CAMPYLOBACTER* IN THE FOOD CHAIN

4-5 December 2008, Rome, Italy

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About EFSA

The European Food Safety Authority (EFSA) was established and funded by the European Community as an independent agency in 2002 following a series of food scares that caused the European public to voice concerns about food safety and the ability of regulatory authorities to fully protect consumers.

In close collaboration with national authorities and in open consultation with its stakeholders, EFSA provides objective scientific advice on all matters with a direct or indirect impact on food and feed safety, including animal health and welfare and plant protection. EFSA is also consulted on nutrition in relation to Community legislation.

EFSA's work falls into two areas: risk assessment and risk communication. In particular, EFSA's risk assessments provide risk managers (EU institutions with political accountability, i.e. the European Commission, European Parliament and Council) with a sound scientific basis for defining policy-driven legislative or regulatory measures required to ensure a high level of consumer protection with regards to food and feed safety.

EFSA communicates to the public in an open and transparent way on all matters within its remit. Collection and analysis of scientific data, identification of emerging risks and scientific support to the Commission, particularly in case of a food crisis, are also part of EFSA's mandate, as laid down in the founding Regulation (EC) No 178/2002 of 28 January 2002.

For more information about EFSA, please contact:

European Food Safety Authority
Largo N. Palli 5/A
I-43121 Parma
Italy

Tel: +39 0521 036 111
Fax: +39 0521 036 110
www.efsa.europa.eu

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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 4-5 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 principal 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 season. 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* in 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 expected 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 organise 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-related 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* in 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 Summary Report on Zoonoses (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 hazards").

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 encountered is 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 in order 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 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, consumer behaviour differ 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 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 they 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 of 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, targets close to the consumer are less practical 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 subsequently decrease. The importance of assessing the effects of any interventions, such as the ban of enrofloxacin in poultry production in the US should be emphasised. The missed opportunity in monitoring effects on antimicrobial resistance in relation to 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 Denmark and USA 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 e.g. *Salmonella* is suspected). 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 of 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 workshop 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 the 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.

Pre-harvest control options

Some aspects of increasing biosecurity can be carried out at relatively low cost 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 increases 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

Measure	Effectiveness	Strength	Weaknesses	Barrier to introduction	Further research needed
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 DG2). 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 be undesirable.

Table 2: Potential post-harvest control options

Measure	Effectiveness	Strength	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

Measure	Effectiveness	Strength	Weaknesses	Barrier to introduction	Further research needed
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

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 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 to be 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 intervention 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.

IV REFERENCES

Ang C. W., Van Pelt W., , Herbrink P., Keijser J., van Duynhoven *Y.*T.H.P. and Visser C.E., 2007. Sero-epidemiology indicates frequent and repeated exposure to *Campylobacter* during childhood. *Zoon Pub Health* 54(Suppl. 1): p. 50.

Campylobacter Sentinel Surveillance Scheme Collaborators, 2002. Ciprofloxacin resistance in *Campylobacter jejuni*: case–case analysis as a tool for elucidating risks at home and abroad. *J Antimicrob Chemother* 50, pp. 561–568.

Coughlin *S.* S., Benichou J. and Weed D.L., 1994. Attributable risk estimation in case-control studies. *Epidemiol Rev.* 16: pp. 51–64.

De Wit M. A., Koopmans M. P., Kortbeek L. M., Wannet W. J., Vinje J., van Leusden F., Bartelds A. I. and van Duynhoven *Y.* T., 2001. Sensor, a population-based cohort study on gastroenteritis in the Netherlands: incidence and etiology. *Am J Epidemiol* 154: pp. 666-74.

Dingle K. *E.*, McCarthy N. D., Cody A. J., Peto T. *E.* A. and Maiden M. C. J., 2008. Extended Sequence Typing of *Campylobacter* spp., United Kingdom. *Em Inf Dis* 14: pp. 1620-1622.

EC (Commission Decision) No 2007/516/EC of 19 July 2007 concerning a financial contribution from the Community towards a survey on the prevalence and antimicrobial resistance of *Campylobacter* spp. in broiler flocks and on the prevalence of *Campylobacter* spp. and *Salmonella* spp. in broiler carcasses to be carried out in the Member States. (OJ L 190, 21.7.2007, pp. 25-37).

ECDC (European Centre for Disease Prevention and Control), 2008. *Annual Epidemiological Report on Communicable Diseases in Europe*.

EFSA (European Food Safety Authority), 2007. The Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents and Antimicrobial Resistance in the European Union in 2006. *The EFSA Journal* 130: pp. 1-352.

EFSA (European Food Safety Authority), 2008a. EFSA-Q-2008-469. *Campylobacter* in broiler meat production. <http://registerofquestions.efsa.europa.eu/roqFrontend/questionsList.jsf>

EFSA (European Food Safety Authority), 2008b. Scientific Opinion of the Panel on Biological Hazards on a request from EFSA on Overview of methods for source attribution for human illness from food borne microbiological hazards. *The EFSA Journal* 764: pp. 1-43.

EFSA (European Food Safety Authority), 2008c. Report of Task Force on Zoonoses Data Collection on proposed technical specifications for a coordinated monitoring programme for *Salmonella* and *Campylobacter* in broiler meats at retail in the EU. *The EFSA Journal* 155: pp. 1-49.

EFSA (European Food Safety Authority), 2008d. Summary report: EFSA Scientific Colloquium on European food consumption database - current and medium to long-term strategies. 28-29 April 2005 in Brussels, Belgium.

EFSA (European Food Safety Authority), 2008e. Guidance Document for the use of the Concise European Food Consumption Database in Exposure Assessment. EFSA/DATEX/2008/01: pp. 1-8; 17 March 2008, Parma, Italy.

EFSA (European Food Safety Authority), 2009. The Community Summary Report on Trends and Sources of Zoonoses and Zoonotic Agents in the European Union in 2007. *The EFSA Journal*, p. 223.

Endtz H.P., Ruijs G.J., van Klingeren B., Jansen W.H., van der Reyden T. and Mouton R.P., 1991. Quinolone resistance in *Campylobacter* isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine. *J Antimicrob Chemother* 27, pp. 199–208.

Evers *E.* G., van Der Fels-Klerx H. J., Nauta M.J., Schijven J.F. and Havelaar A.H., 2008. *Campylobacter* source attribution by exposure assessment. *Int J Risk Ass* Mgt 8: pp. 174-190.

Fallacara D. M., Monahan C. M., Morishita T.Y. and Wack R.F., 2001. Fecal shedding and antimicrobial susceptibility of selected bacterial pathogens and a survey of intestinal parasites in free-living waterfowl. *Avian Dis* 45(1): pp. 128-35.

FDI/236/2005. Enhancing Surveillance of Potentially Foodborne Enteric Diseases in New Zealand: Human Campylobacteriosis in the Manawatu. Massey University, New Zealand.

FSA (Food Standards Agency), 2009. A critical review of interventions and strategies (both biosecurity and non-biosecurity) to reduce *Campylobacter* on the poultry farm. <http://foodbase.org.uk>

Havelaar A. H., van Pelt W., Ang C.W.,. Wagenaar J.A., Gross U., van Putten J.P.M. and Newell D.G., 2009. Immunity to Campylobacter: its role in risk assessment and epidemiology. Critical Reviews in Microbiology, in press.

Havelaar A. H., Vargas Galindo A., Kurowicka D. and Cooke R. M., 2008. Attribution of Foodborne Pathogens Using Structured Expert Elicitation. *Foodborne Pathogens and Disease* 5(5): pp. 649-659.

Helms M., Simonsen J., Olsen K. *E.* and Molbak K., 2005. Apr 1. Adverse health events associated with antimicrobial drug resistance in *Campylobacter* species: a registry-based cohort study. *J Infect Dis.* 191(7): pp. 1050-5.

Leatherbarrow A. J., Hart C. A., Kemp R., Williams N. J., Ridley A., Sharma M., Diggle P. J., Wright *E.* J., Sutherst J. and French N. P., 2004. Genotypic and antibiotic susceptibility characteristics of a *Campylobacter coli* population isolated from dairy farmland in the United Kingdom. *Appl Environ Microbiol* 70(2): pp. 822-30.

Luangtongkum T., Jeon B., Han J., Plummer P., Logue C.M. and Zhang Q., 2009. Antibiotic resistance in Campylobacter: emergence, transmission and persistence. *Future Microbiol*, Mar 4: pp. 189-200.

Nachamkin I., Ung H. and Li M., 2002. Increasing fluoroquinolone resistance in *Campylobacter jejuni*, Pennsylvania, USA, 1982–2001, Emerg Infect Dis 8, pp. 1501–1503.

Nelson J. M., Chiller, T. M., Powers, J. H. and Angulo, F. J., 2007. Fluoroquinolone-resistant *Campylobacter* species and the withdrawal of fluoroquinolones from use in poultry: a public health success story. *Clin Infect Dis.* 44(7): pp. 977-80.

Norström M., Hofshagen M., Stavnes T., Schau J., Lassen J. and Kruse H., 2006. Antimicrobial resistance in *Campylobacter jejuni* from humans and broilers in Norway. *Epidemiol. Infect.* 134:127–130.

Olson C. K. , Ethelberg S., van Pelt W. and Tauxe R.V., 2008. Epidemiology of *Campylobacter jejuni* infections in industrialized countries. In *Campylobacter* 3rd ed., Nachamkin I, Szymanski CM, Blaser MJ. *ASM Press*, Washington DC., pp. 163-189.

Stafford R. J., Schluter P., Kirk M., Wilson A., Unicomb L., Ashbolt R. and Gregory J., 2007. A multi-centre prospective case-control study of *Campylobacter* infection in persons aged 5 years and older in Australia. *Epidemiol. Infect.* 135: pp. 978-988.

Thwaites R.T. and Frost J.A., 1999. Drug resistance in *Campylobacter jejuni*, *C. coli*, and *C. lari* isolated from humans in north west England and Wales, 1997. *J Clin Pathol* 52, pp. 812–814.

Waldenstrom J., Mevius D., Veldman K., Broman T., Hasselquist D. and Olsen B., 2005. Antimicrobial resistance profiles of *Campylobacter jejuni* isolates from wild birds in Sweden. *Appl Environ Microbiol* 71(5): pp. 2438-41.

Wassenaar T.M., Kist M., de Jong A., 2007. Re-analysis of the risks attributed to ciprofloxacin-resistant *Campylobacter jejuni* infections. *Int J Antimicrob Agents*. 30(3): pp. 195-201.

Wheeler J.G., Sethi D., Cowdon J.M., Wall P.G., Rodrigues L.C. Tomkins D.S., 1999. Study of infectious intestinal disease in England: rates in the community, presenting to general practice, and reported to national surveillance. *British Medical Journal*. 318: 1046-1050.

Whittemore, A. S., 1983. Estimating attributable risk from case-control studies. *Am J Epidemiol*. 117: pp. 76–85.

Wilson D. J., Gabriel *E.*, Leatherbarrow A. J. H., Cheesbrough J., Gee S., Bolton *E.*, Fox A., Fearnhead P., Hart C. A. and Diggle P. J., 2008. Tracing the Source of Campylobacteriosis. *PLoS Genetics* 4(9): e1000203.

ANNEXES

V ANNEXES

Annex 1: Programme of the Colloquium

Annex 2: Participants at the Colloquium

Annex 3: Presentations of speakers

Annex 4: Presentations of Discussion Groups

ANNEX 1: PROGRAMME OF THE EFSA COLLOQUIUM

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

4-5 December 2008, Rome, Italy

PROGRAMME

Overall chairs:	Arie Havelaar RIVM, Netherlands
	Marta Hugas BIOHAZ Unit – EFSA
Overall rapporteurs:	Diane Newell United Kingdom
	Tobin Robinson BIOHAZ Unit – EFSA

Day 1

09.00-13.00	**Session 1: INTRODUCTORY PLENARY SESSION**	
09.00-09.15	Welcome and introduction to EFSA	Hubert Deluyker Director Scientific Cooperation & Assistance, EFSA Presented by Marta Hugas
09.15-09.30	Objectives of the Colloquium	Arie Havelaar RIVM, Netherlands
09.30-09.50	New approaches to source attribution and their role in reducing campylobacteriosis notifications in New Zealand	Nigel French Massey University, New Zealand
09.50- 10.00	*Questions*	
10.00-10.20	*Campylobacter* Risk Assessment in the EU: Past, present and future	Maarten Nauta RIVM, Netherlands

10.20- 10.30	*Questions*	
11.00-11.20	Presentation as introduction to DG 3	Frank Aarestrup CRL - Antimicrobial Resistance
11.20-11.30	*Questions*	
11.30-11.50	Measures to control *Campylobacter* in broilers and broiler meat	Hanne Rosenquist Technical University of Denmark
11.50-12.00	*Questions*	
12.00-12.20	General discussion	Chairs
12.20-12.30	Introduction to discussion groups	Stef Bronzwaer Scientific Cooperation Unit, EFSA

14.00-18.00 **Session 2:**
DISCUSSION GROUPS (DG)
Four parallel discussion groups to address:

DG 1 Health impact and attribution of *Campylobacter*
Chair: Kare Molbak
Statens Serum Institute, Denmark
Rapporteur: Paolo Calistri Istituto Zooprofilattico
Sperimentale dell'Abruzzo e del Molise, Italy

DG 2 Quantitative risk assessment
of *Campylobacter* in broiler meat in the EU
Chair: Gilles Salvat
AFSSA, France
Rapporteur: Mieke Uyttendaele
University of Gent, Belgium

DG 3 Fluoroquinolone resistance in *Campylobacter*
Chair: Guenter Klein
University of Veterinary Medicine Hannover, Germany
Rapporteur: Hilde Kruse
WHO Regional Office for Europe

DG 4 Assessment of effectiveness
of control measures in the food chain
Chair: Dan Collins
University College Dublin, Ireland
Rapporteur: Jaap Wagenaar
University of Utrecht, Netherlands

Day 2

09.00-10.00	**Session 3:** **CONTINUATION OF DISCUSSION GROUPS** Including discussion on the outcomes of the discussion groups and the production of reports to the plenary session	
10.30-13.30	**Session 4:** **FINAL PLENARY SESSION**	
10:30-10:50	Report back from discussion group 1	Paolo Calistri Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise, Italy
10:50-11:05	*Discussion*	
11:05-11:25	Report back from discussion group 2	Mieke Uyttendaele University of Gent, Belgium
11:25-11:40	*Discussion*	
11:40-12:00	Report back from discussion group 3	Hilde Kruse WHO Regional Office for Europe
12:00-12:15	*Discussion*	
12:15-12:35	Report back from discussion group 4	Jaap Wagenaar University of Utrecht, Netherlands
12:35-12:50	*Discussion*	
12:50-13:30	General discussion Conclusions and take-home message	Chairs Diane Newell, overall rapporteur
14.30	COLLOQUIUM ADJOURNS	

ANNEX 2: PARTICIPANTS AT THE COLLOQUIUM

Name	Affiliation	Country	Discussion Group (DG)
Dr Frank Aarestrup	National Food Institute (DTU)	DK	3
Dr Thomas Alter	Federal Institute for Risk Assessment (BfR)	DE	4
Dr Antonio Battisti	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Tuscany and Lazio	IT	1
Mr Aivars Berzins	Institute of Food and Environmental Hygiene (FVM)	LV	1
Dr Louise Boysen	National Food Institute (DTU)	DK	1
Prof. Dr Lone Brøndsted	University of Copenhagen	DK	1
Dr Andrea Brtkova	State Veterinary and Food Institute	SE	3
Dr Luca Bucchini	Hylobates Consulting s.r.l.	IT	2
Dr Sabina Buettner	Federal veterinary office (FVO)	CH	3
Dr Paolo Calistri	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Abruzzo and Molise	IT	1
Mr Luca Cocolin	International Journal of Food Microbiology	IT	2
Prof. Pierre Colin	University of Western Britain	FR	3
Prof. John Daniel Collins	University College Dublin (UCD)	IE	4
Dr Roberto Condoleo	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Tuscany and Lazio	IT	2
Mrs Sigurborg Dadadottir	The Icelandic Food and Veterinary Authority	IS	4

Name	Affiliation	Country	Discussion Group (DG)
Dr Paolo Daminelli	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Lombardia and Emilia Romagna	IT	1
Dr Kris De Smet	European Commission, Directorate General for Health and Consumer Affairs	BE	4
Dr Elisabetta Di Giannatale	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Abruzzo and Molise	IT	3
Prof. Dr Zerrin Erginkaya	Çukurova University	TR	4
Dr Maurizio Ferri	Local Health Unit Pescara, Veterinary Service	IT	2
Dr Alessia Franco	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Tuscany and Lazio	IT	3
Prof. Nigel French	Massey University	NZ	1
Dr Norbert Ginten	Emsland-Frischgeflügel	DE	4
Mr Ihab Habib	University of Gent	BE	2
Mrs Marjaana Hakkinen	Finnish Food Safety Authority (EVIRA)	FI	1
Prof. Marja-Liisa Hanninen	University of Helsinki	FI	3
Prof. Arie Havelaar	National Institute for Public Health and the Environment (RIVM)	NL	1
Dr Merete Hofshagen	National Veterinary Institute (NVI)	NO	4
Dr Mary Howell	The Food Standards Agency (FSA)	UK	1
Mrs Andrea Humski	Croatian Veterinary Institute (CVI)	HR	2
Prof. William Keevil	University of Southampton	UK	2
Prof. Dr Günter Klein	University of Veterinary Medicine Hannover	DE	3

Name	Affiliation	Country	Discussion Group (DG)
Dr Günther Kraus	Austrian Agency for Health and Food Safety (AGES)	AT	1
Dr Hilde Kruse	World Health Organization, Regional Office for Europe	IT	3
Dr Roland Lindqvist	Swedish National Food Administration	SE	2
Dr Ida Luzzi	Istituto Superiore di Sanità (ISS)	IT	3
Dr Gerardo Manfreda	University of Bologna	IT	1
Dr Antonio Martinez Lopez	Institute of Agrochemistry and Food Technology (CSIC)	ES	4
Dr Winy Messens	Institute for Agricultural and Fisheries Science	BE	2
Dr Kåre Mølbak	Statens Serum Institut	DK	1
Dr Dominique L. Monnet	European Centre for Disease Prevention and Control (ECDC)	SE	3
Dr Maarten Nauta	National Food Institute (DTU)	DK	2
Prof. Diane Newell	Foodborne Zoonoses Consultancy	UK	4
Dr Lisa O'Connor	Food Safety Authority of Ireland	IE	4
Dr Eva Olsson Engvall	National Veterinary Institute, CRL- *Campylobacter*	SE	4
Dr Antonio Parisi	Collaborating Center for Veterinary Training, Epidemiology, Food Safety and Animal Welfare of Puglia and Basilicata	IT	3
Mr Pavel Pollak	Institute of Public Health of Slovenia	SI	2
Dr Miguel Prieto	University of León	ES	3
Dr Franco Rigo	UNA SITO	IT	4
Dr Mati Roasto	Estonian University of Life Sciences	EE	3
Dr Hanne Rosenquist	Technical University of Denmark	DK	4
Mr Gilles Salvat	French Food Safety Agency (AFSSA)	FR	2
Dr Moez Sanaa	Veterinary School of Alfort	FR	2

Name	Affiliation	Country	Discussion Group (DG)
Dr Snieguole Sceponaviciene	National Food and Veterinary Risk Assessment Institute	LT	2
Dr Pavle Sekulovski	National Food Institute	MK	4
Prof. Peter Silley	MB Consult Limited	UK	3
Prof. Dr Iva Steinhauserova	University of Brno	CZ	3
Dr Anca-Violeta Stoicescu	Institute for Hygiene and Veterinary Public Health	RO	1
Dr Johanna Takkinen	European Centre for Disease Prevention and Control (ECDC)	SE	1
Dr Benno Ter Kuile	Netherlands Food and Consumer Product Safety Authority (VWA)	NL	3
Dr Nicola Tornaletti	UNICEB/Fiorucci	IT	2
Dr Mary Torrence	U. *S.* Department of Agriculture	US	4
Mr Jordi Torren Edo	European Medicines Agency (EMEA)	UK	3
Mrs Mª Esther Tortuero	City Council of Madrid	ES	4
Prof. Dr Mieke Uyttendaele	University of Gent	BE	2
Dr Emanuela Varani	Negroni SpA	IT	4
Dr Peter Van Der Logt	New Zealand Food Safety Authority	NZ	2
Dr Wilfrid Van Pelt	National Institute for Public Health and the Environment (RIVM)	NL	1
Dr Ana Vidal	Veterinary Laboratories Agency (VLA)	UK	4
Prof. Ana Cristina Vilela	University of Lisbon	PT	1
Prof. Jaap Wagenaar	University of Utrecht	NL	4
Dr Paul Whyte	University College Dublin (UCD)	IE	3
Dr Kinga Wieczorek	National Veterinary Research Institute	PL	1
Dr Siamak Yazdankhah	Norwegian Scientific Committee for Food Safety	NO	2
Mrs Carmen Zigorraga	Health Department Basque Government	ES	3

EFSA Staff

Dr Stef Bronzwaer	Scientific Cooperation and Assistance, Scientific Cooperation Unit
Dr Maria Teresa Da Silva Felicio	Scientific Cooperation and Assistance, Zoonoses (Data Collection) Unit
Ms Rita De Bon	Risk Assessment, Biological Hazards Unit (BIOHAZ)
Dr Hubert Deluyker	Director of Scientific Cooperation and Assistance
Dr Marta Hugas	Risk Assessment, Biological Hazards Unit (BIOHAZ)
Dr Ernesto Liebana	Risk Assessment, Biological Hazards Unit (BIOHAZ)
Dr Pia Makela	Scientific Cooperation and Assistance, Zoonoses (Data Collection) Unit
Dr Alessandro Mannelli	Scientific Cooperation and Assistance, Zoonoses (Data Collection) Unit
Ms Francesca Piombini	Communications, Public Information & Events Unit
Dr Valentina Rizzi	Scientific Cooperation and Assistance, Zoonoses (Data Collection) Unit
Dr Tobin Robinson	Risk Assessment, Biological Hazards Unit (BIOHAZ)
Ms Barbara Rotovnik	Communications, Public Information & Events Unit
Dr Eirini Tsigarida	Risk Assessment, Biological Hazards Unit (BIOHAZ)

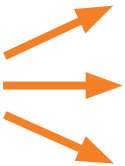
ANNEX 3: PRESENTATIONS OF SPEAKERS

Welcome and introduction to EFSA

MARTA HUGAS
Head of the Biological Hazards Unit

Creation of EFSA: Three main goals

Make a significant contribution to:



- Improving EU food safety
- Re-building consumer confidence in EU food safety
- Re-building confidence of trading partners in the EU food supply

Creation of the EFSA: guiding principles

- Independence
- Scientific excellence:
  - Best experts throughout the EU and beyond
  - Stick to the food safety science
- Openness and Transparency
- Responsiveness

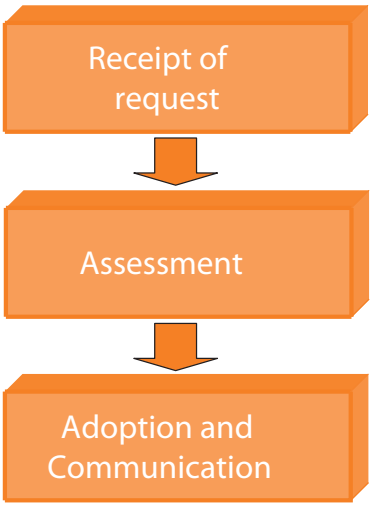
Scientific Priority Objectives

- Provide scientific opinions and advice to the European Commission, the European Parliament and the Member States
  - Applications
  - General opinions
- Enhance risk assessment methodologies and other scientific activities
  - Establish Guidance documents
  - Methodology development

Risk assessment: Scientific Panels

- Panel on dietetic products, nutrition and allergies (NDA)
- Panel on food additives & nutrient sources (ANS)
- Panel on food contact materials, enzymes, flavourings (CEF)
- Panel on contaminants in the food chain (CONTAM)
- Panel on biological hazards (BIOHAZ)
- Panel on Animal health and welfare (AHAW)
- Panel on additives and products or substances used in animal feed (FEEDAP)
- Panel on Genetically Modified Organisms (GMO)
- Panel on plant protection products and their residues (PPR)
- Panel on planth health (PLH)

Risk assessment: Overview on workflow of scientific opinions



- Accepted mandates (Register of Questions)
- Names of panel and working group members
- Declaration of interest of experts

- Agendas of the panel's plenary meetings
- Minutes of the panel's plenary
- Minutes of working group meetings

- Adopted opinions
- Press releases and web stories

Communications

Services and outputs

- Europe-wide Reference service largely via website: **www.efsa.europa.eu**
- Timely and accurate public announcements on risk assessments and key EU-wide issues
- Accessible and relevant messages on food safety issues
- Consistent and targeted output by close co-ordination with Member States

Scientific cooperation and assistance (SCA): Modus operandi

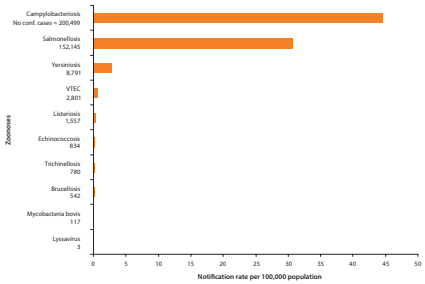
- Not Risk Assessments - Remit of Panels (exception pesticides)
- SCA operates through networks - with representation of all Member States
- Shared best practices with Scientific Panels
  - Working groups: Selection of Experts
  - Transparency: Declaration(s) of Interest
  - Openness: Reports on the web

Scientific Cooperation and Assistance: Data collection activities

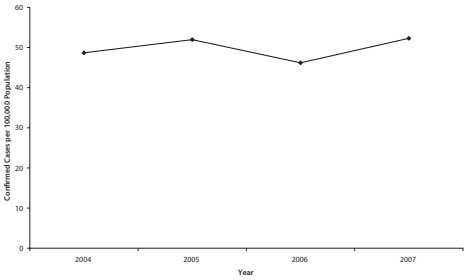
- Data Collection
  - For Scientific Opinions of high quality and Monitoring
  - Operating Procedures developed
- Data collection on food consumption
- Data collection on chemical occurence
- Data collection on pesticide residues
- Emerging risks: new unit established
  - RASFF analysis
  - Hazard Databases
- Data collection on Zoonoses

Notification rates of human zoonoses in EU - Community Summary Report draft 2007

Courtesy, ECDC. Draft Community Summary Report on Zoonoses (CSR) 2007

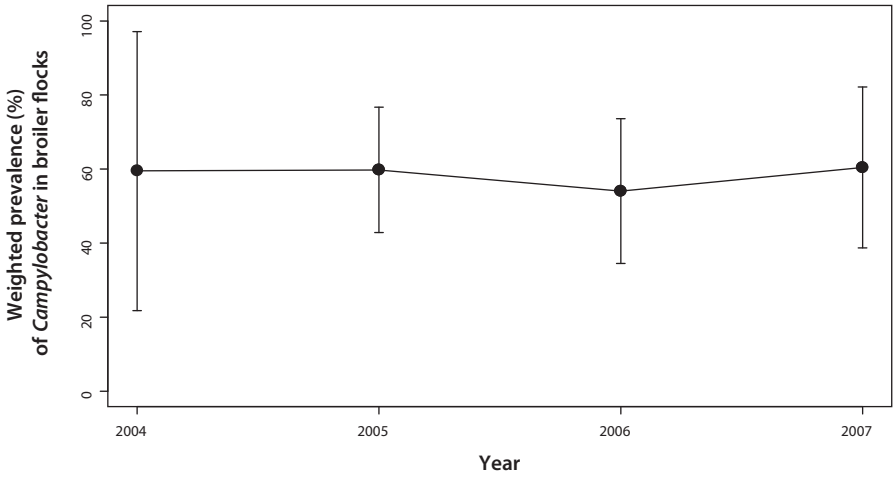


Campylobacteriosis: most frequently reported zoonoses in humans in EU



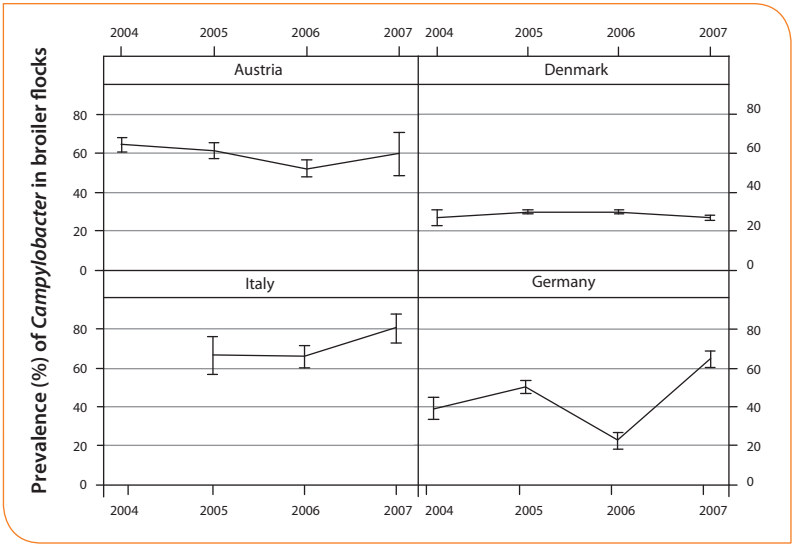
Reported incidence rate stable, data 17 countries

Campylobacter *in broiler flocks in EU 2004-2007 - Community Summary Report draft 2007*



Data from 9 MS, prevalence generally high, no trends apparent …

Campylobacter *in broiler flocks 2004-2007 - Community Summary Report draft 2007*



… but, substantial variation between reporting MS

2005 - BIOHAZ Opinion - Conclusion

Opinion of the Scientific Panel on Biological Hazards related to *Campylobacter* in animals and foodstuffs
(Question N° EFSA-Q-2003-081) - Adopted on 27th of January 2005

Source of risk

- Poultry meat products - major source through
  - Cross contamination to ready-to-eat food
  - Direct hands-to-mouth transfer during food preparation
  - Consumption of undercooked poultry meat (lesser extent)
- Meat from pigs and ruminants - low risk to consumers except for undercooked offal
- Raw milk and contaminated drinking water
- Bivalve molluscs

2008 - Request for a BIOHAZ opinion

Quantitatively update the 2005 Opinion related to *Campylobacter* in animals and foodstuffs as regards broiler meat production (*Gallus gallus*)
(Question No EFSA-Q-2008-469)

- The extent to which meat derived from broilers contributes to human campylobacteriosis at EU level.
- Identify and rank the possible control options within the broiler meat production chain
- Propose potential 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.

EU-wide baseline survey on Campylobacter *in broilers*

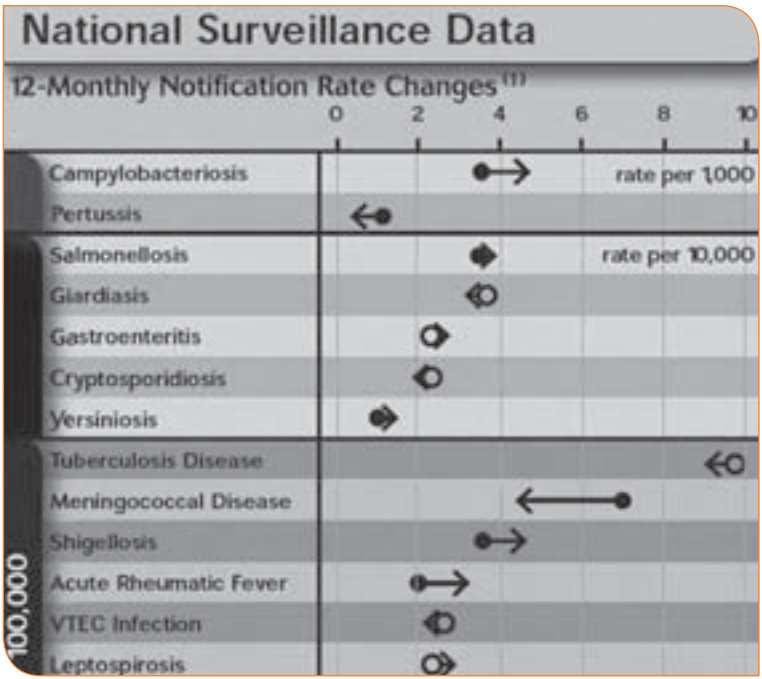
- Fully harmonised, well designed survey across the EU Member States carried out in 2008
- The survey covers
  - *Campylobacter* prevalence in broilers (ceacal samples) and
  - *Salmonella* and *Campylobacter* prevalence + quantitative data on broiler carcasses at slaughterhouse
- EFSA will receive the data in March 2009:
  - the report A (on prevalence estimates) to be published on 31.1.2010 and
  - report B (on risk factors) on 30.4.2010

New approaches to source attribution: their role in reducing campylobacteriosis notifications in New Zealand

NIGEL FRENCH
Massey University, New Zealand

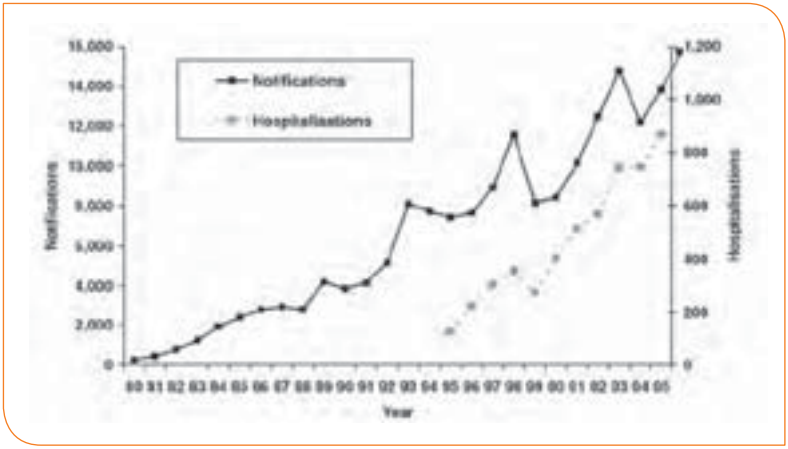
Outline

- Epidemiology
  - Recent studies of human case data
- Genotyping – human and animal reservoirs
  - MLST
- Source attribution modelling
- Recent trends – post intervention



Source: ESR

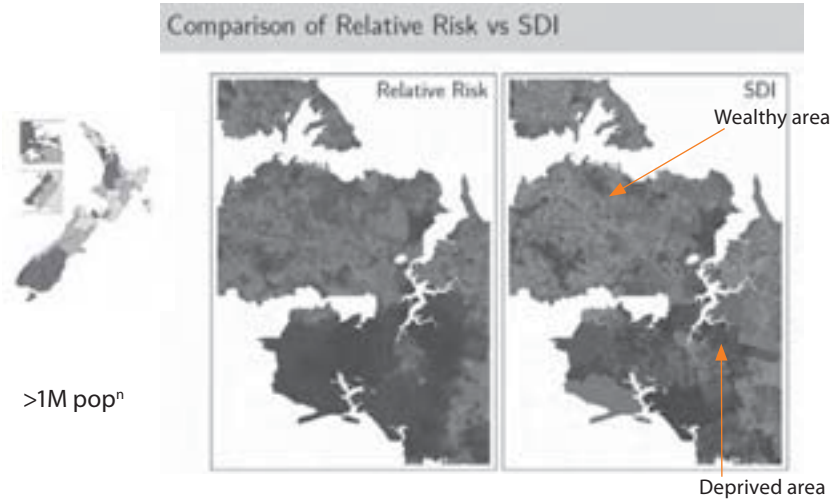
Campylobacteriosis in New Zealand



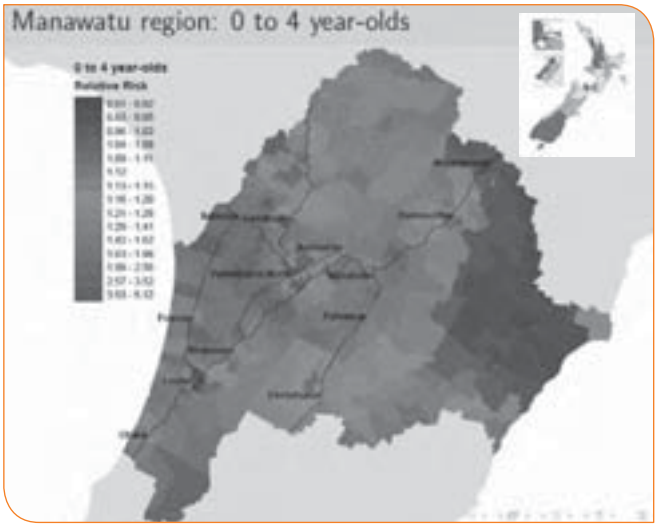
From Baker et al. *2006*

Epidemiology: seasonal pattern

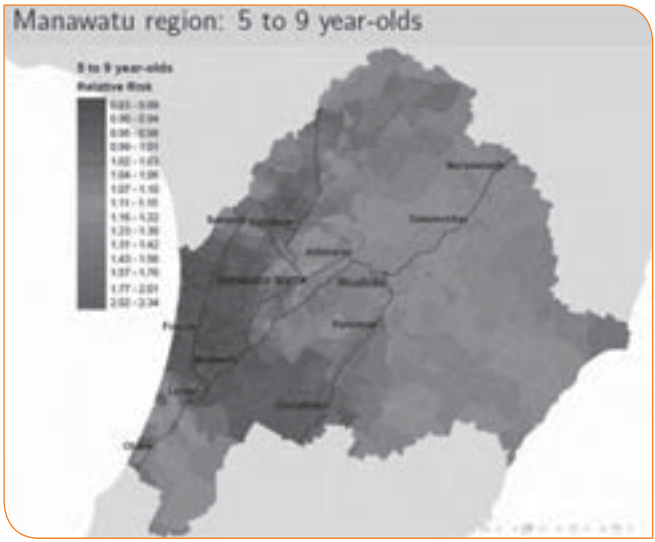
Epidemiology: spatial pattern



Spatial epidemiology - age



Pre-school children predominantly rural



School children predominantly urban

Interventions in poultry industry demanded

THE NEW ZEALAND MEDICAL JOURNAL

Vol 119 No 1243 ISSN 1175 8716

Regulation of chicken contamination urgently needed to control New Zealand's serious campylobacteriosis epidemic

Michael Baker, Nick Wilson, Rosemary Ikram, Steve Chambers, Phil Shoemack, Gregory Cook

Poultry ~ 40% of meat consumption

Source attribution

Essential for:

- Managing public health risks
- Prioritising resources
- Directing research effort

Approaches to 'source attribution'

- (Analytical) epidemiology
  - Population-based epidemiological studies
- Simulation modelling / Risk assessment
- Molecular epidemiology
  - Microbial subtyping / source tracking
  - Applying molecular tools, population genetics and epidemiological modelling to inform public health policy
  - NZFSA and industry funded

(Analytical) epidemiology

Population-based epidemiological studies

- Cross-sectional, cohort, case-control, case-case.
- Can estimate relative risk / odds ratios / PAF for different exposures
  - e.g. *Campylobacter* and eating poultry, foreign travel, environmental, occupational

Source/ exposure ← disease

- Issues with case-control studies
  - Can be very valuable but…
  - Prone to reporting bias
    - "I must have eaten chicken…."
  - If high level immunity, similar exposures in cases and controls – low power

Chicken – confusing / conflicting evidence?

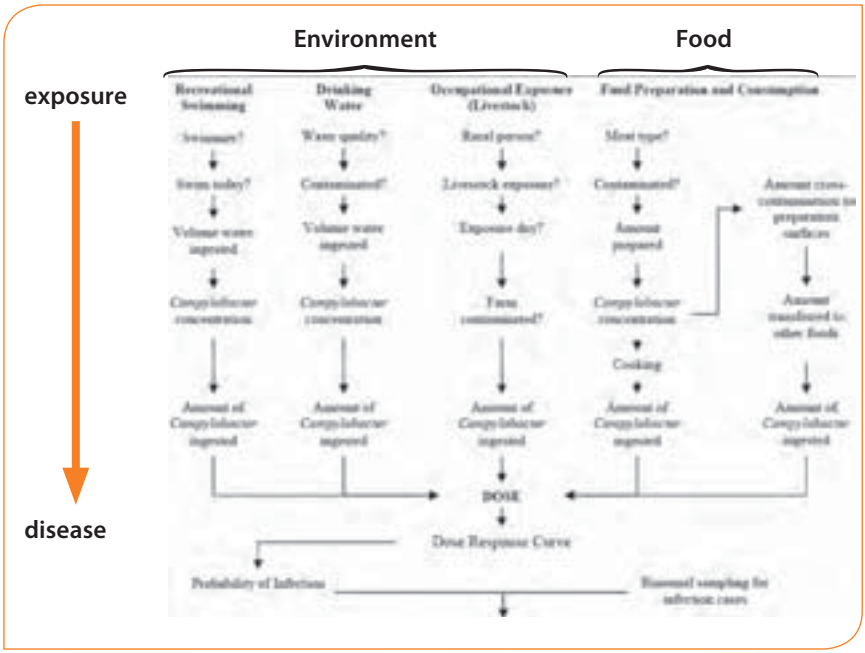
Risk/Protective factor	Odds ratio (CI)
Eating undercooked poultry (risk)	4.94 (1.01, 23.62)
Poultry eaten at a friend's house (risk)	3.18 (1.0, 10.73)
Consuming fresh chicken (as opposed to frozen) (risk)	1.8 (0.82, 3.82)
Eating poultry at home (protective)	0.36 (0.14, 0.9)
Freezing fresh chicken before consuming (protective)	0.58 (0.18, 1.83)
Buying frozen chicken (protective)	0.71 (0.34, 1.31)

Ikram 1994, New Zealand Campylobacter *study*

Simulation (RA) modelling

Multiple pathways / exposures

- **Food and environmental sources**
- **Simulation of propagation of pathogen along pathway**
- **Hazard or risk based (need D-RR)**
- **Good for assessing interventions**

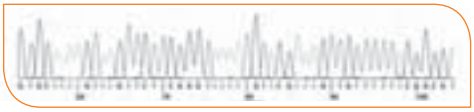


NIWA/ESR model

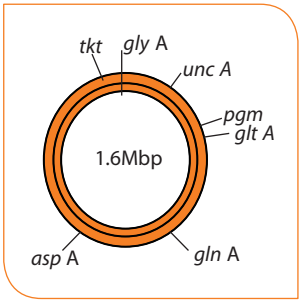
Molecular epidemiology

- Microbial subtyping / source tracking
- Applying molecular tools, population genetics and epidemiological modelling to inform public health policy
- NZFSA funded

Multi Locus Sequence Typing



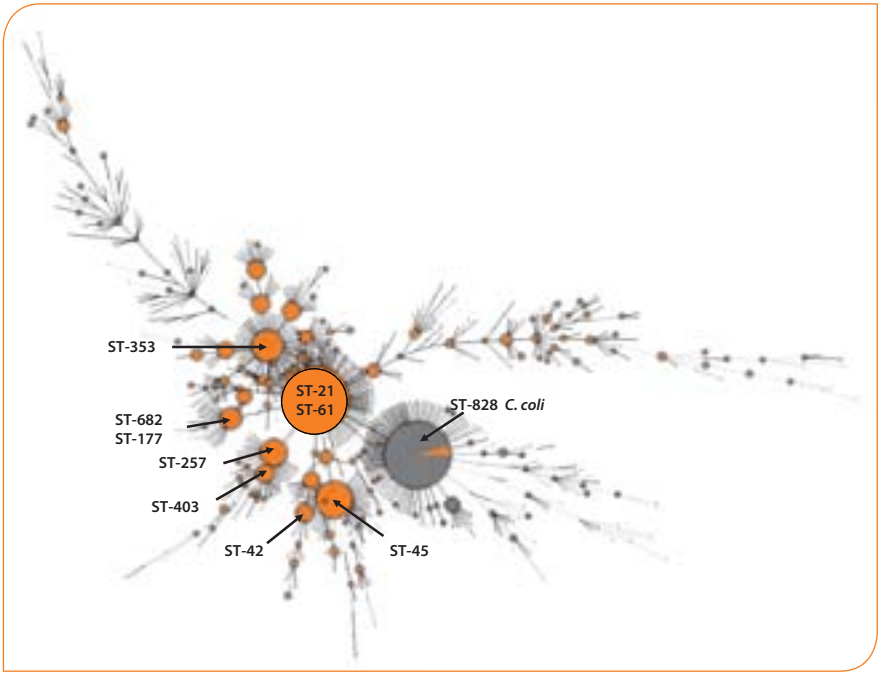
- PCR highly conserved genes
- 7 housekeeping genes
- Use allelic variation to describe subtypes:
  - ST = sequence type – unique pattern of 7 alleles
  - Clonal complex = group of related STs identified by progenitor ST



- Website: Oxford University
  http://campylobacter.mlst.net

Campylobacter *populations*

Minimum spanning tree of all known isolates on PubMLST website
2954 STs, ~5000 isolates



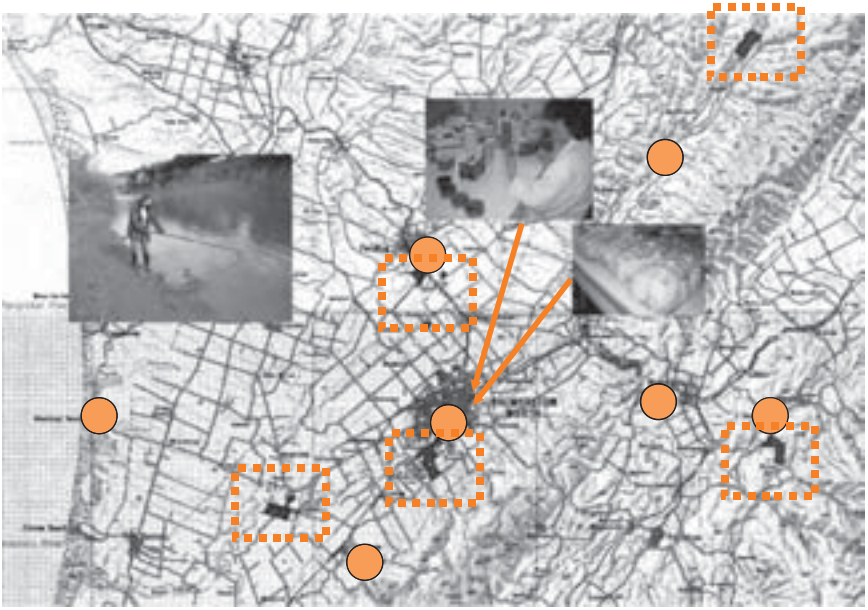
ST-61 complex

source	Frequency	Percentage
human stool	62	35.2%
cattle	53	30.1%
sheep	17	9.7%
ruminant offal/ meat	8	7.9%
lamb	8	4.5%
Chicken	3	1.7%

New Zealand Manawatu study 2005-

- Are human isolates the same as those found in different sources?
- Identify genotypes common to particular sources
- Modelling (risk attribution)
- Feasibility study: useful approach to embed within surveillance in NZ?

Sampling



Numbers of samples/isolates: C. jejuni

- Human 520 (770 samples)
- Poultry 562 samples 75% +ve
- Red meat 1312 samples 12% +ve
- Ruminant faeces 278 samples 58% +ve
- Env. Water 335 samples 30% +ve
- Wild bird 192 samples 13% +ve

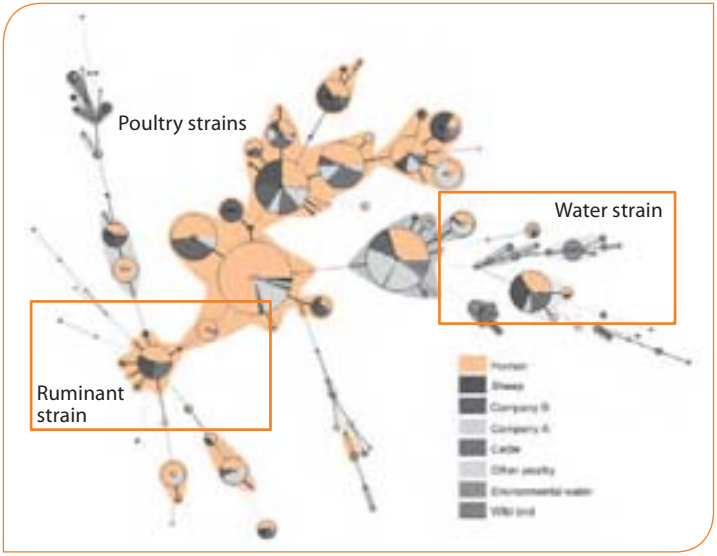
MLST
Human cases in Manawatu

ST	# of cases	%	2006 rank
474	66	27.3	1
48	24	9.9	2
190	18	7.4	4
45	17	7.0	3
53	13	5.4	8
42	11	4.5	5
61	10	4.1	10
50	9	3.7	7
2026	9	3.7	11
257	8	3.3	18
354	6	2.5	6
451	6	2.5	-
520	5	2.1	12
1517	5	2.1	20
38	4	1.7	13
52	3	1.2	9

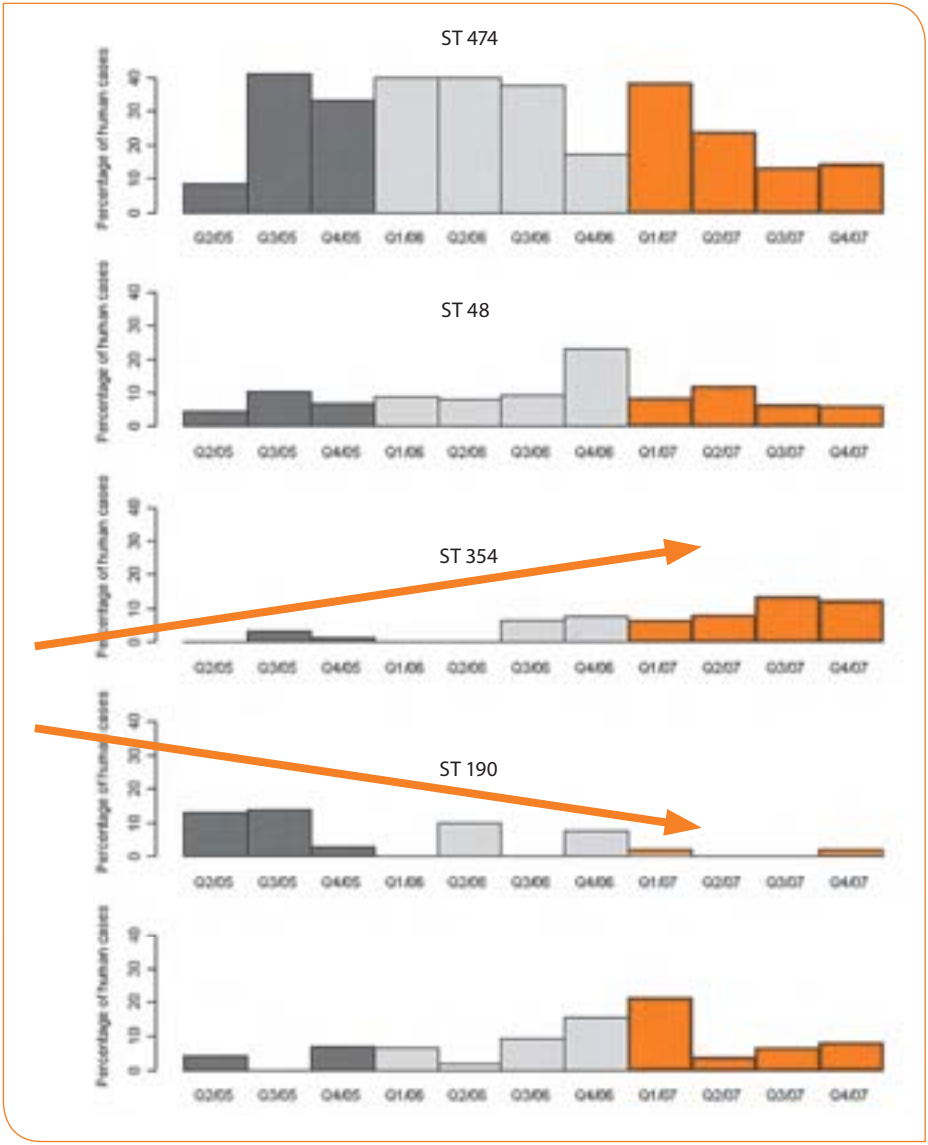
Rare internationally

Orange = Ruminant associated strains

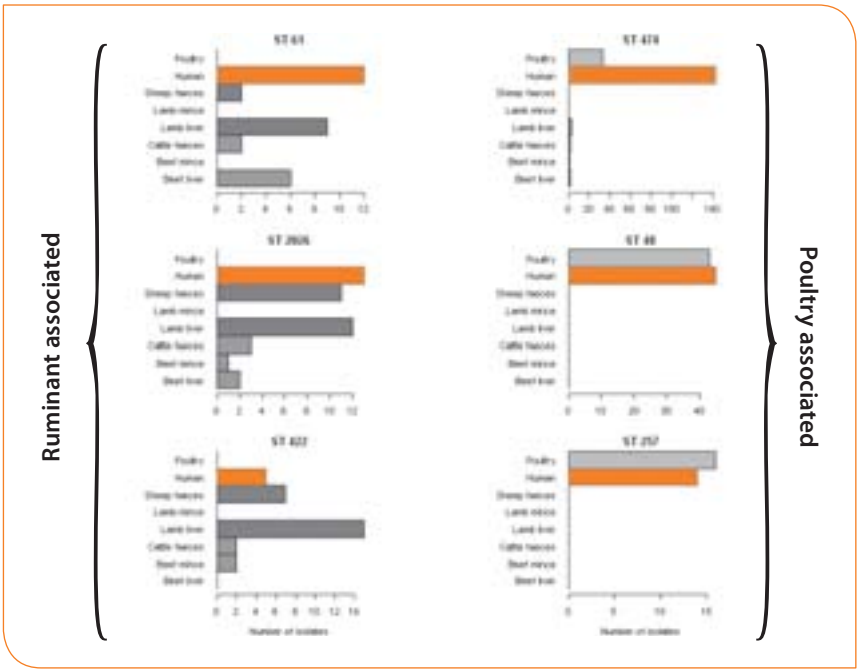
Minimum spanning tree: isolates from the Manawatu

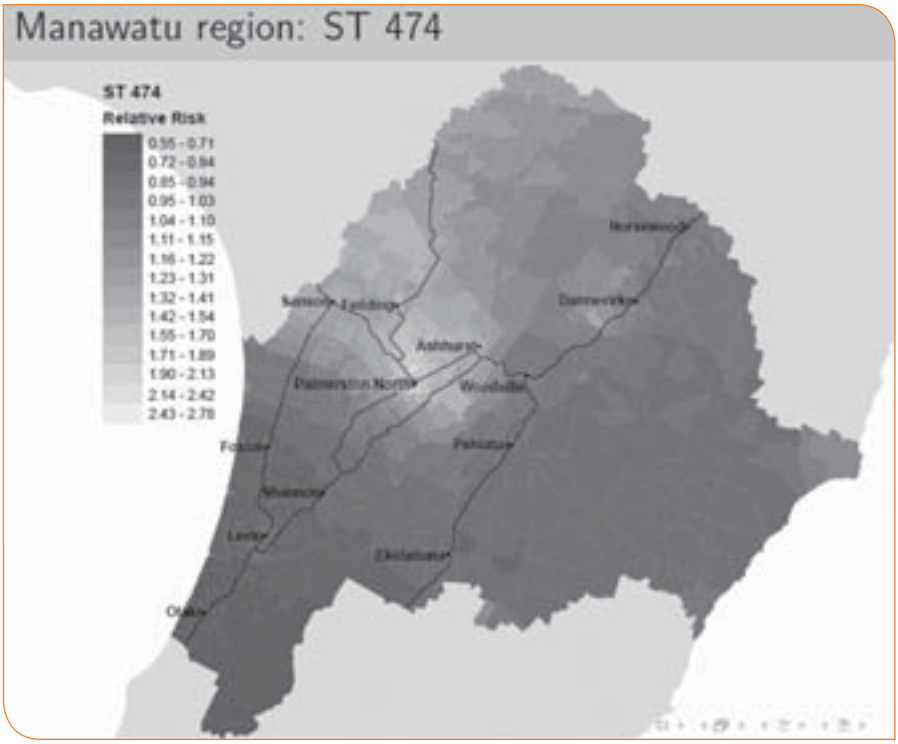


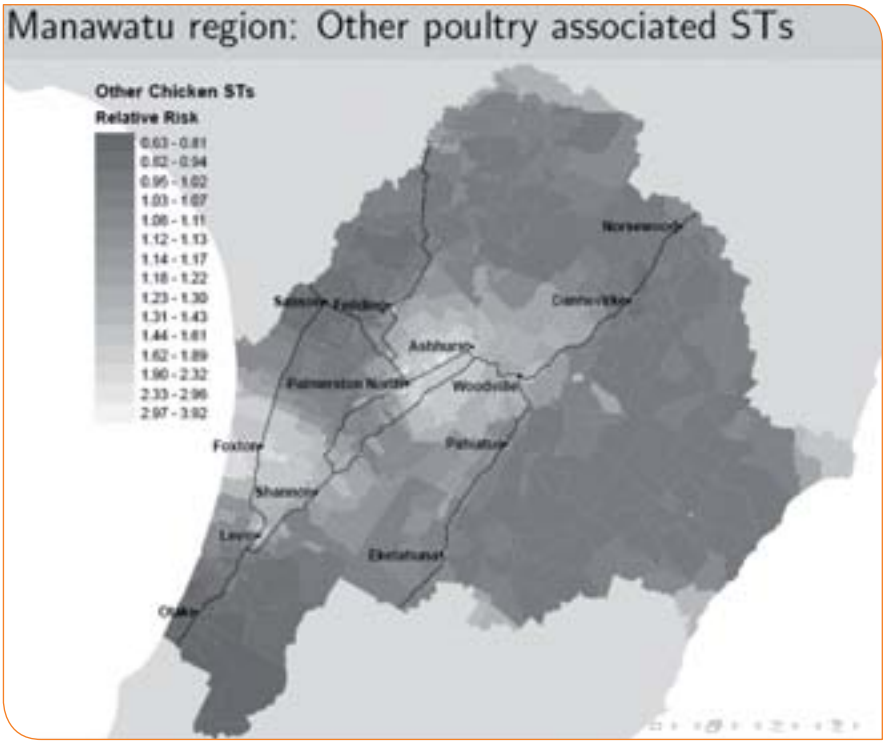
Human cases over 3-year period

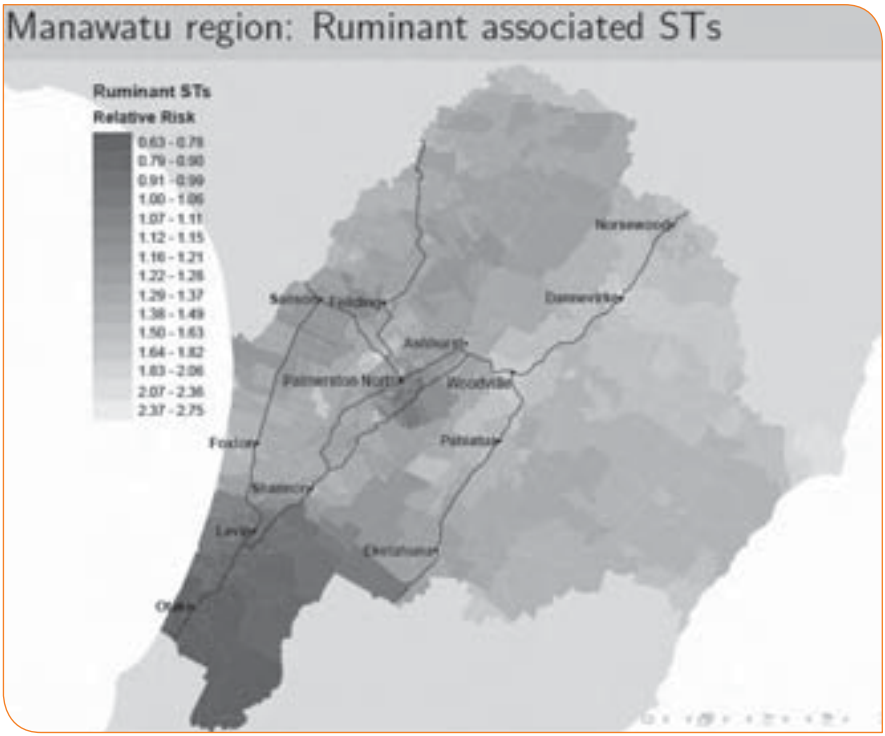


Host associated sequence types in New Zealand

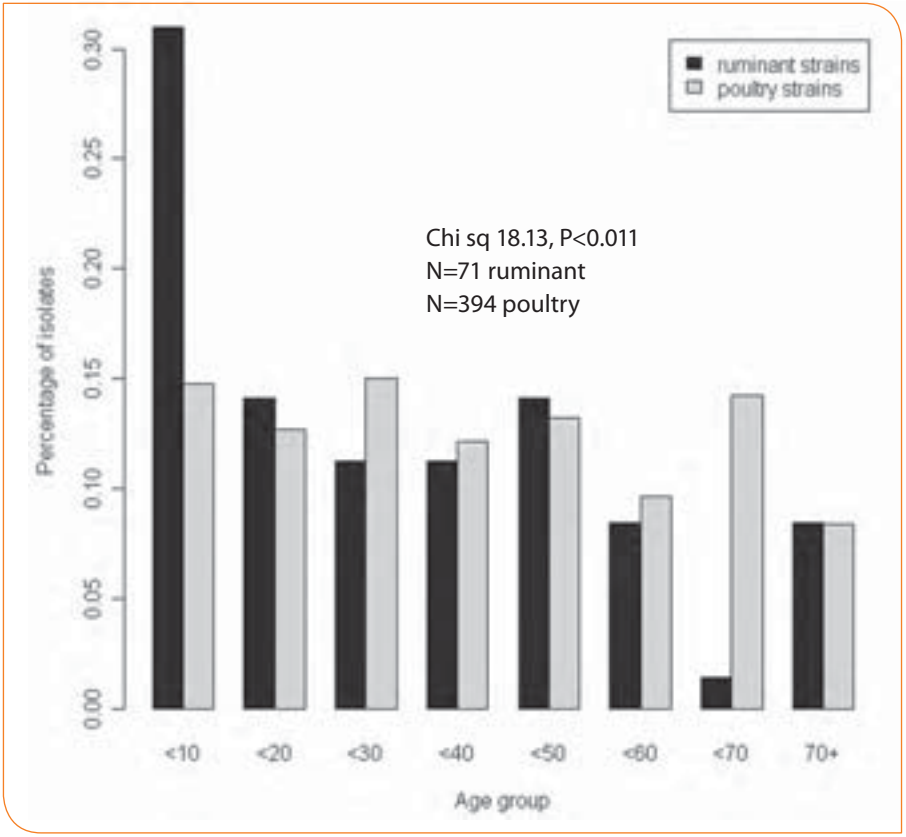



Manawatu region: ST 474
ST 474
Relative Risk
0.55 - 0.71
0.72 - 0.84
0.85 - 0.94
0.95 - 1.03
1.04 - 1.10
1.11 - 1.15
1.16 - 1.22
1.23 - 1.31
1.32 - 1.41
1.42 - 1.54
1.55 - 1.70
1.71 - 1.89
1.90 - 2.13
2.14 - 2.42
2.43 - 2.78
Ashhurst
Palmerston North
Foxton
Pahiatua
Levin
Otaki

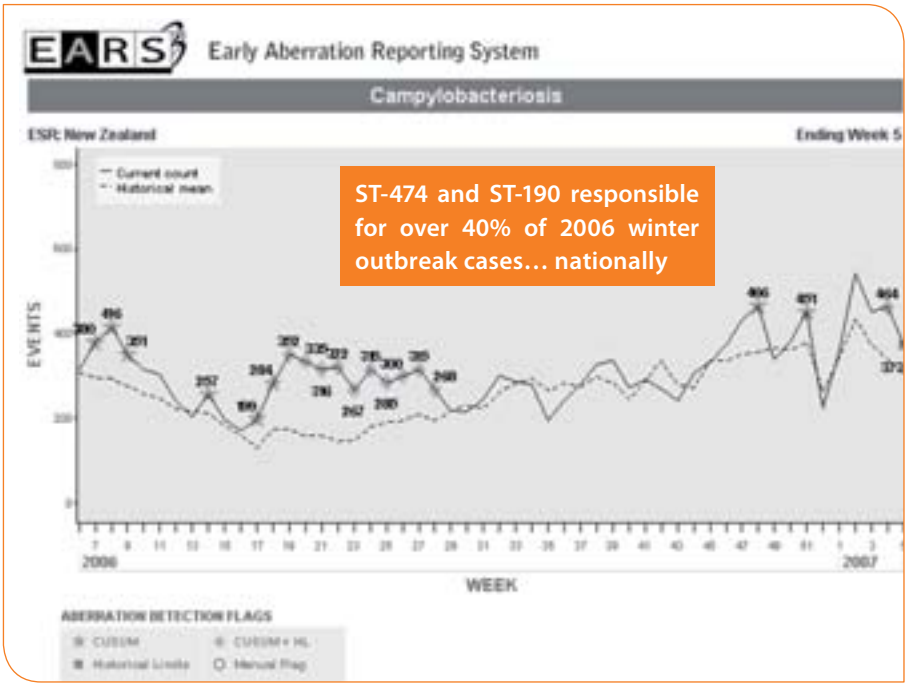

Manawatu region: Other poultry associated STs
Other Chicken STs
Relative Risk
0.63 - 0.81
0.82 - 0.94
0.95 - 1.02
1.03 - 1.07
1.08 - 1.11
1.12 - 1.13
1.14 - 1.17
1.18 - 1.22
1.23 - 1.30
1.31 - 1.43
1.44 - 1.61
1.62 - 1.89
1.90 - 2.32
2.33 - 2.96
2.97 - 3.92
Ashhurst
Woodville
Foxton
Pahiatua


Manawatu region: Ruminant associated STs
Ruminant STs
Relative Risk
0.63 - 0.78
0.79 - 0.90
0.91 - 0.99
1.00 - 1.06
1.07 - 1.11
1.12 - 1.15
1.16 - 1.21
1.22 - 1.28
1.29 - 1.37
1.38 - 1.49
1.50 - 1.63
1.64 - 1.82
1.83 - 2.06
2.07 - 2.36
2.37 - 2.75
Norsewood
Dannevirke
Ashhurst
Palmerston North
Woodville
Foxton
Pahiatua
Shannon
Levin
Otaki

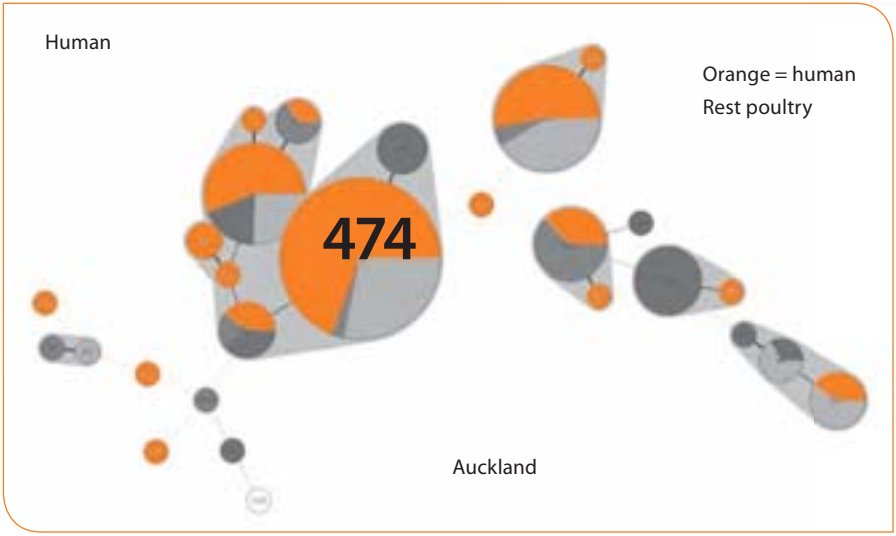
Case-case comparison



Generalised outbreak



Auckland MLST (T. Wong)



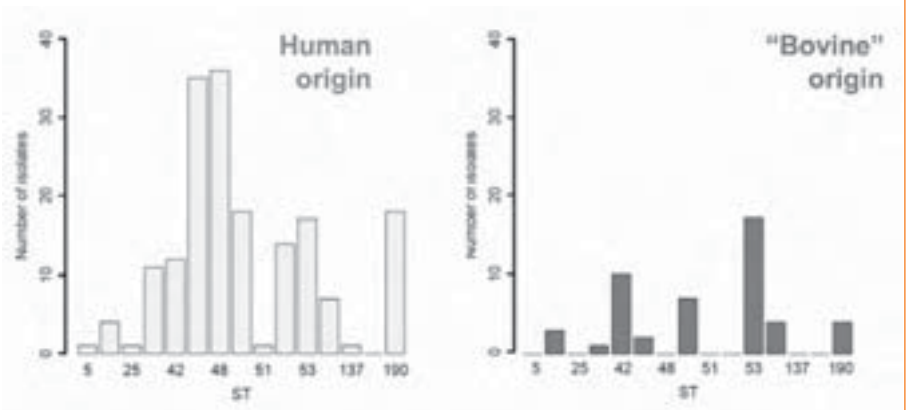
Source attribution

- Molecular tools and modelling
  - Proportional similarity
    - Area of overlap
  - Dutch model
    - Simple deterministic assignment
  - Hald model
    - Bayesian model assignment with uncertainty
  - Island model
    - Population genetics approach

Proportional Similarity Index (PS)

The PS estimates the area of overlap between the frequency distributions of e.g. bacterial sub types from different sources.

Comparison source	Proportional Similarity index	Lower 95% CI	Upper 95% CI
Poultry	0.51	0.45	0.55
Cattle	0.35	0.28	0.40
Sheep	0.30	0.24	0.34
Water	0.15	0.08	0.20
Wild bird	0.10	0.06	0.13



The Hald model (Hald et al 2004)

Number of cases of type i attributable to food source j → $\lambda_{ij} = p_{ij}(M_j a_j) q_i$

- p_{ij} = matrix of prevalence of different strain types
- M_j= relative amount of food consumed
- a_j = relative 'danger' of food (or environmental) sources.
- q_i = relative 'virulence' of strains.

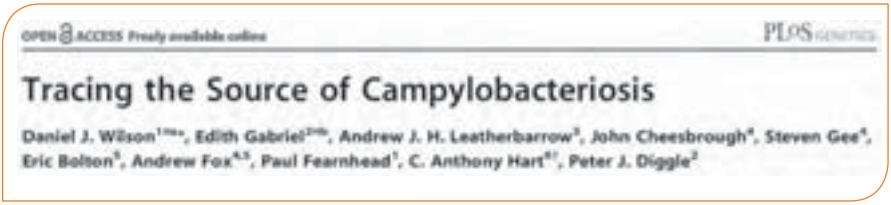
Estimates number of cases with measure of uncertainty (Bayesian inference)

Modified Hald Model

- Model prevalence uncertainty
- Hierarchical model for bacterial parameters (q)
- Exponential prior for source specific parameters (a)
- Omit food consumption weights (M)
- Include potentially pathogenic subtypes

Island model (Wilson et al 2008)

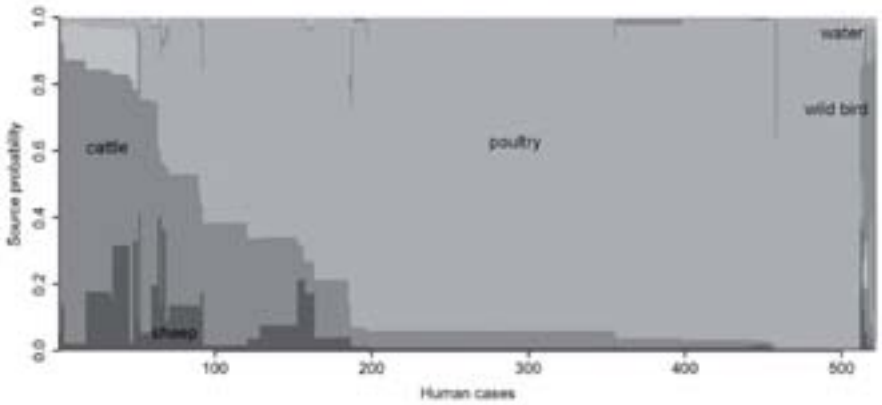
- Population genetics approach
- Genealogical method based on 'coalescent'
  - Cross-validation
- Use MLST data in animal populations ("islands") to estimate:
  - Mutation rates
  - Recombination rates
  - Migration rates (inter-host transmission)
- From these estimate 'migration' into human population
  - Source attribution


OPEN ACCESS Freely available online PLOS GENETICS

Tracing the Source of Campylobacteriosis

Daniel J. Wilson[1]*, Edith Gabriel[2]b, Andrew J. H. Leatherbarrow[3], John Cheesbrough[4], Steven Gee[4], Eric Bolton[5], Andrew Fox[4,5], Paul Fearnhead[1], C. Anthony Hart[6,7], Peter J. Diggle[2]

Source attribution in New Zealand: Island model



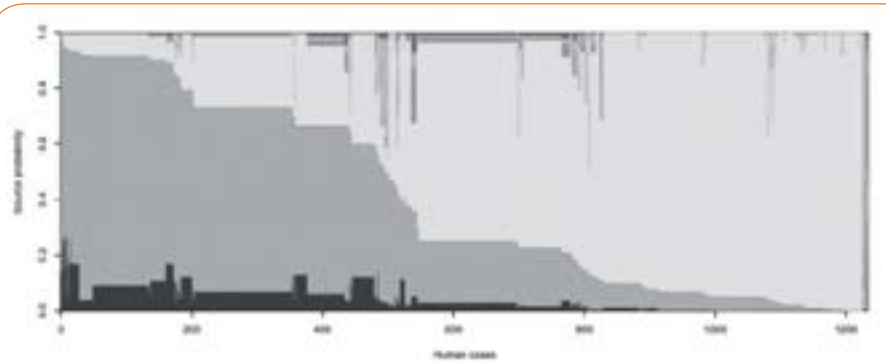
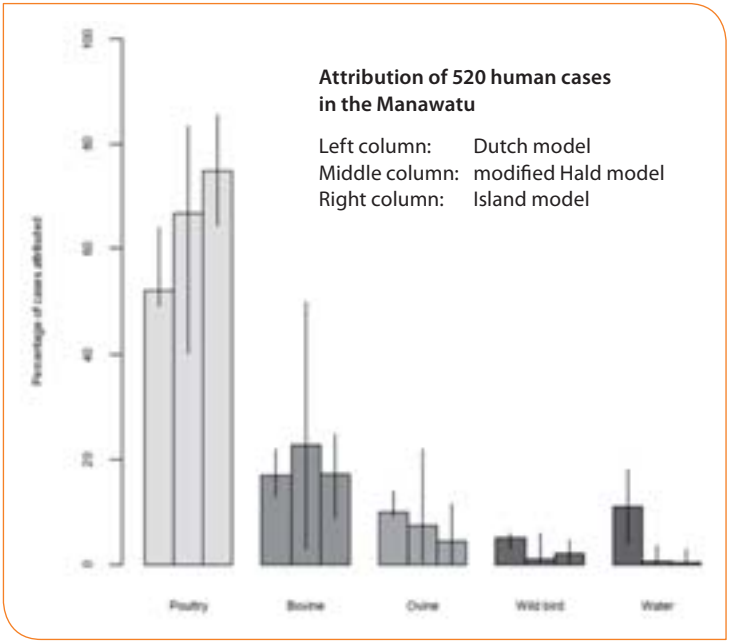


Figure 2. Probability of source for human cases. The source probability for 1,211 human cases (vertical columns) is depicted for Chicken (yellow), Cattle (red), Sheep (blue), Pig (pink), Bird (green), Rabbit (purple), Sand (beige) and Water (cyan). The isolates have been ordered horizontally to aid visualization.

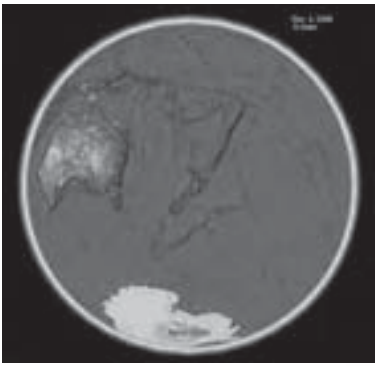
D. Wilson, Lancaster University, UK

Source attribution: comparing models



Comparing models

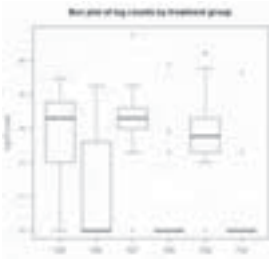
- PS index and Dutch models easy to compute
- m. Hald and Island models include more of information from data – more complex
- m. Hald model captures food and pathogen factors
- Island model can assign all human cases
- Therefore… recommend multiple, comparative approach…



NEW ZEALAND nzfsa FOOD SAFETY AUTHORITY

Campylobacter in Poultry – Risk Management Strategy 2007 - 2010

Poultry industry intervention trials



Post spin-chill:

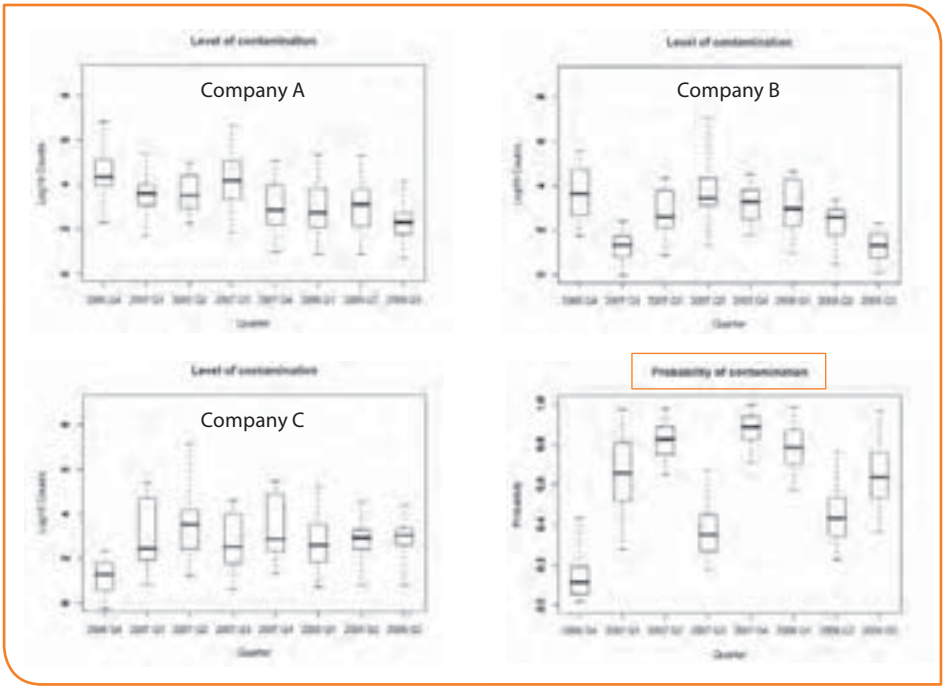
Tasker blue (Sulphuric acid and copper)

Sanova (ASC)

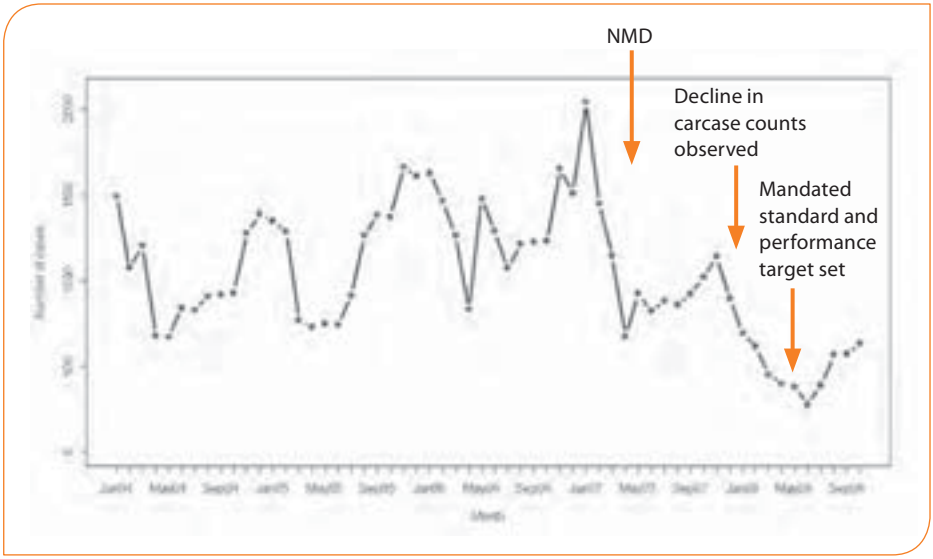
Pre spin chill:

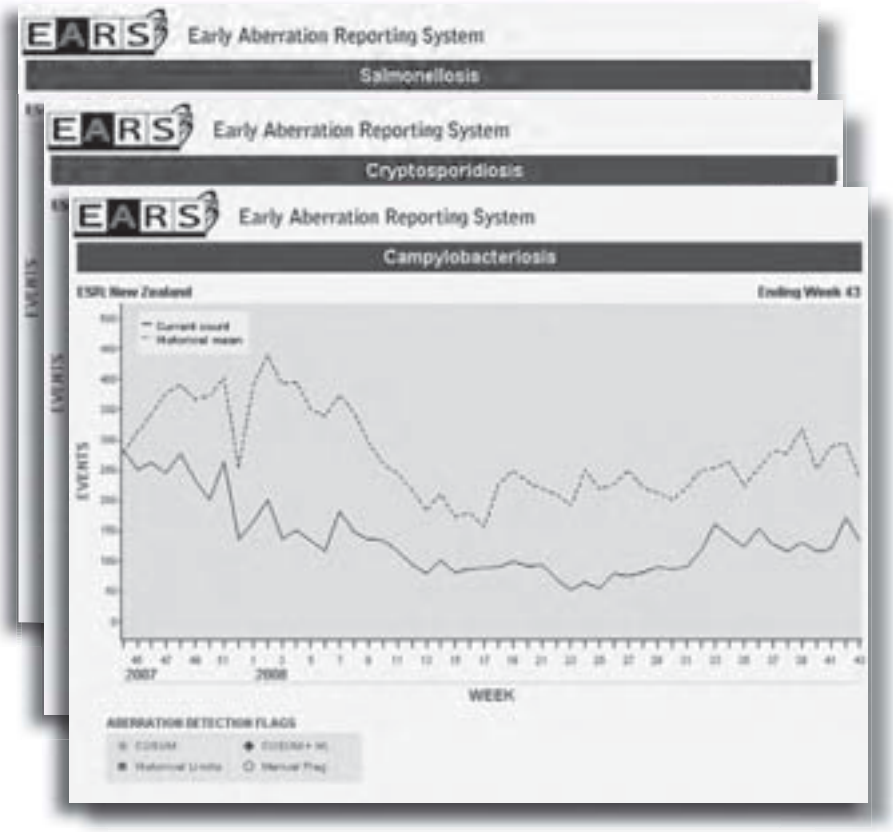
Inspexx
(hydrogen peroxide and peroxyactic acid)

Poultry – count data at retail



Recent trends in New Zealand




EARS
Early Aberration Reporting System
Salmonellosis
EARS
Early Aberration Reporting System
Cryptosporidiosis
EARS
Early Aberration Reporting System
Campylobacteriosis
ESR, New Zealand
Ending Week 43
Current count
Historical mean
EVENTS
2007
2008
WEEK
ABERRATION DETECTION FLAGS

Conclusions

- New Zealand has unique epidemiology
  - Rural ruminant exposure in young children
  - Urban poultry across all ages
  - Dominant strain: ST474
- Source attribution modelling
  - Tools advanced in recent years
  - Applied to Campylobacter identified food, particularly poultry, most important source, cattle second
- Focussing on poultry – early signs of success
- Environmental exposures less well defined
  - May become more important
  - Ruminants and wildlife

Acknowledgements

NZFSA-funded

- Staff - lecturers
  - Dr Eve Pleydell, Dr Deb Prattley
- Postdocs / RAs
  - Dr Simon Spencer,
    Dr Jonathan Marshall,
    Dr Anne Midwinter,
    Dr Julie Collins-Emerson
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  - Rebecca Pattison, Rukhshana Akhter, Errol Kwan,
    Lynn Rogers, Isabel Li, Jim Learmonth, Anthony Pita,
    Sarah Vaughan,
- PhD students
  - Petra Mullner, Vathsala Mohan,
- Masters students
  - Particularly Tui Shadbolt….

- ESR - Phil Carter, Sharla McTavish
- AgResearch – Grant Hotter
- CDRP team
  - NIWA – Graham McBride
  - ESR – Rob Lake
  - NZFSA – Peter van de Logt
- Palmerston North Hospital / MedLab
- Massey – IMBS, IFNHH, IFS
  - Allan Wilson Centre
- Universities of Liverpool, Lancaster, Oxford
- Industry

Campylobacter Risk Assessment in the EU: Past, present and future.

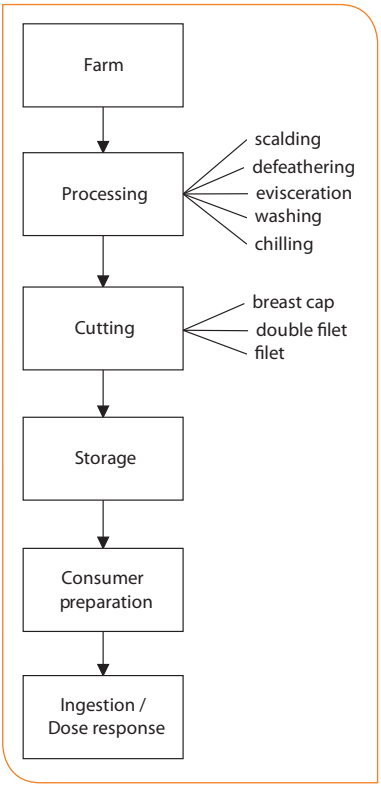
MAARTEN NAUTA
RIVM, The Netherlands

Overview

- Past
  - MedVetNet WP 24: a comparison of *"Campylobacter* in broiler meat risk assessments" in Europe
- Present
  - A consensus framework: CRAF
- Future
  - Challenges of European *Campylobacter* QMRA

Risk assessment: what do I mean?

- Food chain risk assessment
- Model describes transmission and survival of *Campylobacter* in the broiler meat chain: changes in distribution of concentrations
- Exposure assessment
  + Dose response = risk
- Quantitative Microbiological Risk Assessment (QMRA) is still developing!



Why we need risk assessment

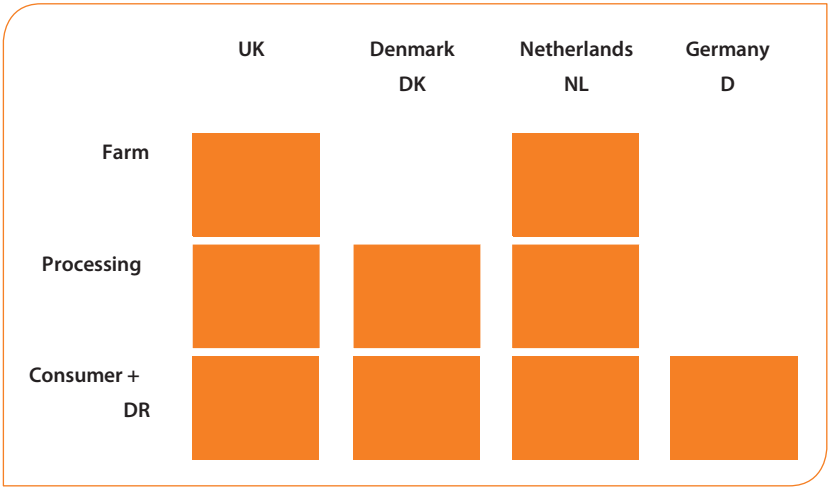
- **Relative** risk estimates
  - The effects of control measures
  - Comparison of interventions all over the food chain
- Added value
  - food chain data
  - epidemiology
  - below the detection limit
  - check our understanding
- Indispensable for PO / target setting

Campylobacter *in broiler meat risk assessments in Europe*

UK	Hartnett	2001
Denmark	Rosenquist, Christensen	2003
Netherlands	Havelaar, Nauta	2005
Germany	Brynestad	2006
Belgium	Uyttendaele	2006
	Gellynck, Messens	2008
Sweden	Lindqvist, Lindblad	2008
Italy	Calistri, Giovannini	2008

MedVetNet Workpackage 24
March 2006 - June 2009

- Objective: consensus on *Campylobacter* QMRA?
- UK, DK, GE, NL models compared
  - Input from New Zealand and FAO/WHO risk assessment
- Differences
  - objectives
  - approach
  - models
  - results
- Similar conclusions



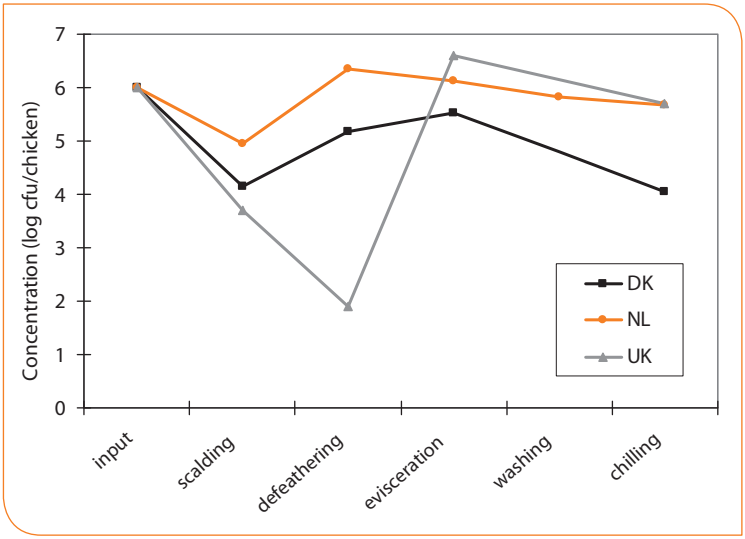
Different objectives

- Gain risk assessment modelling experience
- Human incidence estimation
- Evaluation of risk reduction after intervention and control
  - general
  - specific interventions
  - incl. economic analysis
- Interaction with risk management

Differences between models

- objectives
- expertise of modellers
- national differences
- data and/or expert opinion
- statistical description and/or dynamic model
- details included in the models
- channel assignment
- end product
  - whole carcass
  - specific product
  - side dish
- but all use quantitative risk assessment
  - probabilistic models

Differences between model results
example



Three chicken processing models with the same input

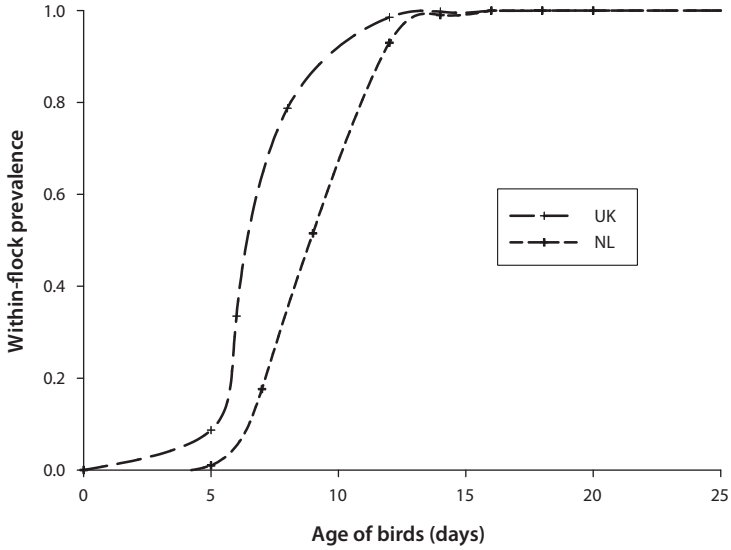
- different dynamics
- similar end results
- similar effects of interventions (?)

Different end results ?

- Varying human incidence estimates
  - Differences in models, (national) data and assumptions
  - Risk estimates are uncertain
  - Not easy to decide what is the "main cause" of differences in results
- Evaluation of risk reduction after intervention
  - In general similar, despite quantitative differences
  - Relative risk estimates are less uncertain

Similar conclusions (1)

- Farm models predict many low prevalent flocks at the farm that may not be detected



source: Nauta et al *IJFM in press*

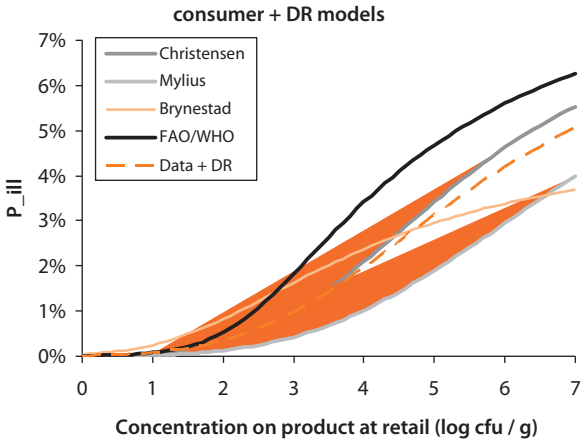
- False negative flocks occur frequently

Similar conclusions (2)

- "Logistic slaughter" has little effect
  - No growth of *Campylobacter* in processing environment
  - Each model MUST predict that concentrations on carcasses of cross contaminated flocks are lower
- Data:
  - Typing shows *Campylobacters* are transmitted from one flock to the other (e.g. Miwa *et al.* 2003)
  - Transferred quantities are small (Johannessen *et al.* 2007)

Similar conclusions (3)

- High concentrations pose the largest risks



Nauta et al, *unpublished results*

  - targetting high concentrations is an effective intervention
  - get data on distributions of concentrations, not just means
  - confirmed by Callicott *et al.* (2008)

Conclusions from WP 24

- QMRA model must be fit for purpose
  - different purposes require different models
  - balance between simple and complex
- Many modelling methods explored
  - try to combine the good qualities of different models
- Similar conclusions !
  - useful insights for risk managers
- No consensus European Risk assessment Model
  - no single purpose, many national differences
- Towards a consensus Approach
  - development of *Campylobacter* Risk Assessment Framework (CRAF)

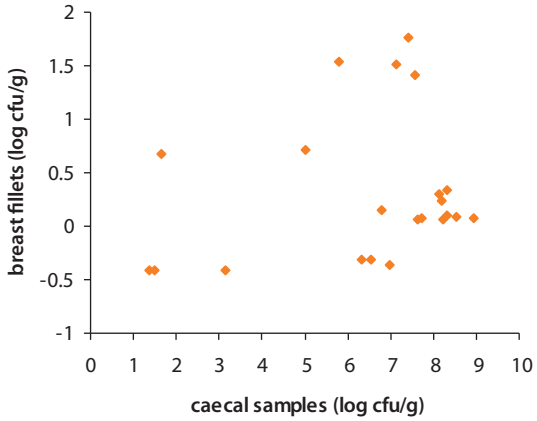
Campylobacter *Risk Assessment Framework CRAF*

- Software tool for risk assessors
- Structured information on five Campy QMRAs
- Compare and link models for modules
- An aid to make your own Campylobacter QMRA

New Campylobacter QMRA in Europe (1)

- Baseline data from caeca and neck skins
- Challenge: how to relate those data to risks?
  - QMRA models don't have either of them as inputs
  - Data don't always show a good link caecal samples - meat products; why not?

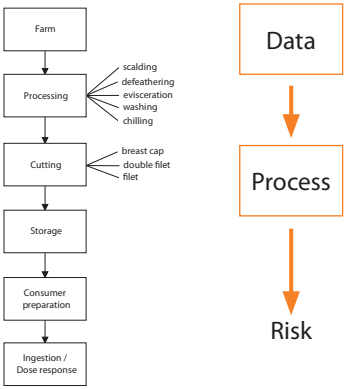
		caeca		
		-	+	tot
product	-	17	19	36
	+	4	22	26
	tot	21	41	62



source: Nauta, Bolder et al, *in prep.*

New Campylobacter QMRA in Europe (2)

- Target setting: link with human health risks



- Challenge: How to model the differences for each MS?
  How important are those?

Take away messages

- Much *Campylobacter* QMRA experience in Europe, but
  - different objectives and approaches
  - different results

  still
  - similar and useful conclusions
- European *Campylobacter* QMRA needs
  - a clear objective
  - further development of QMRA modelling
    - integration of good ideas
    - balance between complexity and simplicity
    - incorporation of differences between MS

Fluoroquinolone resistant *Campylobacter*

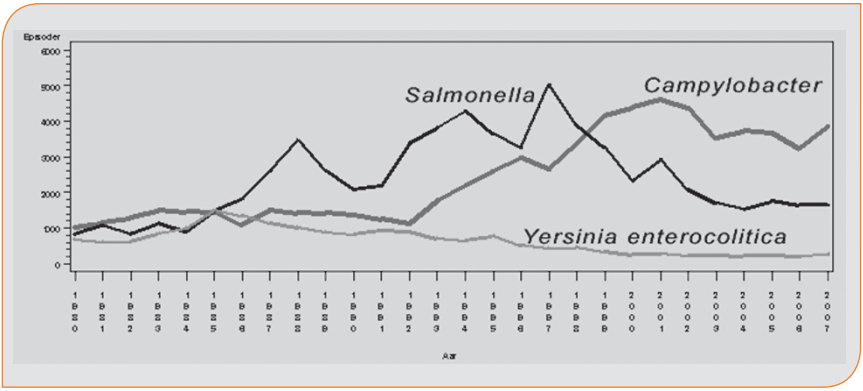
Epidemiology and risk assessment

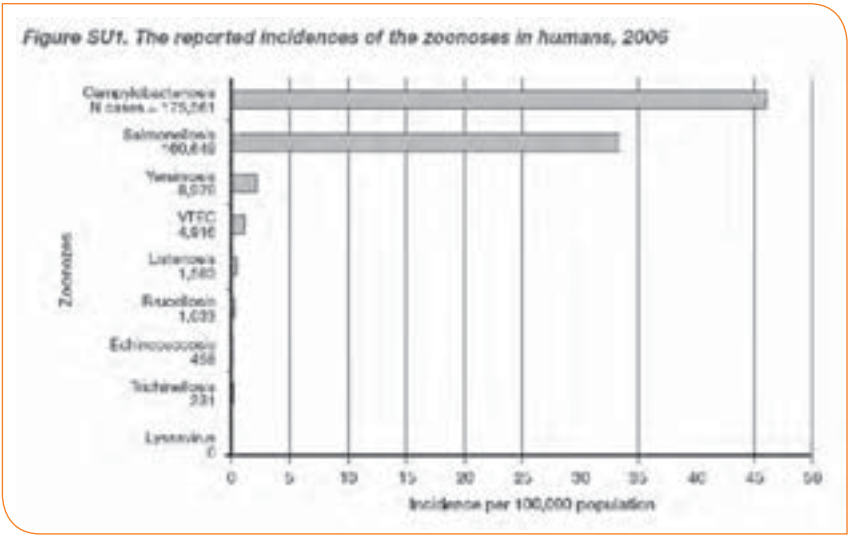
FRANK M. AARESTRUP
CRL Antimicrobial Resistance
National Food Institute, Denmark

Campylobacter jejuni/coli

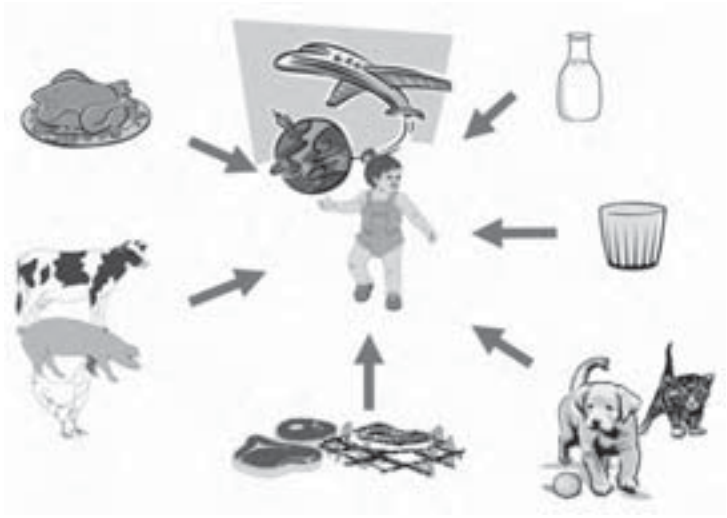
- Primary foodborne pathogen in most developed and developing countries
- Few specific control strategies available
- Antimicrobial resistance a growing concern

Zoonoses in Denmark

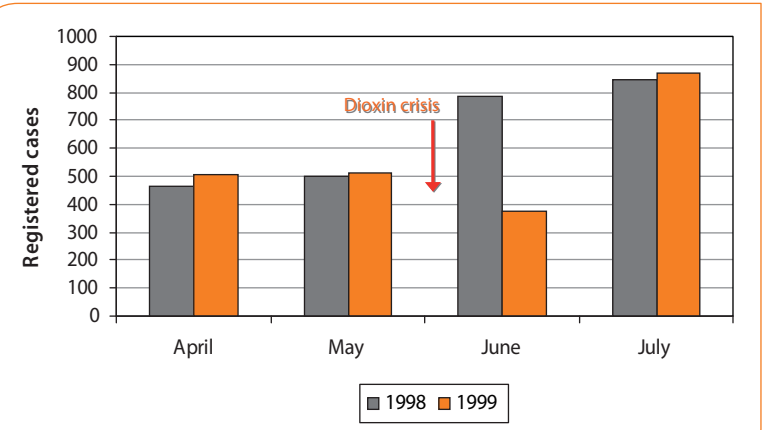




Sources of campylobacteriosis



Campylobacteriosis incidence in Belgium

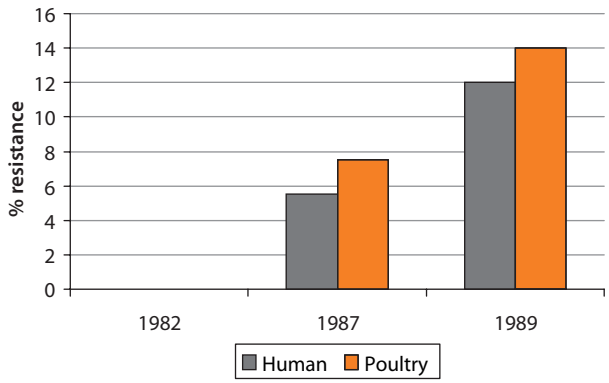


Data: Dr. Frank van Loock

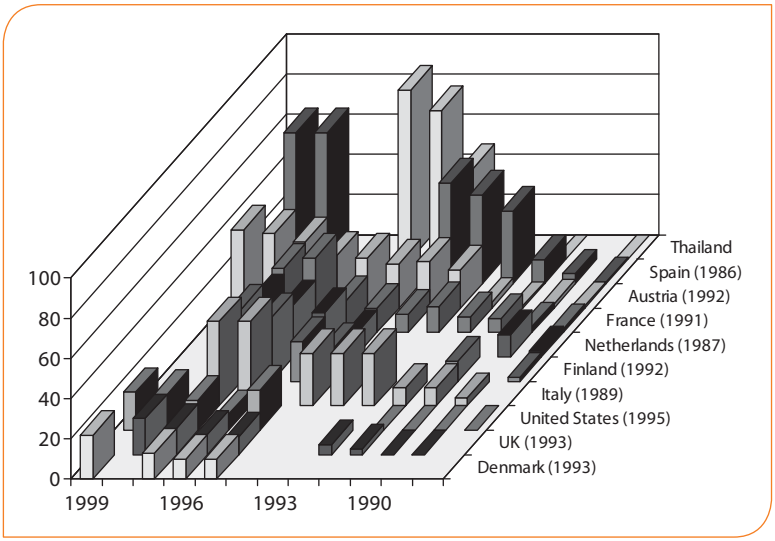
The basics

- Most or second most common zoonoses
- Most studies have indicated poultry as the main reservoir
- Resistance mediated by mutations in gyrA
  - Ala-70 to Thr
  - Thr-86 to **Ile**, Lys, Ala, Val
  - Asp-90 to Ala, Asn, Tyr
- Thus, spread of resistance is with the clone
- Large clonal instability – difficult to determine the spread

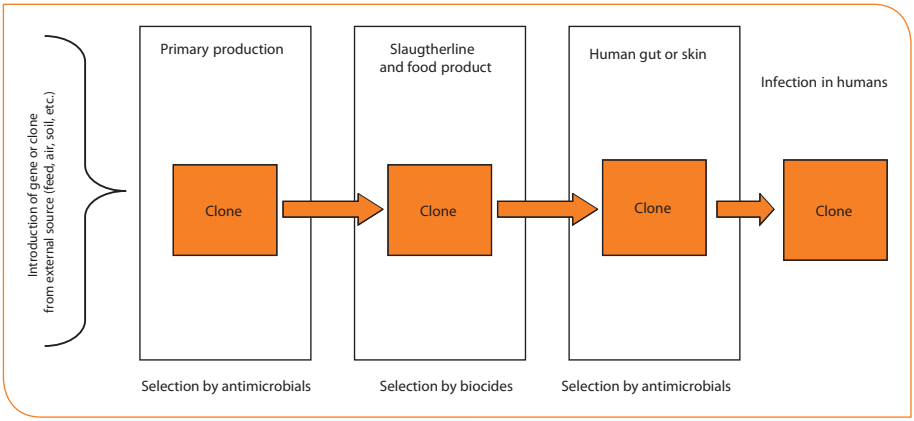
Fluoroquinolone resistance in Campylobacter



Endtz et al. *1991*



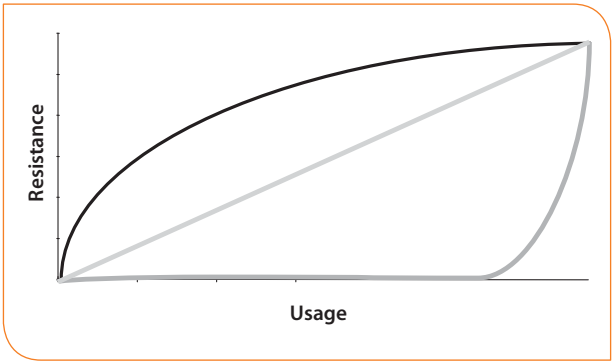
Campylobacter *FQ -resistance epidemiology*



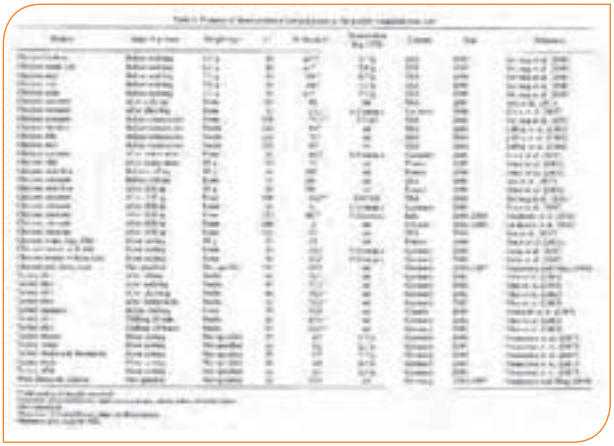
Experimental studies on the emergence of antimicrobial resistance in Campylobacter *following treatment.*

Author and reference	Animal species	Number of experiments and number of animals in each group	Treatment	Outcome
Takahashi *et al.* (112)	Chickens	**Study 1.** Two groups of 15 chickens inoculated with 106 *C. jejuni* ATCC 33560 at day 17. **Study 2.** Two groups of 15 chickens inoculated with 107 and 108 *C. jejuni* ATCC 33560, at day 18 and 23, respectively.	50 ppm enrofloxacin in drinking water for three days to one group	**Study 1.** *C. jejuni* were isolated from approximately 50% of the control group and disappeared from the administration group during treatment. No resistant isolates were found. **Study 2.** Isolation of *C. jejuni* from most chickens and a 100% resistance from the administration group.
Van Boven *et al.* (11)	Chickens	Sixteen individually housed chickens colonized with FQ-susceptible *C. jejuni* at day 8, from day 21 eight chosen for further study.	50 ppm in drinking water from day 21 to 30 to 6 of the 8 chickens	In 5 chickens of the treatment group an emergence of FQ-resistant isolates were observed.
McDermott *et al.* (64)	Broiler chickens	**Study 1.** Two groups (treatment and control) of 25 chickens each. Colonized with a mixture of 5 *C. jejuni* strains. **Study 2.** Two groups (treatment and control) of 50 chickens each. Colonized with a mixture of 5 *C. jejuni* strains.	**Study 1.** Enrofloxacin at 40 ppm in drinking water for five days. **Study 2.** Sarafloxacin at 40 ppm in drinking water for five days.	Rapid and persistent emergence of ciprofloxacin resistance in *C. jejuni*.
Delsol *et al.* (23)	Piglets	Two groups of six piglets	One group given 15 mg enrofloxacin / pig/day for five days.	FQ-resistant *C. coli* found at levels of 40-80% in the treated group.
Lin *et al.* (55)	Broiler chickens	**Study 1.** Three experiments with 10-15 chickens in each group. A control and a treatment group. Experiment A was inoculated with a mixture of two *C. jejuni* strains. Experiment B with a mixture of two *C. coli* strains and experiment c with a *C. jejuni* strain. **Study 2.** Two experiments with 9-11 chickens in each group all inoculated with an *C. jejuni* strain.	**Study 1.** Tylosin at 0.53 g/L in drinking water for three days for experiment A and B. Three times treatment with tylosin at 0.53 g/L in drinking water for three days. **Study 2.** Tylosin at 50 mg/Kg feed for 41 days.	**Study 1.** No emergence of erythromycin resistant isolates. **Study 2.** Erythromycin resistance emerged at 17 and 31 days after inoculation, respectively.

Usage – resistance relationships



Exposure



Exposure and dose-response just as for all other *Campylobacter*

Consequences

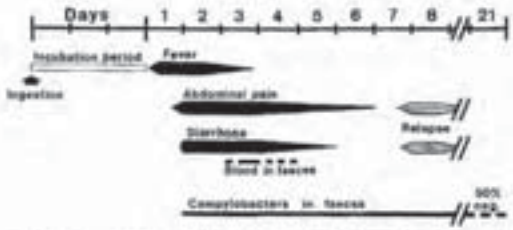


Figure 1. Diagram illustrating the typical course of *Campylobacter* enteritis. Reprinted from D. Greenwood, R. Slack, and J. Peutherer (ed.), *Medical Microbiology*, 13th ed. (Churchill Livingstone, Edinburgh, 1997).

Approx. 2-3 days additional illness

Part conclusion

- Use of FQ selects for resistance
- Exposure and infectivity as for other *Campylobacter* (NB patients in ciprofloxacin treatment)
- Consequences 2-3 days additional illness

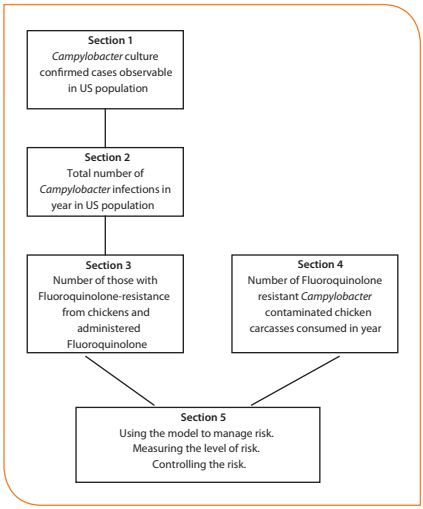
FDA Fluoroquinolone-Resistant Campylobacter *Risk Assessment*

- To determine the feasibility of estimating risk to human health
- Possible regulatory tool for assessing future risks
- Possible tool for establishing regulatory "triggers" based on surveillance

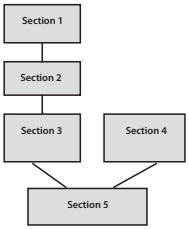
http://www.fda.gov/cvm/default.htm

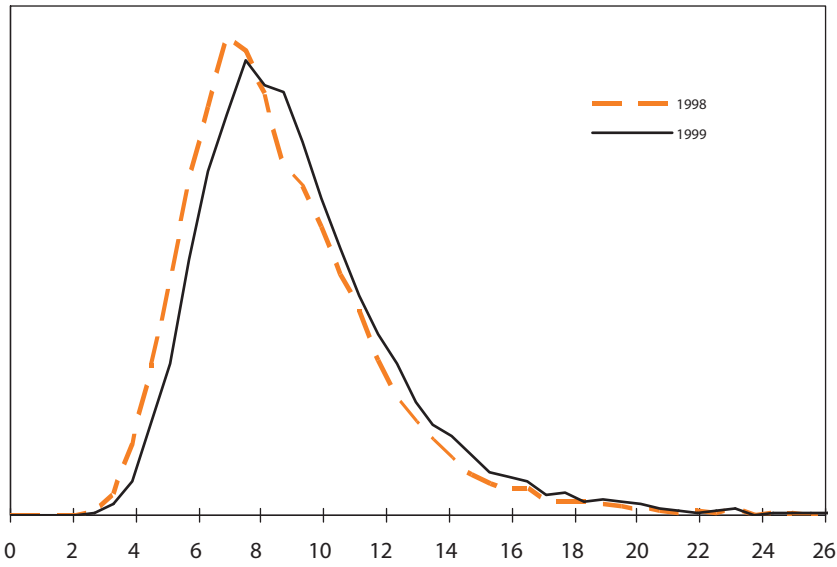
Fluoroquinolone resistant Campylobacter *in poultry*

- FDA-CVM / Vose2000
- This model relates a number of contaminated carcasses N consumed domestically to the number of illnesses I that resulted.
- It then predicts that for a future number of contaminated carcasses n, there will be i infections where: i=n*(I/N)
- Model assumes that practices after production remain the same, but has some ability to make corrections
- Model ends up with exactly the same behaviour as the Danish model!



Symbol	Description	Formula
Section 1	**Expected nominal number of observable confirmed cases**	
n_{US}	US population	Data
n_{FN}	FoodNet catchment population	Data
o_i	FoodNet observed invasive cases of *Campylobacter*	Data
o_e	FoodNet observed enteric cases of *Campylobacter*	Data
λ_i	Expected observed FoodNet invasive cases of *Campylobacter*	=Gamma(o_i,1)
λ_e	Expected observed FoodNet enteric cases of *Campylobacter*	=Gamma(o_e,1)
N_i (= $N1_i$)	Nominal observed mean invasive infections in population	$=\lambda_i * n_{US} / n_{FN}$
N_e	Nominal observed mean enteric infections in population	$=\lambda_e * n_{US} / n_{FN}$
p_b	Proportion of enteric infections with bloody diarrhea	Beta distribution based on data
$N1_{eb}$	Nominal mean number of confirmed enteric infections in population with bloody diarrhea	$=N_e * p_b$
$N1_{en}$	Nominal mean number of confirmed enteric infections in population with non-bloody diarrhea	$=N_e*(1- p_b)$



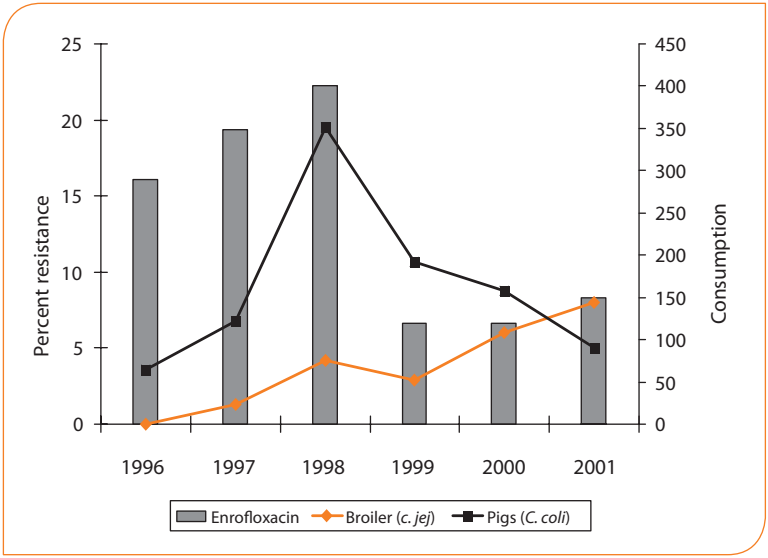


What is an acceptable level of risk?

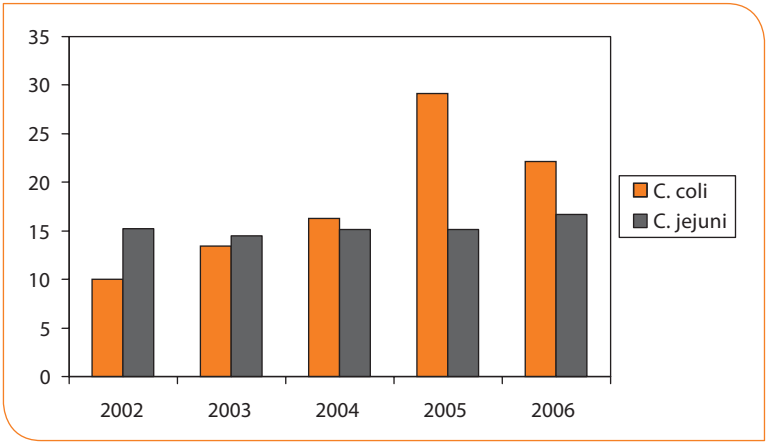
Example Assumptions - FDA Risk Assessment

- Fluoroquinolone resistance (after removal of travelers, those who took a fluoroquinolone prior to culture and those for whom the time of taking the fluoroquinolone was unknown) is attributed to chickens
- The incidence rates for culture-confirmed *Campylobacter* infections in the FoodNet catchment are representative of incidence rates for culture-confirmed *Campylobacter* infections in the United States.
- The CDC study estimate on number of stool samples taken at the doctors office as remembered by the patient (18%) was better than the estimate as remembered by the doctor (78%).

Quinolone resistance among pathogenic Campylobacter



Ciprofloxacin resistance among Campylobacter *from chicken breast in US*

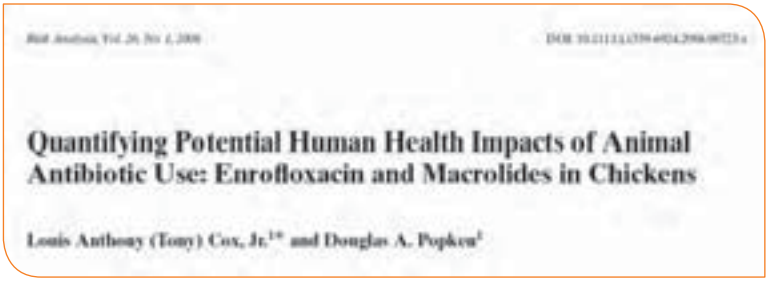


In conclusion

- FQ selects for resistance
  - The effect of different treatment regimes has not been determined
- It is possible to model the expected number of cases and additional effects
  - Requires a lot of data and money to generate those data
- The effect of withdrawal not well documented (however, continuing must be expected to be worse)

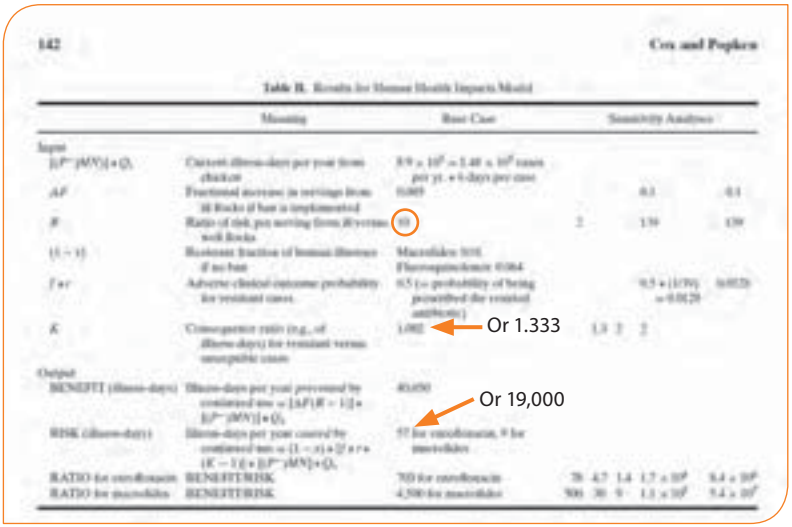
The solution

- Ban all use of fluoroquinolones?

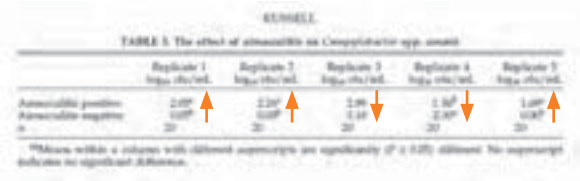


Quantifying Potential Human Health Impacts of Animal Antibiotic Use: Enrofloxacin and Macrolides in Chickens

Louis Anthony (Tony) Cox, Jr.[1*] and Douglas A. Popken[1]



f and r already included in the estimate of K



10.45 / 5 = 2.09
5.45 / 5 = 1.09

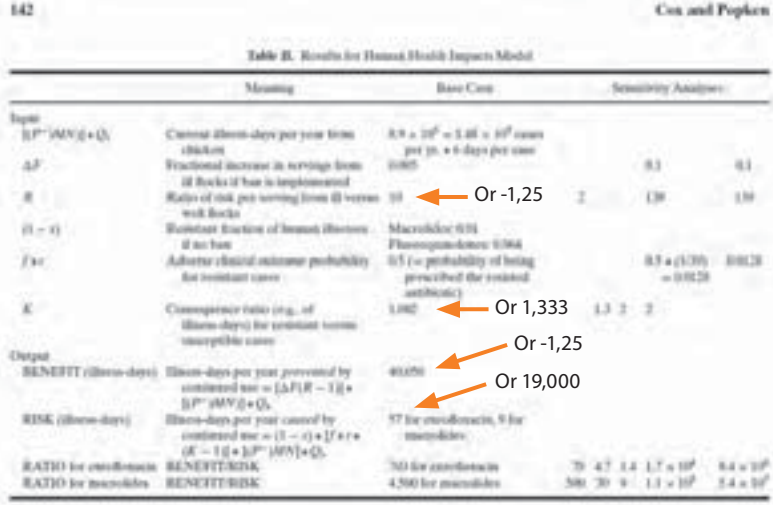
Diff. 10 x higher load of *Campylobacter* from AS positive flocks

Actual numbers:

Positive: 123 + 182 + 776 + 36 + 49 = 1166 / 5 = 233

Negative: 1 + 0 + 1259 + 200 + 0 = 1460 / 5 = 292

Diff. 1,25 x higher load from AS negative flocks



f and r already included in the estimate of K

Conclusions Cox & Popkten

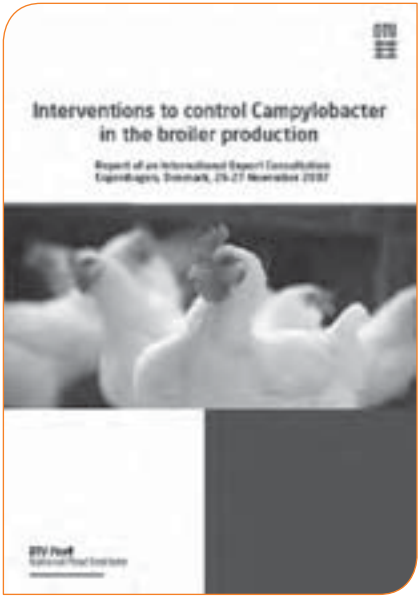
- Some mistaken factors and numbers
- No uncertainty estimates
- Numbers could be looked at differently

- Useful for pointing out that potential benefits might also arise from the use of antimicrobials to animals

Measures to control *Campylobacter* in broilers and broiler meat

HANNE ROSENQUIST
Technical University of Denmark

Report of Expert Consultation



www.vet.dtu.dk/Default.aspx?ID=8561

Talk outline

- Recommendations from an Expert Consultation on interventions to control *Campylobacter* in the broiler production
  - pre-slaughter measures
  - post-slaughter measures
- Experiences from EU countries which have implemented interventions
  - implemented interventions
  - changes in prevalence of broiler flocks
  - changes in number of human cases
- Conclusions

Thanks to

- Ingrid Hansson
- Mats Lindblad
- Merete Hofshagen
- Gro Johannessen
- Sigurborg Dadadottir
- Jarle Reiersen
- Jaap Wagenaar
- Maarten Nauta
- Wilma Jacobs-Reitsma
- Nico Bolder
- Andy Hill
- Viv Allen
- **Frieda Jørgensen**
- Mark Berrang
- Peter van der Logt
- Steen Nordentoft
- Anne Wingstrand
- Birthe Hald
- Ole Heuer
- Flemming Bager
- Helle Sommer
- Bjarke Christensen
- **Birgitte Borck**
- **Louise Boysen**

Aim of expert consultation

- to provide information and recommendations on the most useful interventions in the broiler production for reducing the human exposure to *Campylobacter*
- to facilitate and guide the decision-making for a new Danish five-year action plan for *Campylobacter* in broilers and broiler meat

Experts were asked

- To identify and discuss the pros and cons of different intervention methods, before, at and post slaughter
- To evaluate interventions in terms of effect, cost, applicability, and consumer acceptability
- To prioritise and evaluate the interventions they believed to be most useful under Danish conditions

The conclusions of the expert consultation are, therefore, not necessarily applicable in other countries where the *Campylobacter* prevalence in broilers is different to that of Danish broilers or where different legislation applies, e.g. legislation on the use of chemical decontaminants.

Interventions before slaughter

- Two categories relating to **mechanism**
  1. Interventions aimed at preventing flocks from being colonized
  2. Interventions aimed at reducing the concentration of *Campylobacter* in the broiler chicken gut after colonization

Intervention	Prevents colonization of flocks	Reduces concentration in gut	Ready to implement	Needs further development
Biosecurity				
Farm/farmer hygiene	+	-	+	-
Environment around broiler houses	+	-	+	-
Insect control (fly screens)	+	-	(+)	+
Slaughter broilers young	+	-	+	-
Thinning	+	-	+	-
Drinking water / feed additives Organic acid, lactictic acid bacteria caprylic acid, …	+/-	+	+/-	+
Phage therapy	-	+	-	+
Bacteriocins	-	+	-	+
Vaccination	+	-	-	+
Genetic resistance -broiler breeds able to clear campy	+	-	-	+
Water supply quality (chlorinated, UV)	+	-	+	-
Reduced presence of other animals	+	-	+	-

Interventions before slaughter - given a high score

Intervention	Pros	Cons
Biosecurity		
Farm/farmer hygiene	Applicable, efficient,	Consistent compliance?
Environment around broiler houses	low costs	No guarantee of free flocks
Insect control (fly screens)	Good effect –if other biosecurity measures are in place, relatively low costs	Not commercially available
Slaughter broilers young (31-33 days)	Applicable Effective in Iceland	Relatively costly Not always possible if a special size is required
Thinning – hygiene precautions by catchers	Production more profitable Possibility of different bird sizes	Difficult to thin without causing breach of biosecurity

Interventions before slaughter - given a low score

Intervention	Pros	Cons
Drinking water / feed additives Organic acid, bacteria, caprylic acid, probiotics,fatty acids, …	Easy to apply Relatively cheap	No clear indication that these work efficiently May need legal changes Needs further investigation
Phage therapy	Documented effect	Reduction of *Campylobacter* may be short lived – development of resistance Needs further development
Bacteriocins	Documented effect under experimental conditions	Needs legal changes Needs further investigation
Vaccination	Could be good	Needs investigation
Genetic resistance – broiler breeds able to clear campy	Could be good	Needs investigation
Water supply quality (chlorinated, UV)	Documented effect	Difficult to maintain
Reduced presence of other animals	Evidence that it is a risk factor	Difficult to change on current farms, but relevant in relation to location and design of new farms

Interventions before slaughter - prioritized interventions

- Biosecurity measures in and around farms
- Fly screens
- Improved procedures re thinning of flocks

Biosecurity – farm/farmer hygiene

Ante-room

Empty period, proper cleaning

Biosecurity – environment around broiler houses

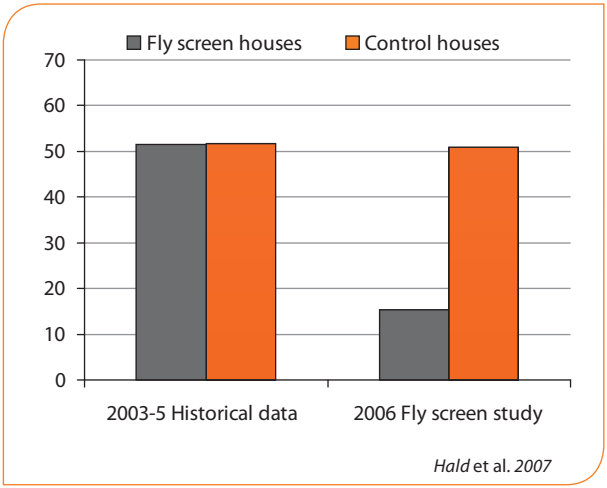
Vegetation free zone

Drained zone

Dust free zone

Biosecurity – insect control, fly screens

% Campylobacter positive flocks at slaughter June - November 2003-5 and 2006



Hald et al. *2007*

Interventions at slaughter

- Two categories:

1. **Hygienic measures** - interventions aimed at reducing fecal contamination (GMP)
2. **Decontamination** - interventions aimed at reducing the concentration on carcasses
   - **Chemical** (**acidified sodium chlorite**, chlorine, **chlorine dioxide**, **trisodium phosphate**, cetylpyridinium chloride, ozone, and peroxy acids)
   - **Physical** (freezing, crust freezing, steam-ultrasound, steam/hot water, forced air chilling, heat treatment, irradiation)

Interventions at and after slaughter - given a high score

Intervention	Pros	Cons
Scheduled slaughter followed by decontamination of positive flocks or production of safe to handle products (e.g. oven-ready or ready-to-eat)	Proven effect May be based on past performance to limit testing Production of safe to handle products may be cheap	Pre-slaughter testing, expensive, needs a low prevalence Needs a marked
Physical decontamination that leaves the meat fresh		
Steam-ultrasound	Fairly effective, relatively low costs	New equipment Needs further development
Crust freezing	Limited effect, may be combined with other methods	Relatively expensive
Forced air chilling	Limited effect, may be combined with other methods	Relatively expensive
Steam or hot water	Fairly effective	Difficult to achieve success i.e. reduction while still maintaining product quality
Marinating – low pH together with food ingredients	May be effective and cheap	Only for a limited production –needs a marked More research needed

Interventions at and after slaughter - given a low score

Intervention	Pros	Cons
Prevention of fecal leakage	May be effective (CARMA)	No equipment developed
Chemical decontamination of all carcasses	Effective, relatively cheap	Needs consumer acceptance Substances needs approval and authorization
Physical decontamination of all positive flocks Freezing Heat-treatment	Effective	Not fresh meat, expensive Risk of marked distortion (opening to imports)
Name and shame - publicity exposing producers and companies, who produce/ sell highly contaminated products	Used in DK (case-by-case risk assessment), seems fairly effective Transparency	Expensive – many batches controlled
Consumer information – labeling about Campy Information on hygiene	Cheap Relatively cheap	Efficacy uncertain Effect minimal
Logistic slaughter – to avoid contamination from positive to negative flocks	Incentive for the industry to do something	Minimal effect, not feasible, expensive
Physical decontamination Irradiation	Very effective	Strong consumer resistance Expensive

Interventions at and after slaughter - prioritized interventions

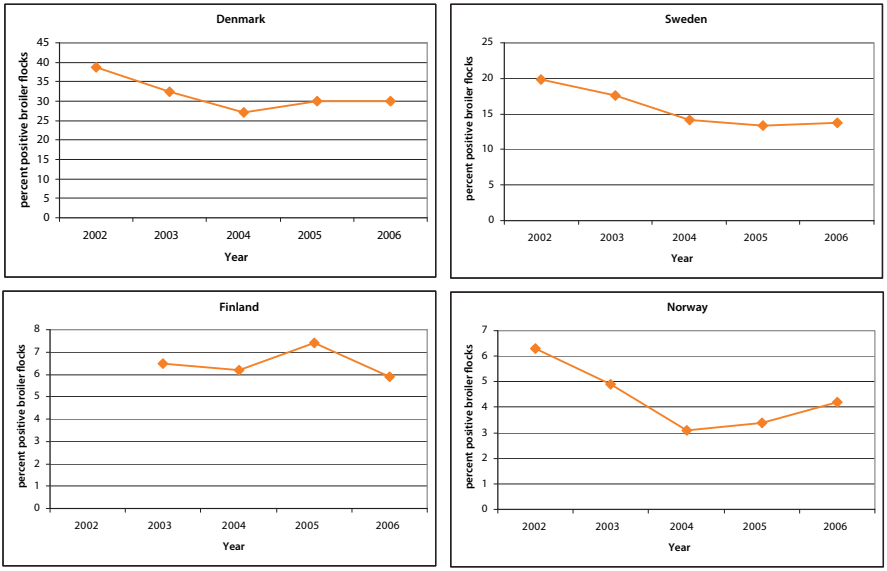
- Channeling of flocks based on Campy history of producers to
  1. decontamination by methods that keep the meat fresh, chilled
  2. Safe to handle products
- Education, especially of children

Table 2. Specific measures within countries with *Campylobacter* control strategies, 2006

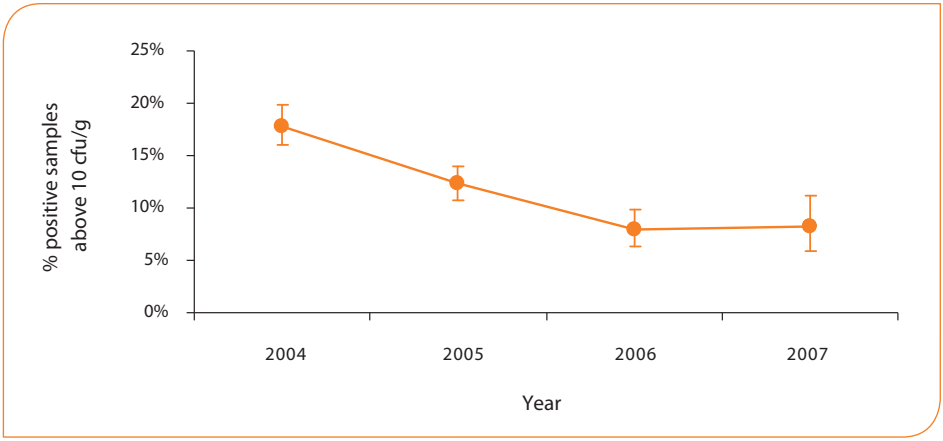
	DK	FI	LT	ES	SE	UK	NO
Year of implementation	2003	2004	2004	N.S.	1991	2003[2]	2001
Mandatory (+/-)	-	+	-	-	+	-	+
Control measures							
FARM							
Biosecurity	√	√	√	√	√	√	√
- Personal hygiene	√	√	√	√	√	√	√
- Buildings	√	√	√	√	√	√	√
- Environment	√	√	√	√	√	√	√
Treatment of drinking water	÷	÷	÷	√	÷	÷	√
Feed additives	√	÷	√	N.S.	÷	÷	÷
ABATTOIR							
Logistic slaughter	√	√	√	÷	÷	÷	÷
Freezing of meat from positive flocks	√	÷	÷	N.S.	÷	÷	√
Heat treatment of meat from positive flocks	÷	÷	√	√	÷	÷	√
Improved GHP[3]	÷	÷	√	√	√	√	√
Removal of faecal contamination	÷	√	√	N.S.	÷	√	√
Use of chemicals	÷	÷	÷	N.S.	÷	÷	÷
RETAIL							
Labelling	÷	÷	÷	÷	÷	√	÷
Leak-proof packaging	√/÷	÷	√	÷	√	√	√/÷
CONSUMERS							
Education	√	÷	√	√	÷	√	÷

Broiler flock prevalences

EU Zoonosis report 2007

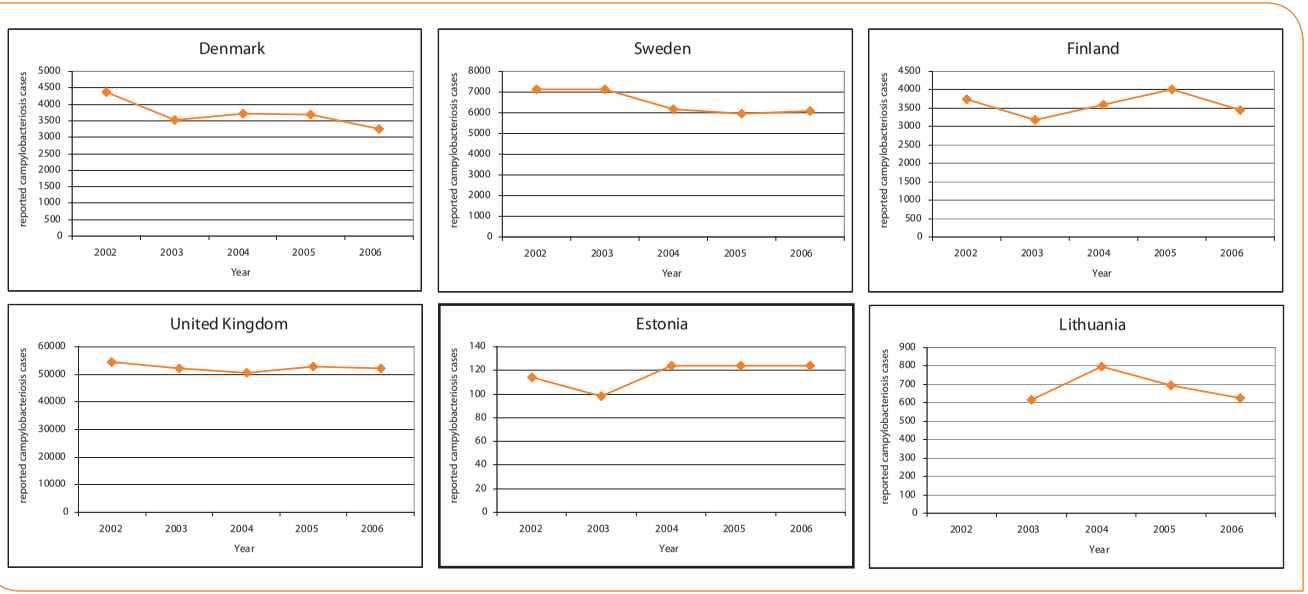


Campylobacter *in broiler meat at two largest Danish processing plants*



Numbers of human Campylobacter *infections*

EU Zoonosis report 2007



Hypothesis of positive effect in Denmark

Economical incentives

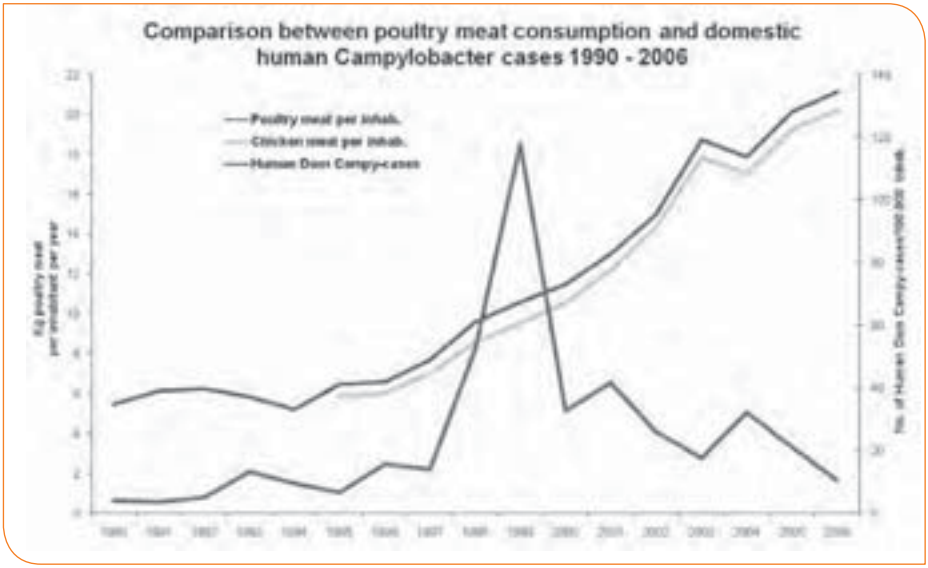
- Rewarding farmers for compliance with industry code of practice
- Rewarding farmers for delivering *Campylobacter* free flocks

Conclusion

With the control measures available:

- It is possible to reduce (not eliminate) the occurrence of *Campylobacter* in broilers and broiler meat
- And to reduce (slightly) the numbers of human *Campylobacter* infections

The Icelandic experience figure borrowed from Sigurborg Dadadottir



ANNEX 4: PRESENTATIONS OF THE DISCUSSION GROUPS

Introduction to Discussion Groups

STEF BRONZWAER
EFSA

Organisation

- 4 discussion groups
- Looking for input from all
- Free scientific debate
- You received briefing notes
- Discussion points: to allow efficient reporting
  - Report back to plenary
  - Summary Report

Programme

- Today: 14.00 – 18.00 Discussion groups
  - Coffee at 16.00 / Buffet 19.00 / Guided Tour 20.30
- Tomorrow: 09.00 – 10.00 Discussion groups
  - Finalise outcome of discussion
- Tomorrow: 10.30 – 13.30 Plenary Discussion
  - Expose groups' work to plenary
  - Provide input to other groups
  - Conclude with overall discussion

Reporting outcome

- Publish PPT-presentations of speakers opening session + short web-story (12 December 2008)
- Planning summary report
  - 1st review by DG chairs and rapporteurs (Jan 2009)
  - Advanced draft to all participants for comments (Feb 2009)
  - Publication of summary report on EFSA website (April 2009)
  - Later in EFSA Science Colloquium Report Series

Composition Discussion Groups

Group number	1	2	3	4
Discussion Group	**Health impact and attribution**	**Quantitative approaches in Risk Assessment in and around the EU**	**Fluoroquinolone resistance in *Campylobacter***	**Assessment of effectiveness of measures**
Chair	Kare MOLBAK	Gilles SALVAT	Guenter KLEIN	Dan COLLINS
Rapporteur	Paolo CALISTRI	Mieke UYTTENDAELE	Hilde KRUSE	Jaap WAGENAAR
	Goutam ADAK	Luca BUCCHINI	Frank AARESTRUP	Thomas ALTER
	Antonio BATTISTI	Luca COCOLIN	Andrea BRTKOVA	Sigurborg DADADOTTIR
	Aivars BERZINS	Roberto CONDOLEO	Sabina BUETTNER	Kris DE SMET
	Maia BERUASHVILI	Ulrike BERNAUER	Paul BRANTOM	Kit Granby
	Louise BOYSEN	Ivelina DAMJANOVA	Pierre COLIN	Zerrin ERGINKAYA
	Lone BRØNDSTED	Maurizio FERRI	Elisabetta DI GIANNATALE	Norbert GINTEN
	Paolo DAMINELLI	Armando GIOVANNINI	Marja-liisa HÄNNINEN	Merete HOFSHAGEN
	Nigel FRENCH	Ihab HABIB	Ida LUZZI	Antonio MARTINEZ LOPEZ
	Marjaana HAKKINEN	Andrea HUMSKI	Dominique MONNET	Diane NEWELL
	Arie HAVELAAR	William KEEVIL	Antonio PARISI	Eva OLSSON ENGVALL
	Mary HOWELL	Roland LINDQVIST	Miguel PRIETO	Lisa O'CONNOR
	Guenter KRAUS	Winy MESSENS	Mati ROASTO	Raymond O'' ROURKE
	Gerardo MANFREDA	Maarten NAUTA	Peter SILLEY	Franco RIGO
	Paolo PASQUALI	Pavel POLLAK	Iva STEINHAUSEROVA	Hanne ROSENQUIST

See overleaf

Composition Discussion Groups ctnd.

Group number	1	2	3	4
Discussion Group	**Health impact and attribution**	**Quantitative approaches in Risk Assessment in and around the EU**	**Fluoroquinolone resistance in *Campylobacter***	**Assessment of effectiveness of measures**
	Anca-violeta STOICESCU	Moez SANAA	Benno TER KUILE	Pavle SEKULOVSKI
	Johanna TAKKINEN	Snieguole SCEPONAVICIENE	Jordi TORREN EDO	Mary TORRENCE
	Wilfrid VAN PELT	Nicola TORNALETTI	Paul WHYTE	Maria Ester TORTUERO
	Ana Cristina VILELA	Peter VAN DER LOGT	Carmen ZIGORRAGA	Emanuela VARANI
	Kinga WIECZOREK	Siamak YAZDANKHAH	Stef BRONZWAER	Ana VIDAL
	Pia MAKELA	Alessandro MANNELLI	Ernesto LIEBANA	Maria Teresa DA SILVA FELICIO
	Eirini TSIGARIDA	Tobin ROBINSON	Valentina RIZZI	Marta HUGAS

An EFSA Colloquium is NOT:

- An attempt to agree on the details of a preferred strategy
- An exercise to define a blue print for the work ahead of us
- A "who is right - who is wrong" discussion

Instead an EFSA Colloquium is:

- Platform for in-depth discussions on scientific approaches, methods available, and tools and data needed for conducting risk assessment
- Event to explore opportunities and limitations
- Opportunity to identify further (research) needs
- Interactive !

Thank you for participating

Wishing you

frank

open and

constructive discussions …

Discussion Group 1

Health impact and attribution of *Campylobacter*

Discussion points

1. Assess the epidemiological evidence on human campylobacteriosis in the EU with a view to identify the extent of the **contribution of foodborne infection**.
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*).
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.
4. Identify possible approaches to establishing the **degree of underreporting** and discuss their applicability at national and EU level.

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

- For those countries where a comprehensive and extensive public health surveillance systems are in place *Campylobacter* is recognised as the leading cause of bacterial zoonotic gastrointestinal illness (refer to ECDC and EFSA)
- Results of epidemiological investigations in sporadic cases and outbreaks indicate the important contribution of *Campylobacter* to the burden of bacterial zoonotic illness
- Substantial number of foodborne outbreaks caused by *Campylobacter* in the last years is observed in the Community Zoonoses Report
- Population-based studies confirm a high campylobacteriosis incidence in humans
- Sero-surveillance studies confirm the high exposure rate to *Campylobacter* by humans
- Studies of burden of foodborne illness suggest that the burden associated to *Campylobacter* infection is substantial particularly when compared with other pathogens that usually are foodborne

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).

- Microbial sub-typing. Some methods coupled with modelling have shown promising results for *Campylobacter* source attribution.
  - Further activities are needed to refine and combine different methods (e.g. PFGE, MLST) to identify the most proper "*markers*" for source attribution purposes.
  - Further work is needed to develop and evaluate models able to assess the contribution of different sources.
  - Culture techniques and sampling procedures may bias the results for source attribution
  - Attention should be given to the interpretation of strains particularly in the environment (source *vs* vehicle)
- Epidemiological studies
  - Case-control studies of sporadic cases have provided useful information.
  - However, they have limitations
    - high degree of exposure and illness limit the applicability
    - Prone to well known biases
    - The interpretation of results may be a challenge (e.g. consumption of ready to cook sliced packed poultry meat as "protective" factor)
  - The combination of this approach with the microbial sub-typing is recommended.
  - The use of spatial analysis methodology for exploring associate risk factors (e.g. age distribution of human cases) may be of benefit.

- **Outbreak investigation** can give useful information on vehicles and pathways.
  - It can not be directly used for source attribution studies, because the distribution of vehicles of sporadic and outbreak cases are unlikely to be the same.
  - However it may give valuable information to better interpret the results of attribution studies, including information on contributing factors (cross-contamination)
  - It can be hampered by the difficulties in obtaining a clear microbiological evidence of the responsible vehicle, but when it combines epidemiology and microbiology in a proper way it is a powerful tool.
- Assessment of interventions should ideally be carried out in the framework of controlled studies.
  - When applied to national control measures the main problem is related to the measurement of PH outcomes, especially when the collection of proper data was not previously planned.
  - Intervention studies should ideally be carried out in pilot areas before the extension to broader scale (pre-test).
  - The results of "*unplanned*" experiments need to be carefully analysed.
- **Expert opinions**. They are useful in particular for risk managers. Should be based on evidence and be updated as knowledge evolves.
- Specific techniques to "weight" the expert opinions exist and should be applied.
- **Exposure assessment**. It addresses pathways taking into account the level of contamination in potential sources. The approach has not been applied broadly and has limitations mainly due to the uncertainty of D-R relationship. At present it can be used to stimulate the generation of hypotheses.

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.

- Data available at **food** chain level:
  - 2008 EU **baseline study** (for chicken only)
  - **Prevalence data** reported in the Community Zoonoses Report derive mainly from (multi)annual national plans. Limited quantitative data are available and data comparability is difficult. They represent a useful background information, but their use in source attribution is limited.
  - **Isolates** are available at some laboratories, but type of collection and related variables are not always known
  - **Production and sales data** are available. The degree of accessibility of these data should be explored. Possible problems for products having a local market.
  - **Import – export and intra-community trade data**. Limitations in accessibility and completeness.
- Data available at **human** level:
  - **Reported cases** in most Countries are available, often at aggregate level
  - **Isolates** are available, but a systematic collection of samples is in place only in few countries.
  - Data from **case-control studies**, **outbreaks**, *etc.* in some Countries
  - Activities to gather **food consumption data** at EU level are ongoing (EFSA)

- Additional data collection at food chain and human level:
  - Priorities to **existing data** sources, availability of which should be explored (general isolates and samples taken during case-control studies).
    An overview of the studies and data suited for source attribution might be of benefit (ECDC – EFSA)
  - Through strengthening public health surveillance systems (case-based reporting of human data, travel history, storage of randomly collected samples)
  - Strengthening surveillance and sampling designs to get comparable information on human disease and food contamination (particularly at retail to be used in exposure assessment approach). "*Sentinel*" sites may be selected around Europe.
  - A consensus should be reached in EU on the methods for *Campylobacter* sub-typing for the future creation of a EU typing database

4. Identify possible approaches to establishing the degree of underreporting and discuss their applicability at national and EU level.

- Differences between under-reporting and under-ascertainment.
  Possible approaches:
  - Estimation of under-ascertainment at each point in the surveillance pyramid (% persons going to doctor, % of stool samples, % false negative lab results, *etc.*).
  - Targeted retrospective or prospective studies (by questionnaires, phone interview, *etc.*) to estimate the burden of diarrhoeal illness. More opportunities given by technologies (SMS, web, *etc.*)
  - Sero-surveillance studies. The main critical aspect is the knowledge on disease/infection rate and the shape of this relationship. Host factors (immunity, medical history, genetic factors and interaction with strains) should be taken into consideration.

Discussion Group 2

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

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.*

- **11 models** (8 EU + 3 non-EU) identified
  - **similar conclusions in a qualitative way**

    A. High concentration (in the meat) **poses the largest risk** (although at consumption low levels are ingested):
    high prevalence carcass contamination but low numbers would be preferred over low prevalence contamination and high numbers (although this is simplification)

    B. Cross-contamination is important but bias in model (set-up only looking at cross-contamination)

    Need to consider further development of models

    - consider for other type of poultry products e.g. minced meat and meat preparations because of other consumer behaviour undercooking should be considered
    - take up expertise of social sciences to finetune module on consumer behaviour – important module to link contamination in the food chain to the public health outcome

C. All the models consider the same **dose-response model** which is based upon a limited data set (extrapolation at low levels?) and not take up genomic variability of the strain (pathotype e.g. link to Guillain Barré syndrome)

Need to consider development of better dose-response models (although this is not an easy task)

- outbreak data ?
- dose response curve for various Seq. Types e.g. In New Zealand ST 474 (important in chicken and in human cases) vs. ST u48 (important in chicken - but not in human cases) – FluorQ. Resistant strains?
- What about multiple exposure – immunity due repeated challenge / multiple strains in mixed infections

Further developments in methodology of risk assessment

- **Bayesian modelling** with ability to update the model estimates and to include prior knowledge (to combine observation and expert opinion) – use as an integrated approach with Monte Carlo simulation (e.g. Apparant prevalence vs. True prevalence) to use all the information available
- Include **variability on processing practices** in models (if data are available)
- Should include/model **uncertainty** (although it is difficult especially if many assumptions made) but important in communication to risk managers

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.*

- Models are often refering to the same data sets that were derived from one specific situation in one specific country – need to be updated
- More Q-data become available on cross-contamination – or distribution of numbers on meat e.g. Baseline survey
- Quality of data – P/A and enumeration data
  - Take into account for input of model Measurement Uncertainty
  - Use the right method, also for sub-lethal injured cells (= can be resuscitated!), especially if evaluating interventions that stress cells (VBNC ? First proof that they are fit = infective/competitive)
  - Need of Best practices on how to treat the quantitative data, to turn them into distributions, especially handling data below detection limit
- List main types of fresh poultry meat and meat preparation in EU - needed to compare the risk derived from various types of poultry meat
- Need to know variability among member states but also among food business operators (slaughter and further processing) within a country among population (cultural differences)
- Data gaps
  - e.g. relation cecal/GI contamination and live birds exterior (feather/skin) contamination : is it linear or depends upon the way you slaughter
  - e.g. frequency of cecal/GI leakage during evisceration
  - e.g. Q-effect of technological interventions (and the way they are implemented = variability!) e.g. air chilling, hygienic design of equipment
  - e.g. consumer behaviour – need of observational data for different scenario's (different countries, different eating habits and food preparation)
  - More Qdata on cross-contamination, also from naturally contaminated samples, also transfer rates from cutting boards to RTE (cooked) product (other adhesion properties of meat)
  - More Qdata on cross-contamination in production environment

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.

Validate= fit for purpose ?

- If purpose is comparison of intervention measures
  - To validate if we have feasible/promising options: pilot studies in plant, field trials to implement and obtain (reproducible) "real life data" to establish cost/benefit and variability e.g. fly screens – ultrasound-steam, consumer campaigns
- Use of (repeated) baseline surveys but to validate ? Many (risk) factors interact – underlying changes/new trends in production practices and consumer behaviour which might intermingle and confuses the effect of intervention measures
- If purpose is to estimate the risk to public health
  - More difficult – need to know contribution of particular product to burden of disease + rely on reporting system whereas for *Campylobacter* often sporadic cases not that much institutional food borne outbreaks and latter are probably biased in reporting
  - Sometimes intervention measures are hard to evaluate by routine surveillance e.g. in Sweden : should divert broilers from producers with high Campy levels only noticeable in reported cases if Swedish broiler meat causes at least 50% of reported human cases otherwise it will be within the baseline fluctuations of reported cases. Maybe only see an effect if setting up targeted epi-studies (e.g. New Zealand)
  - = looking at cost benefit? Will it really matter ?

Disputable outcome on effect of thinning

- Rather disputable because insufficient knowledge on the quantitative effect (e.g. is excretion really significant in numbers of *Campylobacter* at time of slaughter, what about prevalence within the flock, what about influence of age on the numbers of *Campylobacter* excreted)
- Disputable because different practices in different countries

Risk assessment = added value because

- Integrates knowledge
- Brings together data and mulitidisciplinary
- Quantitative – scenario analysis
- Estimate before you start off and invest in further testing of intervention measures in field trials

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.

- Food industry needs guidelines/target (at the end) of the production chain
- Models agree that reducing the numbers is most effective e.g. target (processing criterion?) such as only X% of birds (cecal samples) or fresh meat (carcass or neck skin or end of production line) can have not more than Y cfu/g or cm^2 (defined by the method) at a certain stage of the food chain
- Even with the same target/PO you will have different outcome per country on public health (human cases) depending upon the (evolution) of the consumer behaviour
- Take opportunity of the Q-data from the baseline survey in each country to cut the tails of distribution – to start circle of improvement by setting targets for Food Safety Management Systems in poultry chain

- Models available today are constructed at national level (not for the EU situation). Can we have a generic EU model ? Variability upon MS ! Need to do additional efforts to set it up
- We can use today the national models (conditional if you accept the assumptions it is based upon = valid on generic EU level ?)
- The models agree there is a correlation between concentration on the product at retail and the probability of illness
- If you know the distribution in this particular product you can calculate the risk reduction
- Do we have scientific arguments from the models to decide where in the food chain to put the target
  - the closer to the consumer – the less variability and uncertainty but the less practical and room for corrective action .
  - If at the beginning in the food chain then easier to take measures but the correlation is less because you have more variability in the chain.
- Risk assessment approach versus pragmatic approach e.g. start off with same targets as *Salmonella* in poultry chain to begin with
- Have to think global
- Target within EU should be the same for non-EU countries
- International companies need same rules
- Should link to level of protection – need ALOP to be defined by risk managers
- Setting targets/PO is associated with risk reduction, not with zero tolerance
- Quantitative data throughout the production chain and throughout Europe will help to finetune the models for risk assessment and provide more accurate estimates and help to establish quantitative targets
  - Enumeration of *Campylobacter* with robust methods (microbiological data)
  - Consumer behaviour (relationship to food handling and eating habits)
- The next challenge will be to integrate variability throughout Europe and develop a generic model

Discussion Group 3

Fluoroquinolone resistance 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.

- Some country reports on FQ resistance prevalences (poultry, poultry meat, humans), see EFSA zoonoses report
- Monitoring of both resistance and drug use at the national level is essential
  - Follow trends, basis for risk assessment, guide interventions, monitor effects of interventions
  - Several countries have national drug use monitoring
  - In many other countries drug use data are present, but not easily accessable
  - The systems differ considerable between countries (e.g. based upon prescriptions, sales at species level, or just total sale).
- There are scientific evidence that the use of FQ have lead to emergence of FQ-resistance in *Campylobacter* in poultry flocks.
  - The exact nature of the relationship is not known
  - Not known whether strategic use (e.g. only within the first week of life) would lead to less emergence of resistance.
- Whether there are differences between the different quinolones in the selective ability is unknown.
- There is a correlation between resistance levels in broilers, carcasses and on meat
  - The latter is more difficult to determine because of the effect of cross-contamination and also because meat at retail also come from other sources.
- The effect of withdrawal of FQ is not well understood
  - Major interventions (e.g. ban, stringent compliance) on drug usage are expected to be necessary to obtain a significant effect
  - A full stop of FQ use will probably halt further increase in resistance, but not necessarily mean that resistance will decrease.
  - Effects of interventions should be assessed (e.g. missed opportunities with the growth promoters)

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.*

Significant or added risk of FQ?

- Different studies/reviews/analyses have reached different conclusions whether FQ resistant strains are more hazardous in regard to
  - Prolonged symptoms (diarrhoea)
  - Severity
  - Hospitalization rate
- Studies in DK and US have found increased risks (ref), UK studies and a study of Wassenaar not (ref)
- Different risks for different patient populations:
  - Not severe cases do not require antimicrobial therapy anyway
  - Severe cases of diarrea of uknown origin are normally treated empirically with antimicrobials (generally a FQ if suspicion of e.g. *Salmonella*) and if FQ resistant organisms, including *Campylobacter*, are present there is increased risk of treatment failure and adverse outcome
- Recent indications of increased infection rates of FQ resistant *Campylobacter* strains in humans that are receiving FQ treatment (ref. Molbak)

%Human Camp cases attributable to broiler meat (1)

- A majority of *Campylobacter* infection cases are acquired from broiler meat. Most likely the same with infections with FQ resistant *Campylobacter*
- Other sources for *Campylobacter*, incl FQ resistant strains, than broiler meat, should be taken into consideration
  - Environment and water: indirect contamination from animals (including broilers) and possibly humans

%Human cases of FQ res Camp attributable to broiler meat (2a)

- Need for more studies to assess risk factors for FQ resistant *Campylobacter* infection
  - E.g. longitudinal studies in human volunteers (travel, type of foods – broiler meat, imported foods, patient previous antimicrobial exposure, *etc.*), including susceptibility profile and typing of the isolates, with regular samples from environmental sources & samples from locally-produced and imported food from the same period.
  - Should not focus only on broiler meat, but all poultry meat (e.g. higher antibiotic exposure in turkey production)

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.*

Public health impact of reducing FQ

- FQ resistance is increasing in Camp from humans and poultry
- Studies from many countries: Resistance in humans follows the usage of FQ in food animals and build up of resistance among *Campylobacter* in food animals
- Danish and Norwegian study, % resistant Camp among domestic poultry (low usage of FQ in poultry) and domestically aquired cases low, while travel related cases is very high

Possibilities of reducing in FQ

- Prescription is a requirement in the EU and this should be extended to the rest of the world
  - Compliance / illegal use?
- Some countries have shown that it is possible to produce poultry with limited or without FQ use
  - Australia and NZ
  - Nordic countries
  - US banned FQ in poultry in 2006
- Lack of knowledge of what will be the impact on different management options (ban, only for certain indications, off-label use, only after susceptibility testing *etc.*)
- Carry-over of small quantities of FQ in the poultry environment (FQ used in water)
- FQ slowly degraded in the environment

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

- Need for monitoring of drug usage of antimicrobial agents
  - Progress in some countries
  - Monitoring needs to be harmonised for comparability between countries.
  - A work-shop on best and feasible practices for monitoring drug usage should be held, to recommend a common system for all EU-member countries.
  - A EU database on drug usage in food animals should be established.
- The exact relationship between drug use and resistance needs to be further studied
- Experience from different countries, incl US and Australia needs to be further studied
  - Public health impact?
  - Effects on poultry industry incl animal health?
- Impact on import of FQ res Camp through food from third countries?

- Careful re-analysis of previous work regarding public health risks of FQ resistant strains versus FQ susceptible strains
- Need for more studies to assess risk factors for FQ resistant *Campylobacter* infection
  - *E.*g. longitudinal studies in human volunteers (travel, type of foods – broiler meat, imported foods, patient previous antimicrobial exposure, *etc.*), including susceptibility profile and typing of the isolates, with regular samples from environmental sources & samples from locally-produced and imported food from the same period.
  - Should not focus only on broiler meat, but all poultry meat (e.g. higher antibiotic exposure in turkey production)
- Lack of knowledge regarding whether FQ resistant isolates belong to specific clones and/or have particular properties (e.g. increased fitness, virulence?)

Conclusions

- There is scientific evidence that the use of FQ in poultry has lead to emergence of FQ-resistance in *Campylobacter* in poultry and has further spread to humans
- There is a public health benefit from reducing FQ use in food animals
  - Not yet able to quantify the effect in case of *Campylobacter*
    - Different studies/reviews/analyses have reached different conclusions whether FQ resistant strains are more hazardous than FQ susceptible strains
  - Severe cases of diarrea of uknown origin are normally treated empirically with antimicrobials and if FQ resistant organisms are present there is increased risk of treatment failure and adverse outcome
  - Recent indications of increased infection rates of FQ resistant *Campylobacter* strains in humans that are receiving FQ treatment
- It is possible to produce poultry with limited or without FQ use, but need more data on
  - Public health benefit?
  - Impact on the poultry industry incl animal health?
- FQ is a critical important drug in humans and should therefore be a drug of last resort for therapeutic use in food animals
- Prudent antimicrobial use policy should be promoted and adhered to

Discussion Group 4

Assessment of effectiveness of control measures in the food chain

Additional remarks

- Economic changes: cheaper products (e.g. import)
- Approach for free-range: compromise between welfare and safe product
- What is effectiveness: abscence/reduction? Few human cases
- Inform consumers that all foods including poultry meat carry risks
- Strain specific issues
- Incentives for farmers?

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.

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

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.

- Effect of education:
  1. Producer: short lived, incentive related
  2. Processor: short lived, HACCP compliance
  3. Consumer: short lived, they don't listen; school children

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.

1. where implementation of intervention strategies?
2. Monitor (continuous) effect of strategies
3. Options:
   1. Ideally on-farm (scheduling)
   2. Caeca (yes/no) as in baseline study
   3. End of slaughterline (quantitative?)
   4. Retail?

Key issues

- Fully integrated farm to consumer approach
- Focus on highly contaminated carcasses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European Food Safety Authority

Largo N. Palli 5/A
I-43121 Parma
Italy
Tel: +39 0521 036 111
Fax: +39 0521 036 110
www.efsa.europa.eu

Publications Office
Publications.europa.eu