

ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD

**UPDATE ON THE GOVERNMENT'S ACTIONS TO ADDRESS THE
RECOMMENDATIONS OF THE 1999 ACMSF REPORT ON MICROBIAL
ANTIBIOTIC RESISTANCE IN RELATION TO FOOD SAFETY**

1. In response to a previous request from ACMSF the attached paper updates the actions taken to address the recommendations in the ACMSF 1999 Report on Microbial Antibiotic Resistance in Relation to Food Safety. Members may wish to read this paper in conjunction with initial update presented to the Committee in 2005 by the Defra Antimicrobial Resistance Coordination Group (ACM/730).

**Secretariat
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Update on the Government's Actions to address the Recommendations of the 1999 ACMSF Report on Microbial Antibiotic Resistance in Relation to Food Safety

1. Introduction

- 1.1 In 1996 the Advisory Committee on the Microbiological Safety of Food (ACMSF) set up a Working Group to assess the risks to humans from antibiotic resistant microorganisms entering the food chain and to consider the need to protect public health. The Committee's Report on Microbial Antibiotic Resistance in Relation to Food Safety was published in 1999 (ACMSF, 1999) and listed a series of recommendations, most of which were for Government to consider taking forward.
- 1.2 The Defra Antimicrobial Resistance Coordination (DARC) Group was established in 1999 and part of its remit was to track and update the Government's response to the ACMSF report. In 2005 the DARC secretariat produced a paper (ACM/730) that summarised the actions taken by Government over the five year period since publication of the ACMSF report to address its recommendations. The majority of the recommendations in the ACMSF report had been taken forward and the DARC paper comprehensively covered progress on these. However, progress on some recommendations was at an early stage and would now benefit from a further update. Also, the recommendations of Chapter 12 of the ACMSF report (Research on Antibiotic Resistance in Relation to Food Safety) were not addressed by DARC.
- 1.3 This paper provides an update on recommendations that were outstanding and those where further substantial progress has been made since 2005. It does not cover all the ACMSF recommendations as the majority were covered by the DARC report (ACM/730) and do not require further updating. Also outlined is the research commissioned in relation to the recommendations laid out in Chapter 12.

2. Progress on non-research recommendations

- 2.1 Chapters 3, 4 and 5 of the ACMSF report (ACMSF, 1999) reviewed patterns of antibiotic resistance in bacteria isolated from food animals, foodstuffs and human infections associated with antibiotic-resistant foodborne pathogens. A common recommendation that spanned these chapters was the requirement to bring data covering antimicrobial resistance in organisms from human clinical, veterinary and food sources from different regions across the UK together in a coherent document. This has been addressed by the publication of the Overview of Antimicrobial Usage and Bacterial Resistance in Selected Human and Animal Pathogens in the UK:2004 (VMD, 2007).

- 2.2 Recommendations from Chapters 3 and 5 suggested that comparisons of isolates of *Salmonella* from different regions of the UK and the human and animal sectors using appropriate methodologies should be made. DARC reported to ACMSF on a ring trial that was conducted by the Health Protection Agency (HPA) and Veterinary Laboratories Agency (VLA) to meet these recommendations. The results of the trial were published in 2003 (Threlfall *et al.*, 2003). Further work, resulting from this ring trial, involving molecular comparison of the antibiotic resistance determinants in *Salmonella* isolates from humans and food-producing animals has recently been published (Hopkins *et al.*, 2007).
- 2.3 A recommendation from Chapter 3 (3.134) suggested that Government should initiate studies to identify the key factors that lead to the emergence and disappearance of multi-resistant clones of *Salmonella* Typhimurium. There is currently a Defra funded project and a Med-Vet-Net project on this underway. Additionally, an industry funded study conducted by the HPA was published in 2004 (Hopkins and Threlfall, 2004).
- 2.4 Chapter 6 of the ACMSF report reviewed the evidence of the foodchain contributing to human infections with antibiotic-resistant microorganisms. Gaps in the knowledge base were identified with regards to the prevalence of antibiotic resistance in commensal microorganisms found in food (particularly *E. coli* and enterococci) and investigation of these was recommended (Recommendations 4.72 and 6.121). To our knowledge no work has been commissioned by Government specifically to meet these recommendations.
- 2.5 Sections 8.34 and 8.35 of the ACMSF report reviewed the training arrangements for veterinarians in the UK regarding antibiotic prescribing and antimicrobial resistance. Recommendation 8.51 suggested that veterinary schools and colleges should review their existing courses to ensure that microbial resistance was given a suitably high profile in undergraduate courses. In 2005 DARC reported that the Royal College of Veterinary Surgeons was approached and was reviewing the situation. The Veterinary Medicines Directorate recently wrote to the Universities offering undergraduate degrees in veterinary medicine to confirm that these topics had been incorporated into the degrees and are satisfied that this has been done.
- 2.6 Chapter 9 of the ACMSF report reviewed the use of medicated animal feedingstuffs. Recommendation 9.25 suggested that manufacturers who failed to comply with UKASTA's (United Kingdom Agricultural Supply Trade Association Ltd.) Feed Assurance Scheme should not be considered as suitable for registration by the enforcement authorities. At

the time of the DARC report to the ACMSF in 2005 a review of enforcement arrangements for feed manufacture was being undertaken and this led to new legislation to regulate this sector. The Veterinary Medicines Regulations (2006) state that manufacturers and distributors of premixtures and feedingstuffs containing veterinary medicinal products and premixtures and feedingstuffs containing specified feed additives must be approved. The statutory inspection and approval of these premises is carried out by the Veterinary Medicine's Directorate (VMD) Animal Medicines Inspectorate and is more thorough than the assurance scheme discussed by industry. In light of these developments the industry assurance scheme was not taken forward.

3. Progress to meet recommendations made in Chapter 12: Research on antibiotic resistance in relation to food safety

- 3.1 A large body of research has been conducted since 1999 to meet the recommendations made in Chapter 12 of the ACMSF report. The Microbiological Safety of Food Funders Group (MSFFG) recently published a detailed report on UK publicly funded research on microbial antibiotic resistance in relation to the safety of food that was presented to the ACMSF in March 2007 (MSFFG, 2007).
- 3.2 A summary of how the research covered in the MSFFG report relates to the ACMSF recommendations from Chapter 12 can be found in Table 1. It is important to note that research covering a number of recommendations has been carried out in other countries or funded within the UK by other bodies. Hence, the appearance of gaps in Table 1 does not necessarily represent a lack of scientific evidence relating to a particular recommendation.
- 3.3 Reviewing the recommendations it is apparent that there are two key areas where there may be gaps in Government funded research. Firstly, the occurrence of antibiotic-resistant bacteria in imported food and animal feedingstuffs and, secondly, in the area of microbiological risk assessment.
- 3.4 Government funded surveys specifically testing for antibiotic-resistant bacteria in imported foods only are rare. However, FSA surveys on microbiological contamination in various foodstuffs are designed to allow detection of microbiological contamination (and test for antimicrobial resistance) in particular products available to the consumer at the point of sale. As such, samples taken during these surveys will usually comprise a mixture of home-produced and imported products. Specific surveys of the microbiological contamination of imported foods have been carried out by the FSA only when a significant issue relating to imported foods has emerged (e.g. *Salmonella* contamination of eggs).

- 3.5 The presence of antibiotic-resistant bacteria in imported animal feedstuffs has not yet been investigated but is currently being considered by Defra.
- 3.6 To date, meaningful microbiological risk assessment relating to antibiotic-resistant bacteria has been difficult to carry out due to a lack of data to support the assessment. FSA funded Project B10004 (Assessment of, relative to other pathways, the contribution made by the foodchain to the problem of quinolone resistance in microorganisms causing human infections) is the only project that addresses recommendation 12.36 in its entirety. However, the vast body of research carried out in the last eight years should now allow this work to be undertaken in a more comprehensive manner.
- 3.7 To determine the extent to which the research questions underlying the recommendations of this Chapter have been answered research undertaken in the UK and elsewhere will be further reviewed. This process will contribute to the development of an FSA strategy on antimicrobial resistance in the foodchain.

4. Conclusions

- 4.1 It is evident that the majority of recommendations from the 1999 ACMSF Report on Microbial Antibiotic Resistance in Relation to Food Safety have been taken forward and completed.
- 4.2 Areas that have been highlighted for further consideration by this review of the ACMSF recommendations include antibiotic resistance in commensal microorganisms in food, antibiotic-resistant microorganisms in imported food and animal feed and Microbiological Risk Assessment.
- 4.3 The FSA intends to hold a stakeholder meeting on Antimicrobial resistance in the food chain in November 2007. The topics listed above, as well as issues which have emerged since the publication of the report (such as ESBL-producing *E. coli* and MRSA in pigs), will be considered during this stakeholder meeting. The results of the stakeholder meeting are intended to inform work on an FSA strategy on antimicrobial resistance in the food chain.

References

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VMD (2007). Overview of Antimicrobial Usage and Bacterial Resistance in Selected Human and Animal Pathogens in the UK:2004.

<http://www.vmd.gov.uk/Publications/Antibiotic/antimicrob120707.pdf>

Table 1: Recommendations from Chapter 12 and corresponding research projects

Recommendation	Relevant Research Projects
<p>12.33 Research should be undertaken to:</p> <ul style="list-style-type: none"> • Undertake integrated local surveillance studies to examine prevalence of antibiotic resistance associated with <i>Campylobacter</i>, <i>Salmonella</i> and commensal bacteria throughout slaughter and processing • Assess the prevalence of antibiotic resistance in wild animals, including birds, and food animals on farms in relation to the usage of antibiotics, particularly a) growth promoters and b) fluoroquinolones 	<p>Defra funded project FZ2009 (Abattoir Survey of Foodborne Pathogens in Cattle, Sheep & Pigs in Great Britain 2003)</p> <p>Defra funded projects OD2009, OD2003, OZ0501, VM02100, VM02101, VM02200</p> <p>Scottish Executive funded project SAC/147/97</p>
<p>12.34 Research should be funded to:</p> <ul style="list-style-type: none"> • Identify risk factors for acquiring an infection with an antibiotic resistant pathogen. Such studies need to be conducted in both humans and, where appropriate, animals • Assess the extent of infection in travellers caused by antibiotic-resistant strains and the contribution these make to the burden of IID and antibiotic resistance in the UK • Assess the importance of imported food and animal feed as a source of antibiotic-resistant bacteria • Determine the contribution made by microorganisms of human origin to microbial antibiotic resistance in animals and food • Model current patterns and predict future trends in antibiotic resistance of foodborne pathogens in humans and animals • Determine the socioeconomic costs attributable to antibiotic-resistant foodborne pathogens in humans, above the costs attributable to antibiotic sensitive foodborne pathogens 	<p>FSA funded project B14001</p> <p>FSA funded projects B10004, B14001</p> <p>FSA funded surveys B18002, B18012, B18017, B18018, B18022, B18024, B18025</p> <p>Scottish Executive funded projects SAC/254/00</p> <p>FSA funded project B10004</p>

<p>12.35 Research should be funded to:</p> <ul style="list-style-type: none"> • Develop methods which will characterise the origins of resistance in foodborne pathogens and commensal microorganisms, so as to improve identification of sources and routes of transfer of resistant organisms from farm through food to humans 	<p>BBRSC funded project 4311218 Defra funded projects OD2011, OD2014, OD2020, OZ0132, VM02100, VM02105, VM02136 FSA funded project B10001 MRC funded projects G0501415, G0300020</p>
<p>12.36 In relation to microbiological risk assessment (MRA), research should be funded to:</p> <ul style="list-style-type: none"> • Undertake structured MRA to assess the risk of infectious intestinal disease from antibiotic-resistant foodborne pathogens and commensal bacteria in food animals, foods and the environment • Use MRA to quantify the magnitude of the key pathways by which microbial antibiotic resistance can transfer from food animals to humans via the food chain and environment • Undertake MRA to assess links between a) use of growth promoters and b) fluoroquinolones in food animals and the development of antibiotic-resistant infections in humans 	<p>FSA funded project B10004</p>
<p>12.37 To facilitate a reduction in the usage of antibiotics, research should be funded to:</p> <ul style="list-style-type: none"> • Underpin effective antibiotic management policies in animals, aimed at optimising administration practices to minimise the risk of development of resistance. This will include investigations of the persistence of antibiotic-resistant bacteria in the gastrointestinal tract of food animals after antibiotic withdrawal • Further investigate how particular hygiene practices and interventions can bring about a real reduction in the need for antibiotics in food animal production, without jeopardising animal welfare • Evaluate the potential of vaccines, probiotics and competitive exclusion to 	<p>Defra funded projects OD2003, OD2007, OD2014, OD2015, OZ0501, OZ0502, VM0292, VM02201</p> <p>Scottish Executive funded projects SAC/137/97, SAC/147/97</p> <p>Scottish Executive funded projects SAC/137/97 and</p>

<p>reduce the usage of antibiotics and the level of resistance in microorganisms in food</p>	<p>SAC/147/97</p>
<p>12.38 Research should be conducted to:</p> <ul style="list-style-type: none"> • Determine the relationship between antibiotic resistance and virulence in foodborne pathogens in humans and, where appropriate, animals • Review the clinical picture (duration, severity, treatment and outcome) of cases of IID involving antibiotic-resistant foodborne pathogens as opposed to cases infected with sensitive isolates, and assess whether there are any longterm implications of these infections for the patient 	<p>FSA funded project B14001</p>
<p>12.39 Research should be funded to:</p> <ul style="list-style-type: none"> • Examine the antibiotic-resistant pathogens and commensal organisms from animals an humans to determine their survival characteristics in the environment compared to non-resistant strains • Examine the effect of antibiotic selection pressure on the survival and persistence of antibiotic-resistant strains, both in vitro and in vivo • Examine the transfer of resistance determinants between foodborne pathogens and commensal flora of humans and animals in a) foods and b) the environment 	<p>BBSRC funded projects 772, 4311218, D15925 Defra funded projects OD2002, OD2005, OD2008 SEERAD funded project RRI/743/01</p> <p>BBSRC funded projects 772, 4311218, D15925 SEERAD funded project RRI/743/01</p>