

**ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD**

**INFORMATION PAPER**

**ACMSF Working Group on Antimicrobial Resistance**

1. At the January 2013 ACMSF meeting members considered a paper updating them on recent developments in relation to antimicrobial resistance (AMR) and the food chain. The Committee agreed to establish a subgroup of members to consider the topic in detail and to ensure that appropriate weight was given to the food chain in relation to discussions and developments on AMR.
2. The ACMSF Working Group on AMR met by teleconference on 30<sup>th</sup> July to discuss the terms of reference and scope of their work and had their first formal face-to-face meeting on 9<sup>th</sup> September 2013.
3. This paper provides a summary of the main issues discussed by the subgroup at their September meeting, the conclusions reached and recommendations made.

Terms of reference

4. The group discussed their terms of reference and scope (see annex A). The groups' role will be to assess the risks to humans from foodborne transmission of antimicrobial-resistant microorganisms and provide advice to the ACMSF. Their specific terms of reference are:
  - To brief ACMSF on developments in relation to antimicrobial resistance and the food chain and identify evidence that will assist the group in assessing the risks.
  - To review key documents and identify the risks for the UK food chain and relevant aspects of the feed chain in relation to antimicrobial resistance which may have consequences for human health.
  - To comment on progress in understanding the issue of antimicrobial-resistant microorganisms and the food chain since the ACMSF produced its report in 1999 and subsequent reviews in 2005 and 2007, including the relevance of any outstanding recommendations.
  - To highlight key research or surveillance gaps in relation to antimicrobial-resistant microorganisms and the food/feed chain and identify those which are considered a priority.
5. The group also discussed their workplan for the forthcoming year and identified key documents and issues they wished to review and discuss. The group plan to meet four times a year.

## Outstanding recommendations from ACMSF 1999 report on AMR

6. Members reviewed the outstanding recommendations from ACMSF's 1999 report on Microbial Antibiotic Resistance in Relation to Food Safety and discussed whether these were still relevant. They related to two main areas:
  - Gaps in the knowledge base with regards to the prevalence of antibiotic resistance in commensal microorganisms found in food (particularly *E. coli* and enterococci)
  - Gaps in Government funded research on antibiotic-resistance bacteria in imported food and animal feeding stuffs and in the area of microbiological risk assessment.
7. The group noted that 14 years have elapsed since the report had been published and since then a lot of work has been undertaken. This has meant that some of the recommendations may be out of date and in some cases may no longer be applicable. In addition some recommendations may need updating or re-framing, for example in light of developments in newly-developed, genomic sequence-based methods for identifying resistance genes in bacterial populations.
8. The role of commensals has been identified as important in spreading resistance genes to pathogens. This has been highlighted in a 2011 EFSA Opinion on the public health risks of bacterial strains producing extended-spectrum  $\beta$ -lactamases (ESBLs) and/or AmpC  $\beta$ -lactamases in food and food-producing animals and also in a series of recent papers from The Netherlands. When the ACMSF 1999 report was being written, methods for detection of resistance would have relied heavily on phenotypic methods including the use of surrogate markers. There is now increased emphasis on tracking the spread of resistance genes between organisms which has been facilitated by the use of molecular methods. Hazards in this area are posed by the presence of resistance genes, and their propensity to "move" (e.g. plasmid/integron/transposon *versus* nucleus) from the current commensal host.
9. In relation to imported foods the group commented that the relative importance of imported foods to the development of AMR is unknown and it remains a potentially significant source. This is particularly relevant in that such foods may be imported from countries where production is cheaper and antibiotic usage in food animals is less regulated than in the UK, and in other EU Member States.
10. Some antimicrobial resistance gene/organism combinations are spread by the food-borne route and have had significant effects in some areas e.g. *Salmonella* Kentucky in North Africa and Eastern Europe, but not to a significant extent in the UK. Data to understand these patterns and associated risks would be desirable.
11. The new poultry inspection proposals from the Commission include requirements to define the levels of *E. coli* with ESBLs/AmpC-encoding resistance genes.
12. In summary the group considered that AMR in imported food remains an area of concern, and the knowledge gaps in this area need to be resolved to inform risk management.

13. The working group also considered imported feedstuffs and noted there are differences between bacteria in imported animal feed, and in imported feed that is medicated (including water). It was thought that there is little feed that is imported already medicated, but imported feed may be contaminated with resistant microorganisms. It was considered that it was important to know whether there is an enhanced risk from imported feed and there is still insufficient data to inform assessment of these risks.
14. In relation to the outstanding, and in some cases longstanding, recommendations re AMR (ACMSF 1999, 2005 & 2007) the group noted that some significant gaps in the knowledge base remain. The working group will continue to monitor and report on these gaps, “new gaps”, and re-opening gaps (i.e. areas where the passage of time, and changes in AMR patterns mean that new/additional data is necessary to inform accurate risk assessment).

#### European Medicines Agency (EMA) advice on colistin and tigecycline

15. The European Commission submitted a request to the EMA for advice on the impact on public health and animal health of the use of antibiotics in animals. The EMA published an opinion responding to this request on 19th July 2013 focussing their advice on colistin and tigecycline.
16. The working group reviewed the EMA documents. The group noted that, in the UK, colistin is frequently used in livestock (pigs and poultry), sometimes in combination with critically-important antimicrobials such as fluoroquinolones and very occasionally used in humans. In the past colistin was not used in human medicine because of its toxicity and because more effective antibiotics were available. The emergence of resistance to other first-line or last resort antibiotics now means that colistin is, in some circumstances, becoming the only effective appropriate human antimicrobial. Colistin resistance has not been demonstrated to be plasmid-mediated, and there is no evidence of horizontal transfer of the resistance gene to other bacteria associated with its use in livestock. Emergence of resistance has been observed after colistin use in humans, but there is no suggestion of any link between animal use and resistance in human. As mentioned above, colistin is sometimes used in combination with other antimicrobials in treatment of livestock, which may be of concern. It was also noted that there have been some reports of low level colistin resistance in *E. coli* and/or possibly some *Salmonella* serovars at non-therapeutic levels. The group agreed that the EMA advice, including removing prophylactic use of colistin in animals and monitoring of off-label use, was proportionate.
17. The group noted that tigecycline is currently unlicensed for use in veterinary medicine, and is therefore not used in the UK. As long as this restriction remains the group considered that this antibiotic should not pose a significant concern.

#### Quantification of human deaths due to antibiotic use in chicken

18. The Group considered a letter from Collignon *et al*, published in Emerging Infectious Diseases in August 2013. These authors estimated the number of human deaths

and hospital admissions in European countries (including the UK) resulting from the presence of third generation cephalosporin-resistant *E.coli* in poultry.

19. The authors used a figure from a study in the Netherlands by de Kraker *et al.* (which estimated the number of human infections with cephalosporin-resistant *E. coli* that could be associated with poultry consumption) to estimate the number of such infections in other European countries. The group expressed concerns over such extrapolation, as there is evidence that:

a) ESBL levels in poultry in The Netherlands are much higher than in the UK and;

b) cephalosporin usage in The Netherlands was not the same as in the rest of Europe.

20. The working group also noted that a more recent paper by de Kraker *et al* queried some of the initial research findings. Overall, the group also felt that although some of statements in the letter were currently unsubstantiated, they could usefully be further examined. Members noted that the authors should be commended for attempting a quantitative risk assessment, but felt that uncertainties remained in relation to the validity of the data used to calculate the above estimates, along with potential difficulties around the large confidence intervals associated with the estimates.

#### DH AMR Strategy

21. The group noted that the DH strategy on AMR was due to be published on 10<sup>th</sup> September and agreed to provide comments on the strategy. They also noted DH's intention to produce a draft implementation plan which they would have the opportunity to comment on at a future meeting. Members were updated on some of the groups being established by DH to help with implementing the AMR strategy and it was suggested that ACMSF may be involved/provide advice to one of the implementation groups.

**Secretariat  
October 2013**

## **ACMSF Antimicrobial Resistance Working Group**

### Role

To assess the risks to humans from foodborne transmission of antimicrobial-resistant microorganisms and provide advice to the FSA.

### Terms of Reference

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- To highlight key research or surveillance gaps in relation to antimicrobial-resistant microorganisms and the food/feed chain and identify those which are considered as priorities.

### Membership:

Prof David McDowell (Chair)  
Prof John Coia  
Prof Rick Holliman  
Mr Paul McMullin

Mr Stephen Wyllie (Defra representative)  
Ms Sally Wellsted (DH representative)

### Co-opted members

Prof Stephen Forsythe (ACAF member)  
Mr Chris Teale (AHVLA)  
Dr John Threlfall (consultant microbiologist)

### Secretariat

Ms Kara Thomas  
Dr Paul Cook  
Dr Sophie Rollinson

## Scope

Many other groups are involved in work on antimicrobial resistance (ARHAI, DARC, VRC – see annex). Some of these are concerned with risk management rather than risk assessment which will be the working group's task. The working group will liaise with and co-ordinate their work with these other groups and bodies to avoid duplication.

Both imported food and food produced in the UK are included within the groups remit.

## Outputs

The group will report back to the main Committee meetings on its discussions and recommendations. This may be an oral update or may take the form of a written paper for more significant issues/discussions.