

MONITORING OF ANTIMICROBIAL RESISTANCE IN FOOD PRODUCTION ANIMALS IN EUROPE. HOW TO BUILD A COHERENT SYSTEM

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Introduction

The development of antimicrobial resistance among bacteria from food animals is considered a major public health problem in the European Union. The Zoonoses Directive (2003/99/EC), adopted on 29 September 2003, requires that EU Member States implement a monitoring programme that provides comparable data on the occurrence of antimicrobial resistance in zoonotic agents and other public health threatening agents. A proposal for a Monitoring Programme attempting to specify Article 7 of the Zoonoses Directive is drafted by the Community Reference Laboratory for the Epidemiology of Zoonoses (CRL-E). This draft will be discussed at the annual meeting of the National Salmonella Reference Laboratories in Berlin at the Federal Institute for Risk Assessment (BfR) on 21 and 22 October 2004. Subsequently a final proposal will be forwarded to the Commission to draft a decision on this issue.

There are several factors in monitoring programmes that affect the quality and comparability of the data. Next to sampling strategies, microbial test methodologies used are important factors. Isolation and identification methods used can be standardised, for susceptibility tests this is more complicated because historically, different guidelines are used in different European countries. The optimum goal is to harmonise the quality of the susceptibility data by controlling this data with ATCC quality control strains. Community and National Reference Laboratories (CRLs and NRLs) with adequate expertise in antimicrobial resistance will have to be designated. Coordination of surveillance activities will be done by the CRLs by building an active network of all NRLs. External and Internal Quality Assurance Systems for susceptibility tests need to be developed and stimulated by this network.

In Europe the existing active network of national reference laboratories that monitor antimicrobial resistance is based on two EU-projects. The first project was ARBAO (FAIR5- PL97-3654), which report was published in 2001 (1). The second project, a EU-wide External Quality Assurance Programme (EQAS) has started in 2003 (FP5-EU-project ARBAO-II, QLK2-CT-2002-01146). Both projects are the basis for the coherent system to be built. ARBAO-I was a concerted action focussed at describing well-founded recommendations for EU-wide monitoring of resistance. For standardisation of susceptibility tests three options were given: *i.* no standardisation and as a result the data could only be used as a main alert statistic; *ii.* intercalibration of the results by organising external quality assurance systems; *iii.* a standard method to be used, which was considered to be a future perspective. Based on the recommendations of ARBAO, ARBAO-II started an External Quality Assurance System (EQAS) to harmonise the quality of susceptibility test results in Europe.

Method

In 2003 eighteen veterinary reference laboratories participated. Moreover, 13 regional veterinary laboratories in 4 countries participated on equal terms as the veterinary reference laboratories and these numbers are expanding in 2004. Four laboratories (DFVF Denmark AFSSA France, VLA United Kingdom and CIDC Netherlands) act as reference laboratories. These laboratories select reference panels of isolates of *Salmonella/E. coli*, *Pasteurella* spp./*Actinobacillus pleuropneumoniae*, *Campylobacter* spp., and streptococci/staphylococci/enterococci, respectively. MICs of relevant antimicrobials are determined with NCCLS methods and always confirmed by at least one other laboratory. Four times a year, panels of strains are distributed to all participants for susceptibility testing. The participants use their own routine methods for susceptibility testing and download their results electronically on a web page. They are directly informed of the numbers of deviations compared to the reference results. Deviations are classified as minor, major or very major. Minor deviations are defined as an intermediate result that was determined as sensitive, resistant or vice versa (i.e. I ↔ S or I ↔ R). When a susceptible strain is classified as resistant it is regarded as a major deviation (S ↔ R). When a resistant strain is classified susceptible it is regarded as a very major deviation (R ↔ S). Annually, a two-days meeting is organised by the coordinating laboratory (DFVF). At this meeting, all results are presented and discussed.

Results

A report of the 2003 EQAS results was published in spring 2004 (2). In Figure 1 the results of the EQAS of 2003 for *Salmonella*, *E. coli*, streptococci and staphylococci demonstrate that depending on the bacterial species involved a variety of deviations from the expected results is obtained in the participating laboratories. It also demonstrates that for certain more fastidious bacterial species like streptococci, the numbers of deviations are substantially higher than for the *Enterobacteriaceae* and staphylococci. These results facilitate the introduction of threshold levels for the accuracy of laboratories that supply summary resistance data to a central database (3).

Conclusion

Since approximately 1997 the core laboratories of ARBAO-II form an active network of veterinary reference laboratories that work on antimicrobial resistance. The focus of the cooperation in this network has constantly been aimed at stimulating, improving and implementing resistance monitoring in food animals in the EU. As a result of Directive 2003/99/EC CRLs will be designated for antimicrobial resistance monitoring. Because of the complexity of antimicrobial resistance in the different bacterial species listed in the Directive, the

ARBAO-II group strongly advises to use the expertise in this network as the motor for the European monitoring. The CRLs to be appointed need adequate expertise on antimicrobial resistance to be able to conduct this task properly and to control and stimulate the implementation of the final monitoring programme after adoption by the Commission.

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References

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3. ARBAO-II 2004. Antibiotic Resistance in Bacteria of Animal origin – II. Report of Summary Susceptibility data 2002.. http://www.dfvf.dk/Files/Filer/ARBAO/ARBAO_monitoring_summary__draft.pdf

Figure 1. The percentage of minor, major and very major deviations from the expected susceptibility test results for *E. coli*, *Salmonella*, streptococci and staphylococci for each laboratory participating in the External Quality Assurance System of the ARBAO-II project in 2003, ranked in descending order.

