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EFSA Task Force of Zoonoses Data Collection
2nd specific meeting on antimicrobial resistance (AMR) monitoring and reporting in animals and food
Held in Copenhagen on 16 March 2012

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PARTICIPANTS:

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Observers:

Brigita Hengl (Croatia), Tatjana Babovic (ME), Blazo Janevski (MK), Sahin Guzin (Turkey)

EFSA:

Pierre-Alexandre Belœil (Chair), Pia Mäkelä, Camilla Smeraldi (Science), Miriam Grasselli and Simona Fusar Poli (Administration).

MINUTES:

1. Opening and welcome

The meeting was opened by the Chair welcoming all the participants to the meeting in particular those attending Task Force (TF) meetings for the first time. The Chair thanked Denmark for hosting this meeting in the margins of the conference on 'Combating Antimicrobial Resistance' organised by the Danish Presidency of the Council of the European Union semester. In providing feedback from the conference, the Chair highlighted the importance of collaborating with public health, and to this end the conference marked a good starting point. It was anticipated that the interaction between the animal and food sector and the human counterparts will also be the topic of many of the items on the agenda of the current meeting.

2. Declaration of interest

In accordance with EFSA policy on declaration of interests, participants were asked if they had any interests to declare in relation to the agenda of the meeting. B. ter Kuile informed the Task Force about his recent participation in a Working Group (WG) meeting of the International Life Sciences Institute (ILSI) on risk analysis in food microbiology. No conflicts of interests related to the issues discussed in this meeting were identified

3. Minutes from the previous meeting

The minutes from the previous meeting, adopted through written procedure, have been published on EFSA's website. The Chair asked whether there was any need for amendment. No comments were raised on the adopted minutes.

4. Adoption of the agenda

The agenda was presented by the Chair and adopted with no changes.

5. Communication from the European Commission to the European Parliament and the Council: Action plan against the rising threats from Antimicrobial Resistance

Rosa Peran presented an overview of the European Commission (EC) 'Action plan against the rising threats from Antimicrobial Resistance' and more in detail, the actions that will arise to put this into practice. Overall, the plan is aimed at promoting appropriate use of antimicrobials, preventing microbial infections, developing new effective antimicrobials or alternatives for treatment, including diagnosis, promoting international cooperation in tackling AMR and lastly, reinforcing research and innovation. It was explained how the activities foreseen in the plan stretch across different areas, such as changes to the legislation on medicines for veterinary use and medicated feed, introduction of restrictions of the off-label use; issuing recommendations and guidance to encourage prudent use of antimicrobials and the introduction of animal health law to promote good farming practices thus reducing the spread of infections. As part of the action plan, legal grounds for the data collection on antimicrobial use in animals will be provided, as such a legal basis does not exist in all MSs at present. The action plan of the EC is available online at the following address: *http://ec.europa.eu/dgs/health_consumer/index_en.htm*

The participants raised a number of questions concerning the Action Plan. The EC explained that one of the goals of the action plan from the EC is to strengthen the systems of data collection, in particular that on antimicrobial use, with a target of all MSs reporting data at animal population level by 2014. For what concerns the diffusion of AMR through the environment, it was recalled that this topic is not in the scope of the Action Plan but rather it is falling within the remit of the DG Research.

6. Cooperation on integrated use of and reporting of data on consumption of, and resistance to, antimicrobial agents in human, animals and food in the European Union between the ECDC, EFSA and EMA

The Chair informed the Task Force about a recent agreement signed by EFSA and the other two Agencies of the European Union dealing with matters related to AMR and antimicrobial use in humans and animals, i.e. the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency.

It was explained that the rationale for this agreement stems from the Action Plan of the EC, as presented in the previous agenda item. The aim is to foster collaboration between the three agencies/authority under an agreed governance model and bodies that are yet to be defined in detail. These efforts should be channelled towards the production of a joint report on the analysis of the relationship between AMR and use in humans and animals. It is however anticipated in the near future the establishment of a cross-agencies expert WG that should coordinate this exercise and also define the best methodologies to be used for the analysis of the data. It is foreseen that representatives from the relevant networks of the agencies/authority will seat in this WG, and that agencies/authority will maintain their own existing procedures for the information and consultation of the MSs.

This is of particular relevance when it comes to the publication of data provided by the MSs, for which prior agreement should always be sought. For the purpose, the relevant Standing Committee will be consulted before publication of the final draft report. EFSA confirmed that from its side current practices as regards the information and consultation of the MSs and other reporting countries, through the Zoonoses Task Force, will be followed. Similarly, as requested by the Zoonoses Task Force, the intention is to pay special attention to the way data submitted by the reporting countries are to be presented to the public, ensuring that these are put in the right context and when quoted, possible limitations of the data and applied methodologies should be highlighted before drawing firm conclusions.

7. 2010 European Union Summary Report on Antimicrobial Resistance: main findings

Camilla Smeraldi presented an overview of the structure and main findings of the 2010 European Union Summary Report on AMR . Task Force members were made aware that the report had just been published on EFSA's and ECDC's website concomitantly with the Danish Presidency conference on AMR. The publication has been accompanied by a joint press release from the two agencies and the publication appeared to be picked up by several media. MSs were thanked again for their contributions in the drafting and review of the Summary Report.

It was highlighted that some of the points raised at the previous Task Force meeting have been already taken into consideration in the drafting of the Report, such as limiting the number of maps to the most significant ones, using the same colour for a given MS throughout the graphs of the report, and the inclusion of a list of contributing laboratories and institutions.

As regards the main findings, no major changes had been detected compared to the previous year. In the report for the first time trends had been tested for statistical significance, resulting in some MSs reporting significant decreasing and increasing trends. Also, for the first time it was possible to produce a separate analysis of the data from turkeys deriving from the *Salmonella* control programmes.

As regards the comments received during the finalisation of the Report, a point raised by one of the networks collaborating with ECDC concerned the use of the term microbiological resistance, considered to be somehow misleading. The Task Force members were in agreement that the concept of microbiological resistance is well and thoroughly explained throughout the report and at this stage it was not felt the need to revise the terminology used. Some Task Force members underlined the fact that also for this year the data have been presented in the report under broad animal species categories (such as cattle, *Gallus gallus*) and not detailed per production type and/or animal age. It was explained that this is due to the fact that despite some countries reporting very detailed information on the origin of the samples, there are still others that report the data under the broad categories. This topic was discussed in more detail under the agenda item 11.

8. Results of the 2010 AMR isolate-based analysis

At the previous meeting in October 2011, a presentation was given to the Task Force members on the plan of analysis of the 2010 AMR isolate-based data to be performed by the contractor Hasselt University. The objectives of the analyses were to apply to the pilot dataset a number of methodologies envisaged *a priori* to investigate the multi-resistance and analyse its relationship with the animal and geographical origins of the isolates. An extract of the outcomes of the analyses performed was circulated to the Task Force Members in advance to the meeting, with data anonymised for what concerns the country providing voluntarily the data.

At the current meeting, the analyses were exemplified by presenting exemplary tabulations of antibiotype frequencies, multi-/co-resistant pattern inventories as well as outcomes of Principal Components Analysis (PCA) and cluster analysis. It was also explained how an attempt was made at defining an indicator of diversity of antibiotypes that was based on the concept of 'weighted entropy'. It was highlighted how the application of PCA would be considered an interesting approach to investigate multi-resistance in a large MIC dataset.

A question was raised on the possible application of these methodologies to draw predictions on the possible evolution of resistance and it was confirmed that PCA, for example, should make it possible to follow evolution over time of the different patterns of resistance, whenever data from successive years will be available. It was also indicated that possible differences in the dilution ranges between the reporting countries might have an effect on the outcomes of the PCA, although laboratory methods should be harmonised.

The complexity of the analysis of the multi-resistance at EU level, the limited number of references on the analysis of the multi-resistance, the limitations inextricably linked with the analysis of truncated datasets (submitted in the framework of a pilot transmission exercise) as well as the importance of this pioneering work were acknowledged. It was explained that the final report from the contractor will be published on EFSA's website as an external report.

9. Insertion of multi-resistance analysis in the 2011 EU Summary Report on AMR: first discussion

Further to his presentation on the results of the 2010 AMR isolate based analysis, the Chair opened the floor for discussion on whether and how outcomes of these new analyses of the multi-resistance could be incorporated in the EU Summary Report on AMR as of next year. It was proposed that only a selection of the most meaningful results will be included in the EU Summary Report, in particular, 'summary indicators' of the multi-resistance, such as the proportions of fully susceptible isolates, the proportions of multi-resistant isolates, the antibiotype diversity illustrated through graphs, and the related weighted entropy. To this end, it was indicated that EFSA has recently launched a call for tender to select a contractor that would take care of conducting similar analyses as those performed on the 2010 pilot dataset and producing results that would be inserted in the 2011 report.

It was clarified that, whilst the data on multi-resistance from the 2010 pilot project will be published in the external scientific report in an anonymised way, for the 2011 data to be included in the EU Summary Report the name of the country that reported them will be shown next to the results. None of the Task Force members voiced concerns over this and therefore it was agreed that as of next year results of the analyses on multi-resistance will be included in the EU Summary Report on AMR.

10. New mandate from the European Commission on harmonised monitoring of AMR

I. Presentation of the proposals for monitoring from the expert Working Group

The Task Force Members were informed about a new mandate received by EFSA from the EC as regards a planned review of the current monitoring of AMR in animals and food. Under this mandate, scientific and technical assistance from EFSA is requested to formulate proposals that should take into account recent scientific opinions on AMR, latest technical developments, recent trends in AMR occurrence and relevance for human health.

The Chair explained that, in order to accomplish the mandate within the short deadline (end of April 2012) assigned to it, EFSA has established a small dedicated WG. The EC will use the technical recommendations from the WG to engage in discussion with the MSs and formulate proposals for updating existing legislation. Subsequently, an update of the EFSA's technical specifications is also foreseen to translate the general recommendations into more detailed and practical monitoring guidance. Christopher Teale, on behalf of the expert WG, presented the main conclusions reached so far by the WG on the terms of reference included in the mandate.

For what concerns the combination of bacterial species and animal/food categories, one of the recommendations from the WG would be to introduce mandatory monitoring of AMR in commensal bacteria *E.coli* and enterococci, in addition to those species that are already subject to mandatory monitoring *Salmonella* and *Campylobacter*. As regards the food and animal species, the WG is recommending the introduction of a threshold mechanism (e.g. on the basis of the tons of animals slaughtered) for the monitoring to become mandatory in a given animal species in a given MS. Mandatory monitoring would be on a yearly

basis for those combinations of bacteria/food and animal categories that are of most relevance in terms of consumers' exposure, whereas for other species this could be performed on a regular basis only, such as every three years. For what concerns monitoring of AMR in meat, the WG would suggest leaving some flexibility as regards the sampling point (either at retail or at cutting plant) to take into account national specificities.

As regards the methods, current phenotypic monitoring is primarily recommended to be retained within the core monitoring programme. Additional typing of certain isolates is considered desirable, for instance for ESBL producing *E.* coli and MRSA, since this would provide the opportunity for further analysis of linked characteristics (for example, resistance and virulence). The WG also acknowledged the existing differences at the level of the MSs as regards the use of molecular typing techniques, and a baseline survey on ESBL producing *E.* coli was suggested as a possible way of piloting these techniques across the EU.

The list of antimicrobials to be included in the testing panel had also been reviewed and some proposals were made as regards inclusion of new substances mainly to discriminate between ESBL and AmpC resistance and to monitor resistance to antimicrobials relevant for human medicines. Additionally, it is proposed to perform a "second-stage" test of only the very few *Salmonella* and indicator *E. coli* cephalosporin-resistant isolates to further characterise the mechanisms of resistance involved. In selecting the antimicrobials and the corresponding concentration ranges to be tested calculations were made in order not to keep as limited as possible the number of plates. The use of epidemiological cut off values (ECOFF) for the interpretation of resistance will be maintained.

In response to the terms of reference regarding the AMR monitoring in VTEC, the WG concluded that pathogenicity of VTEC is unrelated to presence of AMR genes and VTEC infections are not usually treated with antimicrobials. In light of the considerations above, specific monitoring of this subset was not considered recommended. However, resistance phenotype may provide some useful epidemiological information; such as in the case of the major O104 outbreak strain.

As regards the format for the collection and reporting of the data, it was explained that the WG will make reference to the recently issued scientific report 'Technical specifications for the analysis and reporting of data on antimicrobial resistance (AMR) in the European Union Summary Report' and the use of dilution methods and reporting at isolate based level will be recommended.

It was finally indicated that the proposals presented were however still draft and that a meeting of the WG will take place the following week. Also the views of the WG will be shared with the ECDC and the EU-RL on AMR prior to the finalisation of the report. Consultation of the draft report with the Task Force members is planned to be launched in the first half of April 2012.

II. Open discussion on preliminary proposals from Working Group

Further to the presentation on the preliminary proposals from the WG, the Chair invited the Task Force to a first round of comments. No major objections were raised against the preliminary recommendations presented.

A question was raised as regards the reporting of clinical isolates, given that these are currently excluded to favour data deriving from monitoring programmes. It was explained that data from clinical isolates are not covered by the current mandate, for which the focus remains on monitoring of healthy animals.

Task Force Members were also reminded of another mandate that is currently being addressed by EFSA as regards meat inspection. The presence of ESBL/AMPc in *E.coli* in poultry has been identified as a hazard and an existing WG is currently defining harmonised epidemiological indicators. Current proposals include

sampling at farm and at the end of the slaughter lines. Coordination between the two WGs is therefore desirable in order to try to minimise the sampling to be performed by MSs.

11. Reporting of AMR data for the reporting year 2011

I. The 2011 data Reporting Season – reporting of aggregated and isolate-based data

Camilla Smeraldi presented an overview of the planned activities for the 2011 data Reporting Season that will run from 10 April 2012 until 4 June 2012 and of the main changes from last year reporting system.

As in previous years, it will be possible to manually enter the AMR data through the Zoonoses Web Application and from there to create the national reports. This method of transmission is limited to the submission of quantitative and qualitative data in an aggregated format. Transmission of data will also be made possible using EFSA's Data Collection Framework (DCF) and this method will be enhanced for this reporting season, thus allowing the transmission of data not only at isolate level, but also in an aggregated fashion **(**both quantitative and qualitative data**)**. It was explained that data submitted through the DCF system will then be migrated into the Zoonoses Database. As regards the format of the files for the transmission to the DCF, it was confirmed that the system accepts Excel, CSV and XML files, the latter being the preferred option.

Task Force members were informed that the Excel data entry tool provided by EFSA last year to facilitate the creation of XML files compliant with the DCF will not be available for this year. A sample mapping tool will be provided to show how mapping between national terms and EFSA's picklists could be performed. Additionally, EFSA is planning to organise a training session targeted at the reporting officer and a member of the IT staff from the reporting authorities to support the preparation of the transmission.

This year the data collection model has been slightly amended compared with the one in use last year, in particular as regards the splitting of the sampling description. In the model in use for this year the information will be broken down by 'sampling stage', 'sample type', 'sampling context' and 'sampler' as part of the annual revision of EFSA's picklists by scientists and TF members. These same modifications have been implemented in both the pick lists in use in the web application reporting tool as well as in the data collection model for the DCF.

As regards the manual for reporting aggregated quantitative and qualitative data and the data dictionary for the isolate-based data, draft versions were circulated in advance to the Task Force meeting and will be finalised before the start of the reporting season. The guidance documents for reporting have been aligned to the recommendations issued by the previously established Expert WG, particularly for what concern the way information on the animal populations should be reported (i.e. broken down by age and production type). Recommendations have also been given as regards the *Salmonella* serovars of public health relevance that should be reported. Task Force Members were invited to provide comments to these documents by 21 March 2012.

In conclusion, reporting countries were strongly encouraged to move to the isolate-based format for reporting AMR data, in consideration of the fact that this data collection system enables reporting of more detailed information and consequently, allows for more in-depth analyses to be performed. With a view to support transmission of the data through the DCF system and therefore in compliance with EFSA's data models, MSs were reminded about the opportunity to apply to a call for grants launched under Article 36. It was explained that applications can also be submitted for the 'cleaning' of the historical data set

II. Tour de Table on Member States' intention to report isolate based data

Further to this presentation, the Chair invited the Task Force members to a tour de table to gather their views and intentions to report AMR data as isolate based data during this reporting season. The majority of the MSs declared that their intention to submit isolate based data for 2011, some of them limitedly to *Salmonella*.

Several MSs expressed their views over the fact that, at least for *Salmonella* data from *Gallus gallus*, as of the 2011 report data should be presented in the EU Summary Report broken down by production type. This proposal was accepted in principle provided that a majority of the MSs reports AMR data per production type. A similar approach should also be followed for the presentation of the data from cattle.

Lastly, a question was raised by one of the reporting countries, concerning the reporting of data on ESBL obtained with selective enrichment. This question will be followed up by EFSA.

12. Any other business

No other business was raised.

13. Closing remarks and date of next meeting

The Chair thanked all the participants for their contributions to this fruitful meeting. It was reminded that this specific TF meeting on AMR should take place on a yearly basis and therefore the next meeting will take place in 2013, most likely as a joint meeting with ECDC.