



Defra Antimicrobial Resistance Coordination (DARC) Group

REPORT OF FIFTY-EIGHTH MEETING

09 February 2016

Present: Agri-Food and Biosciences Institute (AFBI)
Animal and Plant Health Agency (APHA)
Biotechnology and Biological Sciences research Council (BBSRC)
Centre for Environment, Fisheries and Aquaculture Science (Cefas)
Department for Environment, Food and Rural Affairs (Defra)
Department of Health (DH)
Food Standards Agency (FSA)
Health Protection Scotland (HPS)
Public Health England (PHE)
Scottish Government (SG)
Scotland's Rural College (SRUC)
Veterinary Medicines Directorate (VMD)

1. Update on Recent Findings (August- December 2015)

1.1 England and Wales

- Eighty-two and 67 isolates of Monophasic *Salmonella* Typhimurium 4,12:i:- and 4,5,12:i:- were identified, predominantly from pigs. ASSuT was the most common resistance profile.
- Numbers of CTX-M-15 (24) ESBLs are starting to overtake the number of CTX-M-14 (9) in cattle. Interestingly, half of the CTX-M-15s in cattle also have the OXA-1 gene. In *E. coli* from chickens, CTX-M-1 ESBLs are most commonly seen.
- There was one finding of MRSA *spa*-type t899 from a turkey flock. Further tests to confirm whether the isolate is a Livestock Associated (LA) strain are pending.
- One isolate of *Haemophilus parasuis* with penicillin and ampicillin resistance was identified from a pig; this is the first isolation of this resistant pathogen since 2011.

1.2 Northern Ireland

- Seven *S. Typhimurium* isolates were detected from food products (pork factories), animal feed and a poultry farm. One *S. Typhimurium* was isolated from manufactured pork with resistance profile ACSSuTTmNX.
- Eighteen Monophasic *Salmonella* Typhimurium (4,5,12:i:- and 4,12:i:-) were isolated from a variety of sources, including: pigs, battered sausages, pork, bacon, trotters, sausage meat.
- No multi-resistant *Salmonella* were detected during this period.
- 16/257 *E. coli* isolates were phenotypically consistent with ESBL production. Isolates originated from a variety of sources, including: calf faeces (8), bovine milk (1), bovine faeces (2), calf liver (2), calf lung (1), chicken liver (1), and turkey liver (1).
- 36 *S. aureus* were tested for resistance to cefoxitin during the reporting period and all were sensitive.

1.3 Scotland

- There have been 20 isolations of *S. Typhimurium* between August-December 2015.
- No isolations of Monophasic *Salmonella* Typhimurium in this period.

- All non-Typhimurium *Salmonella* were fully sensitive to all antimicrobials tested.
- No ESBL producers were recovered from Scottish samples during this period. Two ESBL *E. coli* were isolated from two canine samples (suspected to be from the same dog) from England. Additionally an ESBL *E. coli* was found in a pig from the Republic of Ireland – the pig had rotavirus.
- Two MRSAs were isolated from cat wound infections (t379 CC22 and t15289). One CC8 MRSA was isolated from a macaque. Four Methicillin Resistant *Staphylococcus pseudointermedius* (MRSP) were isolated from dogs (2 wound, 1 skin and 1 urine infection). The reference laboratory is examining historic isolates of MRSP.

1.4 Recent findings relating to colistin resistant isolates

The group discussed the resistance profiles of *mcr-1* positive isolates: in both human and animal isolates resistance to other antimicrobials is seen either chromosomally or on another plasmid. However no other resistances are seen on the *mcr-1* plasmid.

APHA confirmed that they will be submitting a paper to JAC detailing the results from analysing isolates from GB surveillance.

The Chair thanked colleagues from APHA, FSA and PHE for the work which was undertaken as a result of these findings and commended all involved for the collaborative, inter-departmental approach.

2. LA-MRSA

PHE presented preliminary results from a human LA-MRSA study; volunteers for this study were sampled at the London Vet Show in 2015. PHE also discussed the results of a retail meat survey.

VMD informed the group that a zoonoses leaflet offering guidance on how to limit the dissemination of LA-MRSA on farm was now available on GOV.UK. This leaflet is now being amended so that it can be applicable to those working in abattoirs. A biosecurity leaflet is also being drafted, and will be circulated for information prior to publication.

3. VARSS – Changes to Structure and Content in 2015

VMD gave an overview of some of the changes to the most recent VARSS Report:

- The report now contains four key chapters covering results from the two areas of surveillance carried out by the VMD.
- The results chapters now include a 'key messages' section.
- Various changes to the content of the report, such as: addition of a chapter on antibiotic consumption data, publication of historical sales data in the report Annex, and inclusion of results from the first year of EU harmonised monitoring.

When comment was sought from the group on the report it was suggested that a questionnaire which readers can fill out and return might be helpful.

4. Independent Review on AMR

The 'Antimicrobials in agriculture and the environment' report was published in December 2015, this is one of many interim papers in the review and that any recommendations are subject to change until the final report to the Prime Minister is published. The UK is committed to take forward

recommendations from the whole report, and a sub group will be coordinating the actions of the UK Government.

An economic forum held in January produced a declaration signed by 85 companies affirming that they would commit to antibiotic stewardship.

Feedback from the report was encouraged; this can be sent directly to the Independent Review team.

5. EU Update

5.1 CVMP

VMD provided an update of CVMP activities between November 2015 and January 2016; the accompanying paper was circulated prior to the meeting. In summary;

- Following advice from the CVMP, the Commission has sent a request to the EMA to update the scientific advice of 2013 on the risk to public and animal health of the use of colistin in animals. The deadline for this is 30 June, 2016.
- The Commission has sent a request for EFSA to provide a scientific opinion on the risk for the development of antimicrobial resistance due to the feeding of calves with milk containing residues of antibiotics. The CVMP will be represented on this working group.
- The CVMP Strategy on Antimicrobials 2016-2020 was adopted for release for a 3 month period of public consultation.

5.2 HMA-V Taskforce on Antimicrobials

VMD provided an update to the group on the recent HMA-V Taskforce teleconference. In summary:

- There have been discussions surrounding stratification of sales data per animal species as an interim measure whilst countries are establishing methods for collecting consumption data. This will be taken forward at the ESVAC network meeting in March.
- The Czech Republic have completed the pilot TPMP (Target species Pathogen Monitoring Programme), the main conclusions from this pilot were: local, independent data are important, followed by evidence based risk management policies and vets and farmers need to see practical results from any interventions. There is a need to identify a minimum set of veterinary pathogens to which countries could agree to provide data.
- There is support for the VetCast initiative. EMA will be discussing the setting of clinical breakpoints and other regulatory issues with VetCast.

6. Colistin Workshop

Colleagues from DH and PHE, as well as representatives from the livestock industry, joined the meeting for a joint DARC/ARHAI afternoon workshop to share knowledge on colistin use and resistance in the UK.

6.1 Use and Levels of Resistance in Human Medicine

PHE shared data on trends in colistin use in human medicine in the UK. The key points were that:

- Colistin is an antibiotic of last resort in human medicine.
- Colistin use (in Defined Daily Dose) is higher in the Community than in Hospitals (75% of all colistin is prescribed in the Community).

- The UK has the highest Community use of colistin in Europe.
- The use of colistin is predominantly in a nebulised (inhalable) form for the treatment of Cystic Fibrosis (CF) related respiratory infections – approximately 1/3 of CF patients receive it.
- Prescription items of colistin are increasing: from 1998-2014 prescription items of colistin have increased from 22,500-45,219 per annum.
- Carbapenem resistance in gram negative infections is climbing and as a result colistin use may be increasing, but this is hidden among CF patient data.
- In the EU countries where there are higher levels of MDR the use of colistin in hospitals is higher than use in the community.

PHE also shared findings on investigations into the presence of the *mcr-1* gene:

- Of the *Salmonella*, *Klebsiella* and *E. coli* isolates which were tested 15/24000 contained the *mcr-1* gene.
- Three of these *E. coli* isolates can be associated with travel to South Asia and all *E. coli* isolates were ESBL producing.
- The *mcr-1* gene has been found on multiple plasmids and in different genetic environments, no fitness attributes for these plasmids have been observed in human medicine.

6.2 Use and Levels of Resistance in Veterinary Medicine

VMD shared data on sales of colistin for use in veterinary medicine:

- In 2014 sales of colistin represented 0.3% of sales of all antimicrobials sold for use in livestock.
- Between 2004-2014 sales have consistently been less than a tonne per annum.
- Colistin was first authorised for use in animals (pigs) in 2004 and has since been authorised for use in lambs, calves and chickens
- Of the authorised products which contain colistin most have cross-species indications, so it is not currently possible to identify what is being used in which sector, though the meeting was informed that use in the poultry sector was very low.
- In the EU, three countries report no sales of colistin for use in animals. Of the countries which do report sales, the UK is the second lowest.

APHA presented on colistin resistance seen in UK livestock:

- Based on the results of testing of 2015 EU monitoring samples, less than 1% of GB pig herds were positive for *mcr-1* mediated colistin resistance. None of the individual *E. coli* examined from these samples were colistin resistant.
- A very low number of *Salmonella* isolates from laying hens collected under EU monitoring in 2014 were colistin resistant; however none were positive for *mcr-1*.
- Two pig farms have been identified as *mcr-1* positive through clinical surveillance in GB. In *E. coli* from the first affected farm, no resistance to other antimicrobials has been found on the *mcr-1* plasmid specifically; however other resistance plasmids were often present in the *E. coli*.
- After *mcr-1* was identified, both farms voluntarily ceased use of colistin.

6.3 Treatment Guidelines

Human Medicine

PHE detailed the role of colistin within human medicine. Colistin has a role in secondary prophylaxis in chronic CF cases. Colistin is neurotoxic and nephrotoxic. Outside of CF treatment it is an antibiotic of last resort; it is never used empirically.

Veterinary Medicine – Pig Sector

A representative from the PVS detailed that colistin is highly effective in controlling colibacillosis in the immediate post-weaning period in piglets. Colibacillosis is difficult to control, as the pig gut undergoes large changes at this time – zinc oxide can also be used. Colistin is used in pigs as a 5 day course in water. The PVS has ranked the antibiotics it uses by their importance to the medical profession.

- Category 1 – Can be used freely, with prescription.
- Category 2 – Further consideration required prior to prescribing.
- Category 3 – Use should be based on proven need and the results of culture and sensitivity testing. *Colistin has been put in category three.*

Veterinary Medicine - Poultry Sector

A representative from the British Veterinary Poultry Association (BVPA) and British Poultry Council (BPC) detailed that the use of colistin in poultry is similar to pigs, in that it is most commonly used for the treatment of colibacillosis in younger neonatal chickens, and also in commercial layers as they come into lay. In both cases, it would be extremely uncommon for it to be used empirically – there would be culture and sensitivity testing (disc diffusion method) of the bacteria causing the problem prior to prescribing.

The BPC antibiotic stewardship group have reported that the BPC membership (meat poultry sector) had not used colistin their stock since before October 2015 and there are no plans to use this active ingredient in the future.

6.4 Evidence Gaps and Next Steps

The meeting discussed current evidence gaps around the mechanisms and dissemination of the *mcr-1* plasmid. These were grouped into themes ‘microbiology’, ‘epidemiology’ and ‘antibiotic usage.’

The next steps that need to be taken in order to fill these evidence gaps was discussed and it was agreed that VMD, PHE and APHA would discuss future surveillance ahead of publication of the next One Health Report in 2017.

7. Date of Next Meeting

Wednesday 1 June 2016

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