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Surveillance of veterinary antimicrobial agents in Europe - the ESVAC project

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Outline

1. Mandate ESVAC Project. Cooperation with EFSA, ECDC and EURL-AR
2. State of the art before the ESVAC project
3. ESVAC project plan
4. Main deliverables from the ESVAC project
5. Major challenge: How to report the data
6. Opportunities for collaboration with EURL-AR?

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Mandate ESVAC project described in Letter from Commission [SANCO/E2/KDS/rz D(2008) 520915]

- Requests the EMEA to take the lead in collecting data on the use of antimicrobial agents in animals
- In order to guarantee an integrated approach, the ECDC, the EFSA and the CRL* should be consulted

*EURL-AR

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Mandate ESVAC project cont

- To identify the existing data/surveillance systems established for collection of sales and use of antibacterial drugs in the Member States;
- To develop a harmonised approach for the collection and reporting of data
 - based on national sales figures
 - combined with estimations of usage in at least major groups of species (poultry, pigs, veal, other ruminants, pets and fish);

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Mandate ESVAC project: Purpose of collecting data on usage of veterinary AM agents

(Reference document: EMEA/507682/2008)

- To obtain reliable data for
 - Input into risk profiling and risk assessment regarding AMR
 - Setting risk management priorities regarding AMR
- As a basis for evaluation of control measures being implemented
- To assess the impact of measures taken in relation to prudent use
- To identify emerging use of veterinary AM agents, e.g. of specific classes of AM agents such as those identified by WHO as critical important for human medicine
- To aid comparison of usage of antibacterial drugs between time periods, countries etc

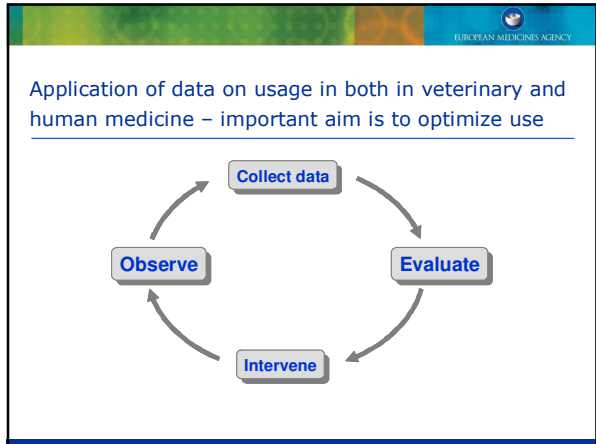
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Request from Commission to EMA

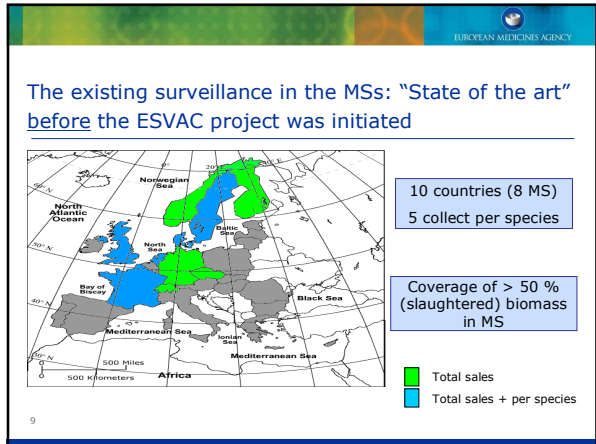
Appendix to letter from Commission: C.8/MN/sx. D(2009)42527


5. Cooperation with other agencies and committees of the Commission

As indicated above, the Commission would like to see more details in the EMA proposal on cooperation with other agencies and committees of the Commission, for example the ECDC and EFSA. One deliverable in phase II of the project could be a draft working agreement between relevant parties on how the data would be collected and used and specifying in detail the responsibilities and output of each party.




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- ### ESVAC project plan
- **ESVAC I.** Pilot project (2009-2011).
 - Investigate "state of the art"
 - Development of ESVAC Protocol and ESVAC Data Collection Form (template) to obtain reliable and harmonized data
 - Collection of overall sales from MSs willing to provide data in accordance with ESVAC Protocol and Template
 - **ESVAC II.** Operational Phase: Collating overall sales data from all Member States (2012-onwards) and on estimations per species
 - **ESVAC III.** Collating data on overall sales, estimates per species and on actual usage of antimicrobials by animal species, production category, indication etc (2013-onwards)




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Surveillance and reporting of data not transparent or harmonized

- Identical data coverage?
 - Which veterinary AM agents included in the surveillance programs for the 10 countries were for several of the countries insufficiently described or were lacking
 - Whether all wholesalers, market authorization holders etc that sells veterinary identified and included as data source
- Sales of veterinary antimicrobial agents reported differently among the ten countries
- Usage of AM classes characterized by the WHO as critically important antimicrobial agents (CIA) for human medicine insufficiently reported, e.g. use of 3rd and 4th generation cephalosporins could not be identified


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Main deliverables so far in **ESVAC I. Pilot project** (Sept. 2009 -2011)

- Technical Consultative Group (**TCG**) appointed with representatives from
 - 10 European countries (8MSs)
 - ECDC, EFSA and EURL-AMR (DG Sanco, DG Enterprise) in order to ensure harmonization
- Version 1 of **ESVAC Protocol** and **Data Collection Form (ESVAC Template)** to collect harmonised and reliable data on sales of veterinary antimicrobials developed in cooperation with TCG
- Version 1 of ESVAC Protocol and ESVAC Template **tested in pilot, training** and by application of **the software** developed
- Following the pilot minor revision of **ESVAC Protocol** and **ESVAC Template** (versions 2)


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Groups of AM agents included in ESVAC I

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/04/WC500089584.pdf

Groups of antimicrobial agents	ATCvet codes
Antimicrobial agents for intestinal use	QA07AA; QA07AB
Antimicrobial agents for intrauterine use	QG01AA; QG01AE; QG51AX QG51BA; QG51BC; QG51BE
Antimicrobial agents for systemic use	QJ01
Antimicrobial agents for intramammary use	QJ51
Antimicrobial agents used as antiparasitic agents	QP51AG

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Main deliverables so far in **ESVAC I. Pilot project** (Sept. 2009 -2011) cont

- A call for 2010 data according to ESVAC Protocol and ESVAC Template (version 2) sent to all countries agreeing to participate sent in January 2011 (23 countries of which 21 are MSs)
- Harmonized aggregated sales data (2005-2009) collated from 9 European countries according to agreed format (not ESVAC Template)
 - To be published when how to report the data agreed on

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Historical data – how it looks like. Example data from Norway

	2005	2006	2007	2008	2009
Tetracyclines	0.23	0.28	0.32	0.25	0.22
Amphenicols	0.00	0.00	0.00	0.02	0.02
β-lactams, penicillins	2.97	3.02	3.03	3.10	3.13
Cephalosporins	0.00	0.00	0.00	0.00	0.001
Sulfonamides	1.54	1.62	1.55	1.55	1.56
Trimethoprim	0.22	0.22	0.23	0.22	0.24
Macrolides	0.00	0.00	0.00	0.00	0.00
Lincosamides	0.02	0.02	0.02	0.02	0.02
Aminoglycosides	1.16	1.11	0.99	0.89	0.83
Quinolones	0.03	0.03	0.03	0.03	0.03
Pleuromutilins	0.14	0.15	0.20	0.13	0.10
Grand total	6.31	6.46	6.36	6.22	6.17

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How to report overall sales data? Example by use of pre ESVAC data. Sales reported in tons

Do not take into account differences between the countries regarding animal population at risk of being treated with antimicrobial agents

Overall sales data – retrieved from national reports and represent 2007 (*DE 2005 data)

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Expression of usage data human and vet med

- Human medicine
 - DDD/1000 inhabitants/year/country or DDD/1000 inhabitants/day/country
 - ESAC core data - DDD/1000 inhabitants/day/country
 - Hospital data - DDD/bed days/hospital
- Veterinary medicine?
 - g/ton biomass/year/country or g/ton biomass/day/country
 - DDDanimal/1000 animals/days /country - but DDDanimal not assigned at international (or European) level

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Biomass carcass + biomass live weight dairy cow (2007 data, 2005 for Germany)

Grave et al., J Antimicrobial Chemotherapy, 2010, 65, 2037-2040.


	Netherlands	France	United Kingdom	Czech republic	Switzerland	Germany*	Denmark	Finland	Sweden	Norway
Dairy cattle	745	1879	999	204	354	2082	276	148	183	127
Cattle	386	1532	882	79	133	1167	130	89	134	85
Dairy	721	1716	1454	217	60	994	171	95	104	70
Pigs	1290	2281	739	360	242	4500	1802	213	265	118

How to report overall sales data? Example by use of pre-ESVAC data. Sales normalized for biomass at risk

Do not take into account

- Differences in dosing between the various substances (and formulations)
- All animals species at risk of being treated
- Biomass animals transported to other countries for fattening or slaughter

Overall sales data – retrieved from national reports and represent 2007 (*DE 2005 data)


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Antimicrobial agents for all animal species included in pilot project. How to report data to allow for analysis of data together with data on AMR?

AMR data in zoonotic agents and indicator enterococci from

Species

Cattle
Pig
Poultry (*Gallus gallus*); broiler meat


Sales data

Major Species

Cattle
Pigs
Poultry


Others

Horse
Sheep and goat
Farmed fish
Rabbits
Dogs and cats


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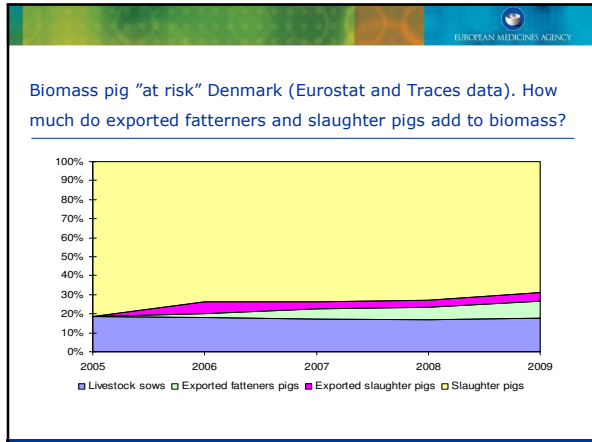
Example on calculation of biomass - France

Pigs	Numbers	Average weight	Biomass (in 100 tons)
No. slaughtered pigs x AW	25,484,411	65	1656.49
No. net import slaughter pigs (-) x AW		65	0.00
or No. net export slaughter pigs (+) x AW	358,194	65	23.28
No. net import fatteners (-) x AW	18,530	25	-0.46
or No. net export fatteners (+) x AW		25	0.00
No. living (1000 heads) sows x AW	1,264	240	303.36


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Example on calculation of biomass - France

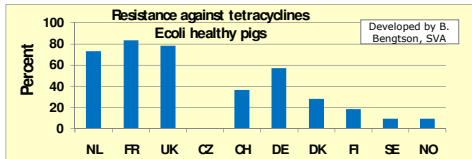
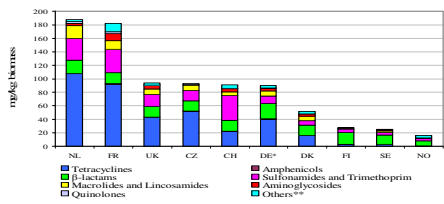
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- Challenge: How to analyse and report future ESVAC data and the historical data
- Prerequisites
 - Fit with TOR for as many of the bullet points as possible
 - Applicable for integrated analysis with data on AMR and usage in humans
 - Includes
 - Selection of/model on how to calculate denominator - including which species
 - How to express usage/exposure

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- Use of ESVAC sales data in relation to TOR – how much can the data be "stretched"
- Input into risk profiling and risk assessment regarding AMR
 - Setting risk management priorities (?) regarding AMR
 - As a basis for evaluation of control measures being implemented
 - To assess the impact of measures taken in relation to prudent use
 - To identify emerging use of CIA
 - To aid comparison of usage of antibacterial drugs between time periods, countries etc

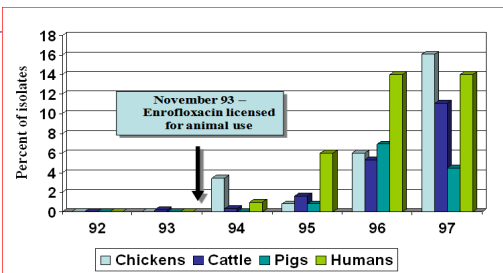
Can we conclude from this that there is an association between use of AM agents and occurrence of AMR?



Overall sales data - retrieved from national reports and represent 2007 (*DE 2005 data)

Data for 2007, from EFSA (2010)

Temporal study on quinolone-resistant MDR *Salmonella* Typhimurium DT104, UK, 1992-97



European Medicines Agency Reference EMEA/CVMP/447259/2009; EFSA Journal 2009; 7(11):1372

Opportunities for collaboration with EURL-AR?



Thank you for your attention
