Combating the risk of antimicrobial resistance in animals for the benefit of human health in Denmark

A case study of emerging risks related to AMR for the International Risk Governance Council (IRGC)

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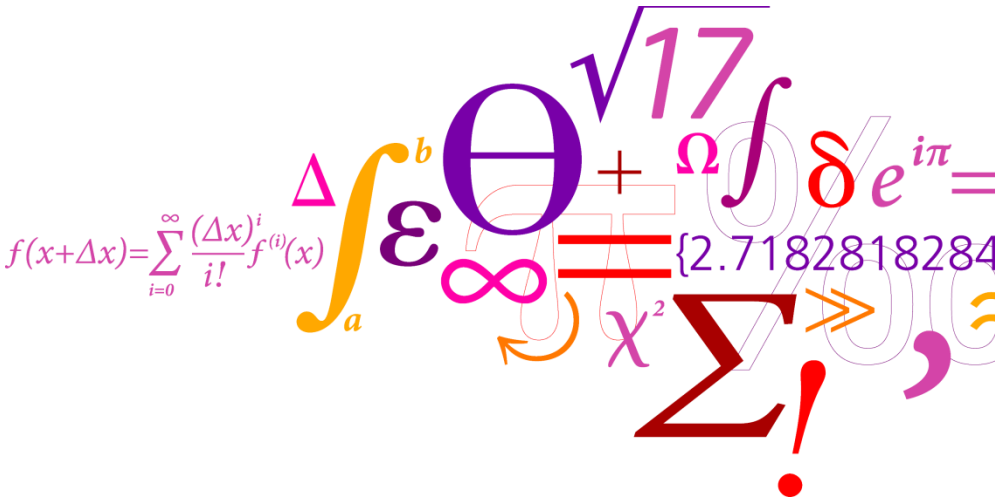

DTU Food
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Antibiotic use

First introduced in humans before World War II to cure bacterial infections

- Its success (e.g. that of penicillin) lead to the introduction in human medicine and development/discovery of many classes of antibiotics

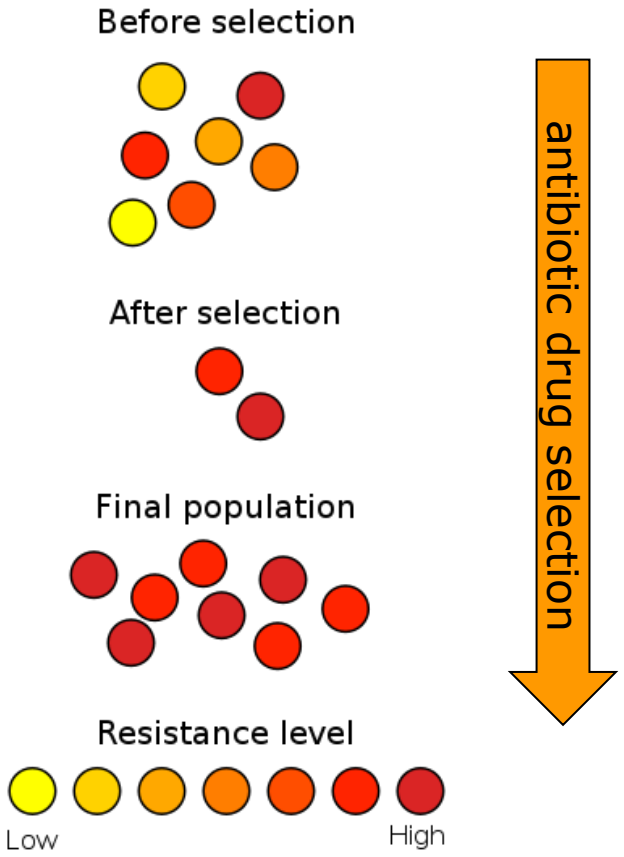
Its success in humans let to the introduction in animals and foodanimal production in the 1950s

Its uses in food animals there are:

- Animal growth promotor (AGP) – subtherapeutic levels
- Preventive treatment (flock treatment)
- Treatment of individual animals

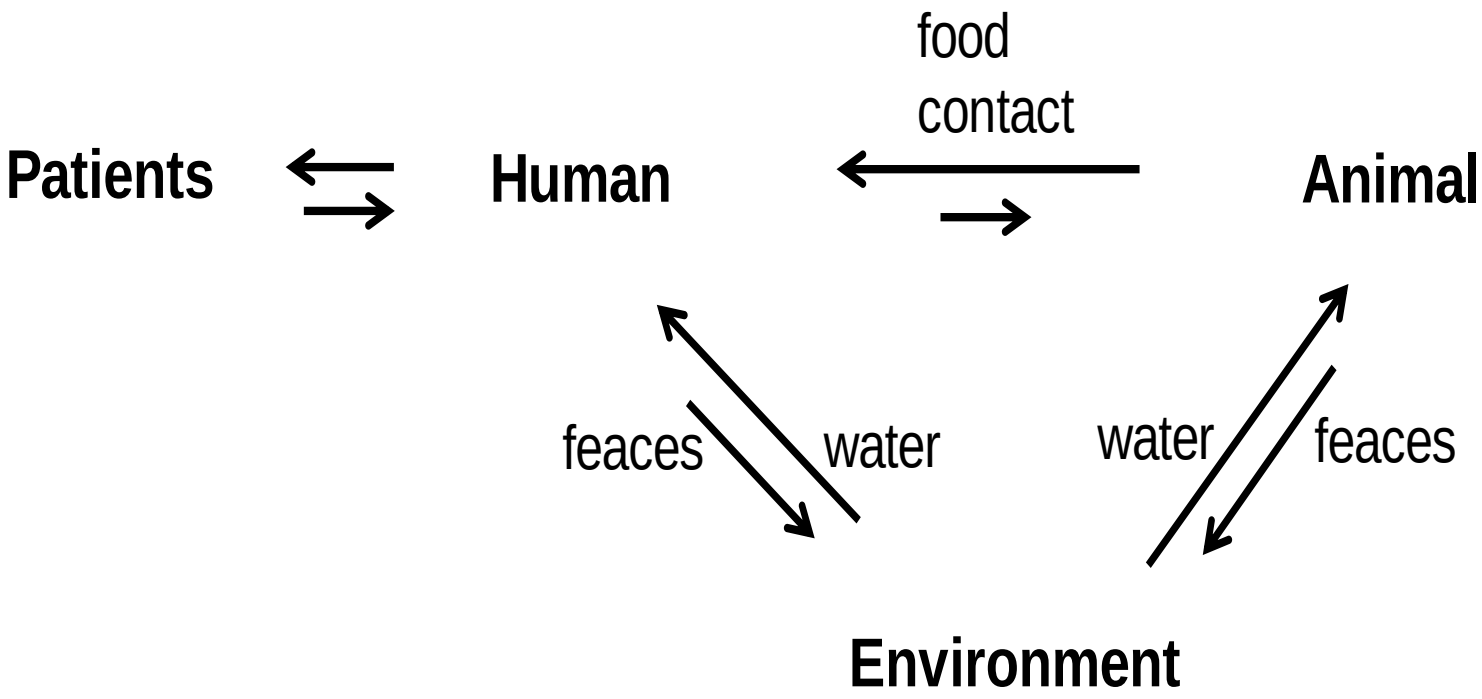
Antibiotic resistance (amr) – survival of the fittest

1. AMR is not new and the prolonged use of antibiotics in general will lead to the occurrence of resistant bacteria, simply through survival of the fittest.
2. Given the many trillions of bacteria in the animal- and human flora, the use of antimicrobials will almost always lead to the occurrence of AMR bacteria.



Transmission routes

Through food, direct contact, and via the environment the human and the animal bacterial flora interact and bacteria from animals end up in people and *vice-versa*.



Antibiotic use as AGP animals led to resistance problems in humans

1969 the UK-Swann report recommended:

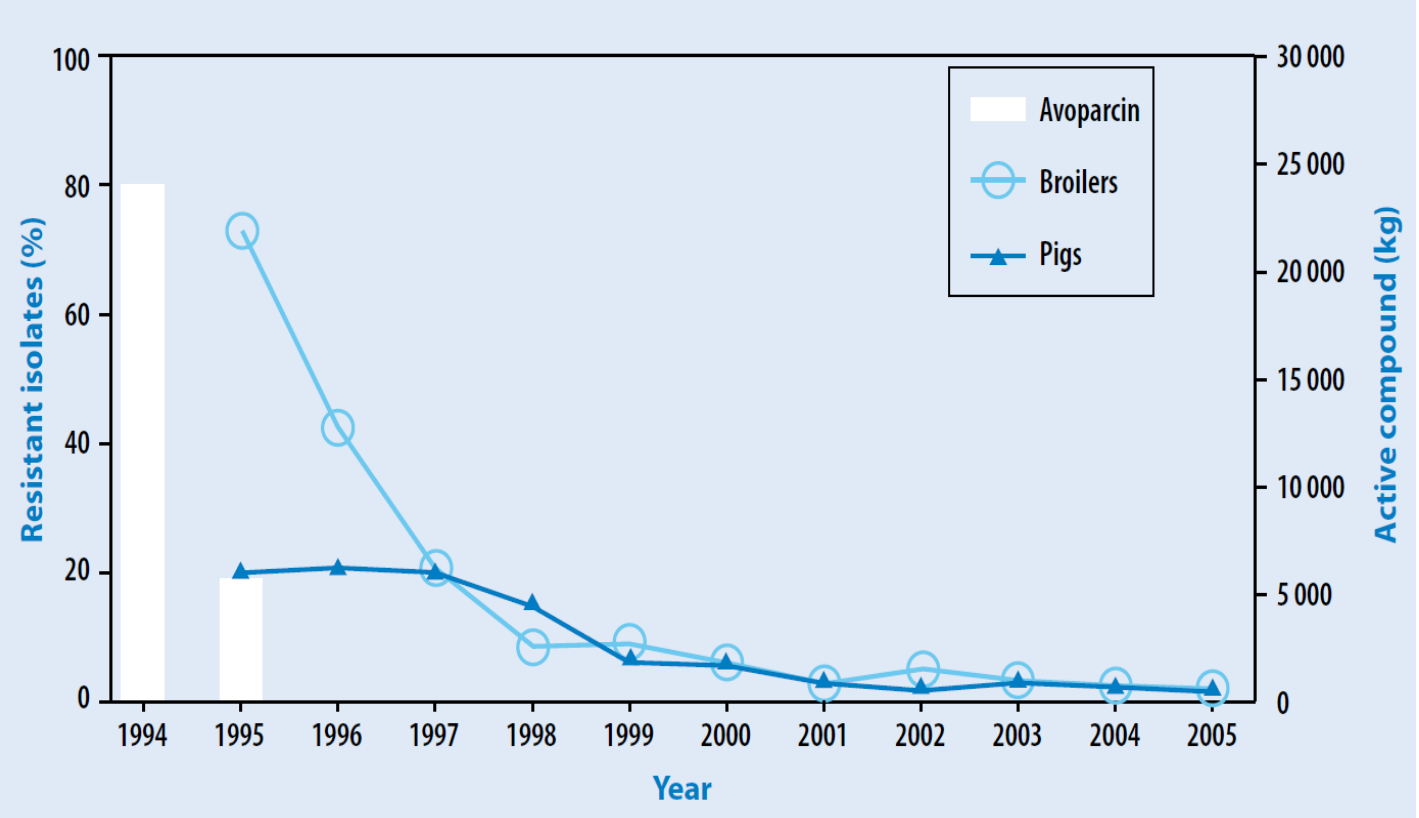
- antibiotics should not be used as **AGP**s if they were used as therapeutic agents in human or animal medicine, or when they were associated with the development of cross-resistance to antibiotics used in people
- This led to a ban of all use of AGP in food-animals if these antimicrobials were also important for therapeutic use in humans
    - First UK and subsequently EU followed

The action was enforced on individual antimicrobials and did not consider analogues of these drugs. Therefore the use of AGP in effect continued for most types

The Avoparcin case: antibiotic in animals formed continued risk for human health

- 1988 Avoparcin first introduced in animals
  - Denmark avoparcin was broadly used as AGP both in pigs and chickens
  - Vets sold the antibiotics they prescribed themselves which may have let to over- and unnecessary use
  - The total use and sales of antibiotics was not known to the authorities
- 1995 an study found vancomycin-resistant *Enterococcus* bacteria (**VRE**) in **80%** of the chickens from **conventional**, avoparcin using farms whereas (none were found in chickens from organic farms)
  - Note that active surveillance was not yet taking place, so there was no historical data to compare to!
- 1995-ish
  - VRE caused problems in humans
  - VRE/Avoparcin problems also found in other countries: Germany/UK…
  - Danish authorities and farmers were shocked, and the farmer agreed to voluntary withdrawal the use of avoparcin

Avoparcin resistance and use in food-animals



- Note that these data were generated by the DANMAP initiate executed after the events in 1995 (explained in the next slide)

Events that followed…

- More data and suggestions followed from the risk assessment side that other animal antibiotics might cause problems in humans as well

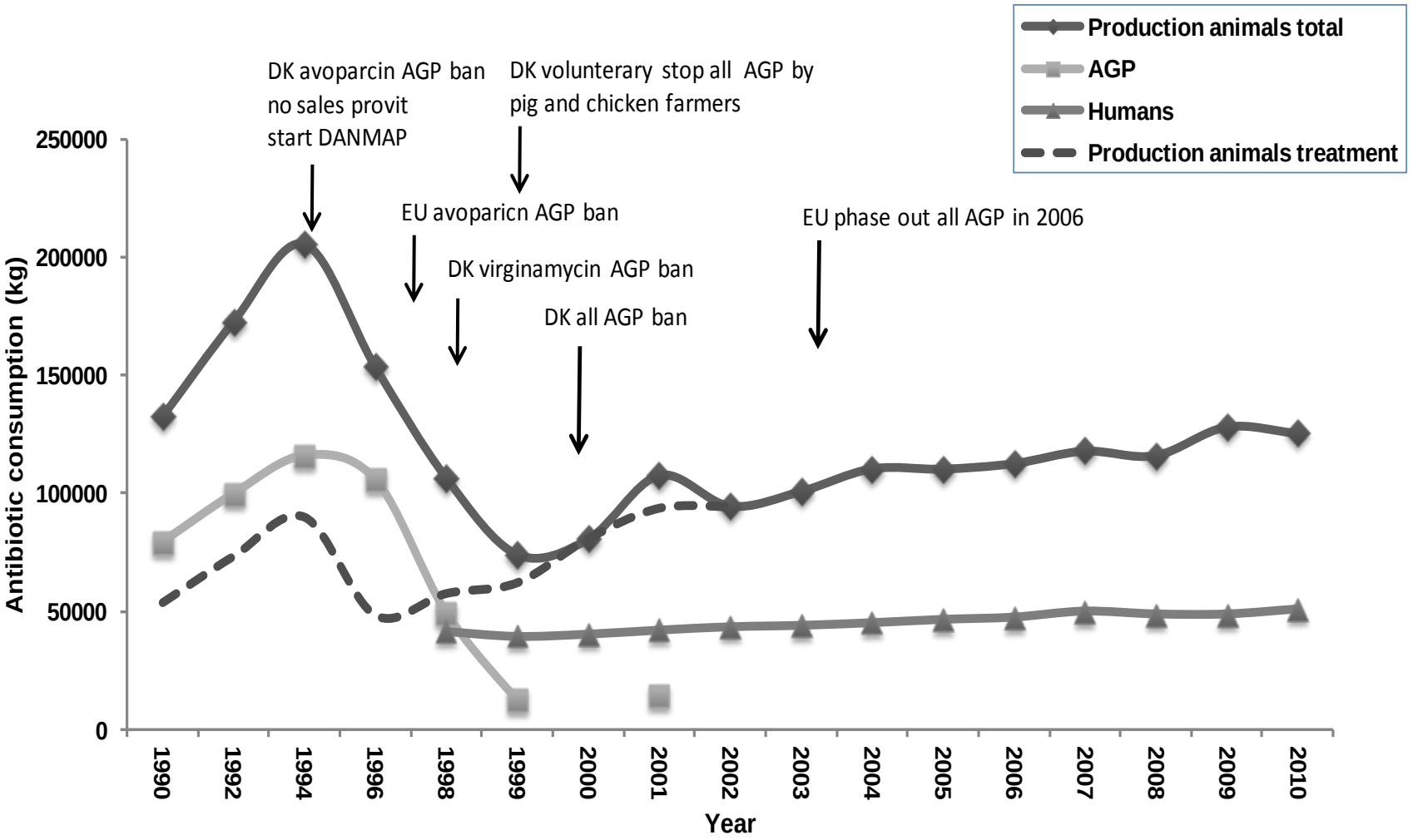
- Industry and Vets opposed the idea AGP caused problems in humans

- This latter claim could be understandable because of:
  - the complex transmission routes between humans and animals
  - the complexity of the microbiology needed for source attribution
  - The fact that human and animal doctors did not communicate/collaborate
  - The fact that different ministries did not communicate to find general solution and in fact tried to protect different groups in society (not only consumers!)

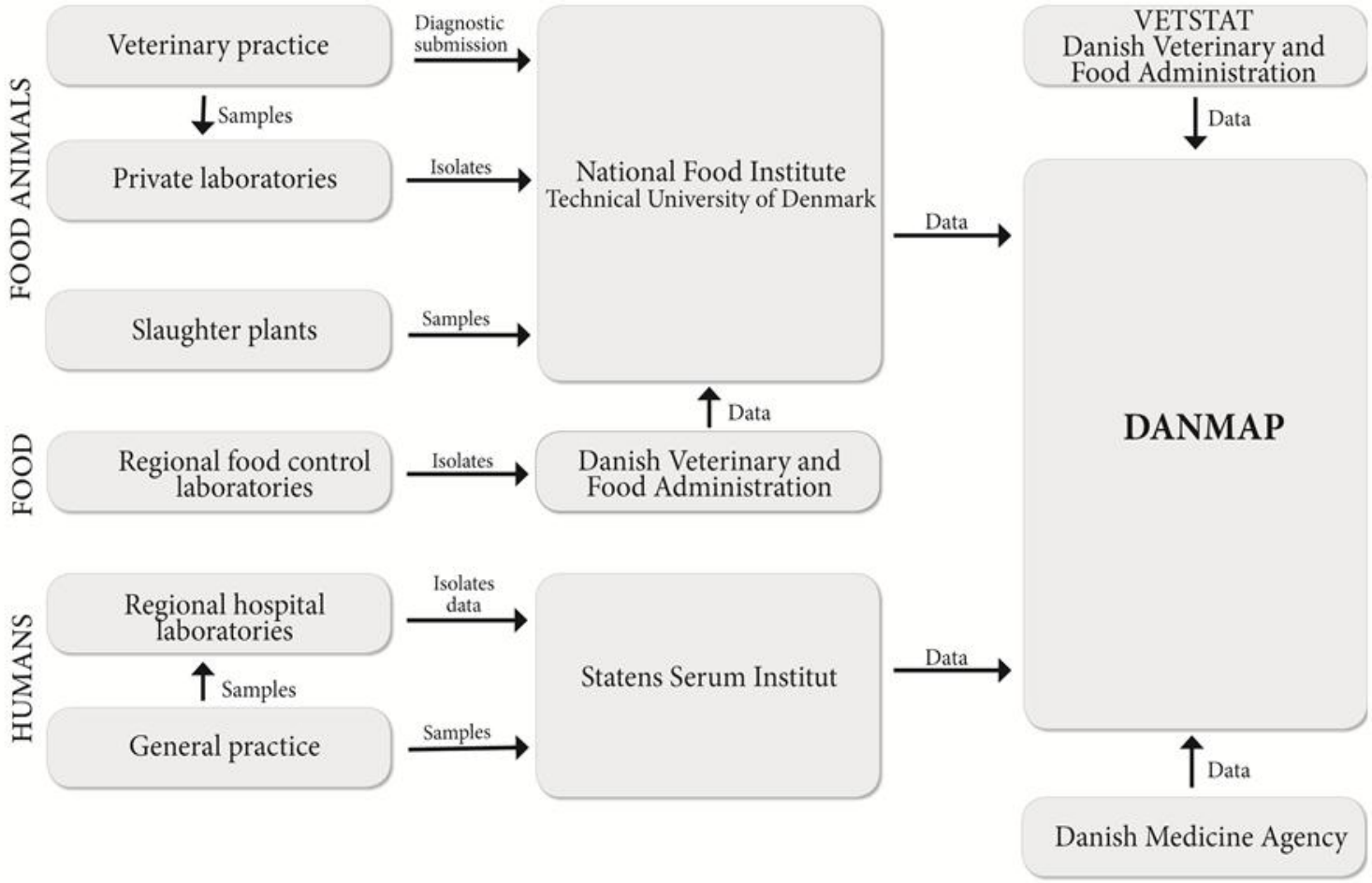
- However, following convincing data, problems were recognized by all stakeholders

- It followed that the Danish Minister of Food and Agriculture & the Minister of Health shared goals through an **integrated surveillance** approach, the Danish Integrated Antimicrobial Resistance Monitoring and Research Program (**DANMAP)**

Timeline of events



1) Integration:
DANMAP: Structure



2) Prioritizing risk - Focused intervention

- Survey foodborne disease and food contamination
- Assess the risk and the main factors affecting it
- Isolate major foods linked to disease
- Define efficient intervention(s) and monitor effect
  e.g. resistance in zoonotic pathogens through DANMAP

3) Accountability

DANMAP was maybe Worlds' first integrated national, cross-sector, surveillance programs to asses the risk of AMR (& 'en passant' some other zoonoses).

Key features:

- Science based and the data are open for all
- Separation of the risk-management and risk-assessment – to prevent conflicts of interest
- System leaves some level of accountability with primary producers and veterinarians, because antimicrobial use is linked to antimicrobial resistance

DANMAP continuity ensures flexibility

- Human health sectors is able to follow AMR development
- Animal production sector is able to compare resistance developed from animal use with resistance developed from human use
- Old practices of pointing fingers at the other use in stead of taking responsibilty for own use is (to some degree) avoided
- Joint reporting promotes joint action

5) Creating transparency

DANMAP promotes open, comparable reporting

- All use data can be linked down to single farm / single Vet / single MD
- Annual reporting ensures continued interest in society
- Positive achievements result in positive feed-back loop (e.g. decrease in antimicrobial use through ‘Yellow Card’ – see next slide)

6) Inclusive Governance

DANMAP integration fosters inclusive thinking

- Collaboration between all stakeholder (private/governmental)
- Authorities making decisions based on best science
- Stakeholders respecting science and decisions

(Newest example the ‘Yellow Card’ system, dramatically lowering use by pointing out farmers with highest use, who gets a ‘Yellow Card’ warning)

7) Convincing methods

DANMAP provides convincing tool for risk assessment and risk management + risk communication

- Data relates to – and are defined by – best contemporary science
- Data directly presents an evaluation of risk mitigation efficiency
- Both risk assessors and risk managers are involved in communication

8) Demonstrating Value

DANMAP as a pioneer project

Based on the Danish approach & findings:

- DANMAP-like projects have been started e.g. in EU
- All use of antibiotics as AGP has been banned in the EU
- More prudent uses of antibiotics being put forward e.g. by WHO and FAO and the OECD
- Antibiotic sales are being monitored e.g. within the EU

Conclusion

- Emergence of the risk:
  - Analogues of human antibiotics were not banned for use in animals after 1969
  - The continued and long term use of antibiotics led to resistance levels approaching 100%
  - Mixed incentives for Vets: both animal (and human) health and own financial gain may govern their level of antibiotics use
  - a lack of knowledge of the prevalence of AMR in animals and the real risks of it for human health
- Caging the risk and the DANMAP approach:
  - Discussion between the human, food and veterinarian sectors
  - Collecting scientific evidence to make a case
  - Conflict of interest (CoI) prevention: separation of risk management and assessment
  - CoI prevention: banning Vet profit from AM sales
  - Working across sectors (human & animal science & policy) and involvement of all stakeholders (private & public)
  - No secrecy: all information public available