

LARAS
LATIN AMERICAN
RISK ASSESSMENT
SYMPOSIUM



Risk assessment of antimicrobial resistance

Dr. Anja Buschulte

Methodological aspects for AMR Risk Assessment

General principles for Risk Assessments apply



CAC/GL 77-2011

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GUIDELINES FOR RISK ANALYSIS OF FOODBORNE ANTIMICROBIAL RESISTANCE

CAC/GL 77-2011

Hazard Identification

Risk Assessment

1. **Hazard identification**
2. Hazard characterisation
3. Exposure assessment
4. Risk characterisation

What exactly is the **hazard** with AMR?

- The **drug**, i. e. residues of the drug?
- The **bacterial** species?
- The **resistance determinant**, i.e. the resistance gene?
- The **DNA** carrying the resistance gene (Plasmid, Integron etc.)?

Hazard Identification

Risk Assessment

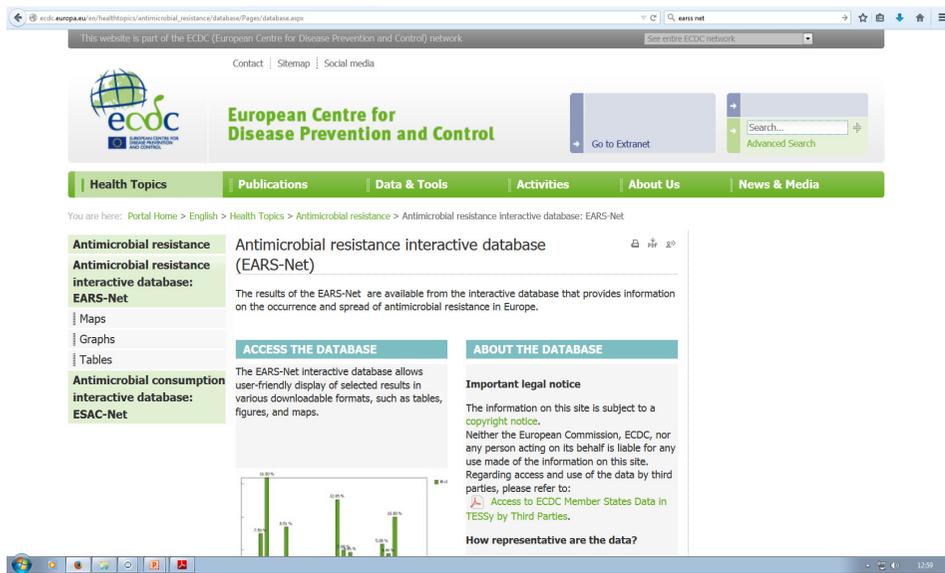
1. **Hazard identification**
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Aim: to **describe** the foodborne AMR **hazard** of concern

Specific **strains** or genotypes of foodborne **microorganisms**

that may pose risks by a particular **combination** of

- **food** commodity,
- **AMR microorganism** and / or determinants and
- **antimicrobial agents** which are affected by resistance.



Risk Assessment

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Information on the **biology** of **AMR** microorganisms / determinants within different **environments** / niches e.g.

- interactions with other bacteria
 - in animal **feeds**,
 - **aquaculture** or
 - the **gut** environment
 - in **food** matrices

Information on **susceptible strains** of the same organisms or related AMR microorganisms and / or determinants are useful.

Hazard Identification (Annex 2)

1.1 Identification of **hazard of concern**:

foodborne AMR microorganisms and / or determinants

1.2 **Microorganisms** and **resistance** related information

- **Potential human pathogens** (phenotypic and genotypic characterization) that are likely to acquire resistance in non-human hosts
- **Commensals with AMR determinants** (phenotypic and genotypic characterization) and the ability to transfer them to human pathogens
- **Mechanisms of AMR**, location of AMR determinants, frequency of transfer and prevalence among human and non-human microflora
- **Co- and cross-resistance** and importance of other antimicrobial agents whose efficacy is likely to be compromised
- **Pathogenicity, virulence** and their linkage to resistance

1.3 The **antimicrobial agent** and its properties

- Description of the antimicrobial agent – name, formulation, etc.
- Class of antimicrobial agent
- Mode of action and spectrum of activity
- Pharmacokinetics of the antimicrobial agent
- Existing or potential human and non-human uses of the antimicrobial agents and related drugs

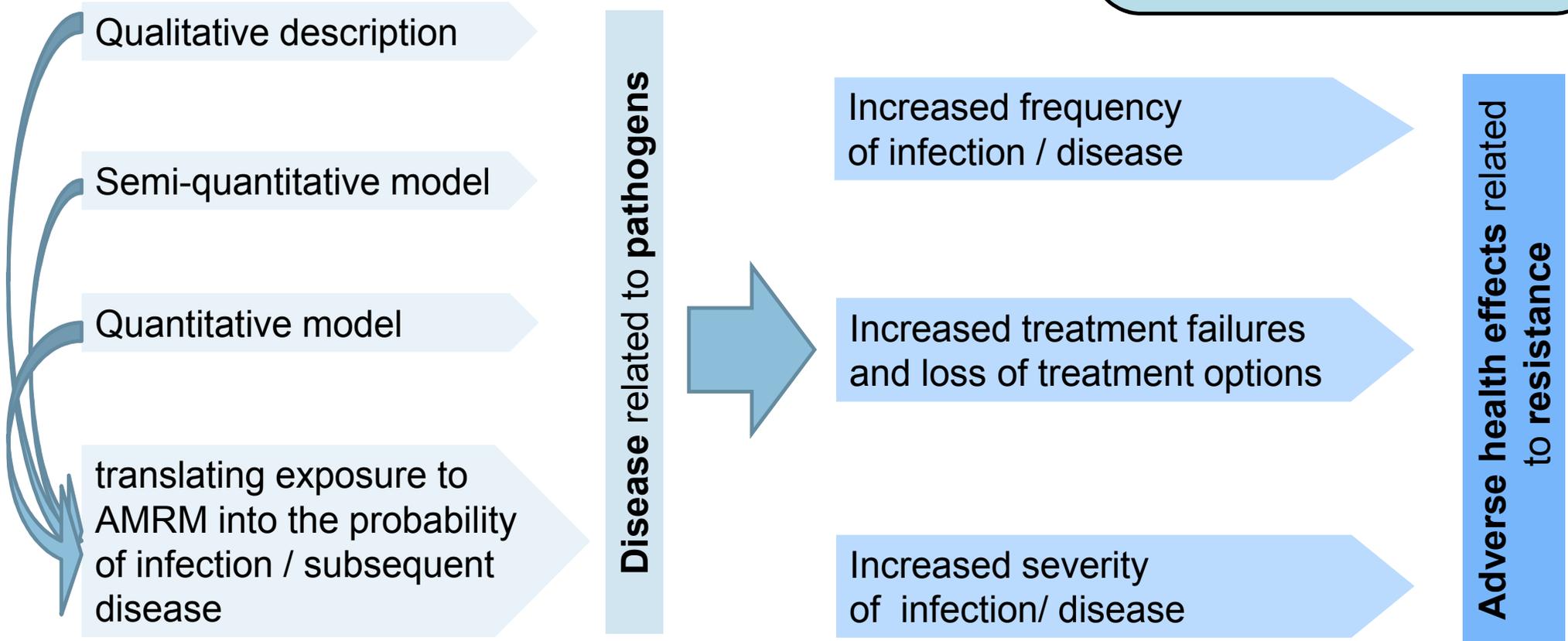


Hazard characterisation

Which adverse health effects could be relevant?

Risk Assessment

1. Hazard identification
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→ **Estimation of diseases and infections** (= adverse health effects) related to AMRM

Hazard Characterisation (Annex 2)

3.1 Human host and adverse health effects

- Host factors and susceptible population
- Nature of the infection, disease
- Diagnostic aspects
- Epidemiological pattern (outbreak or sporadic)
- Antimicrobial therapy and hospitalization
- Importance of the antimicrobial agents
- Increased frequency of infections and treatment failures
- Increased severity of infections (duration↑, frequency↑, hospitalization↑, mortality↑)
- Persistence of hazards in humans

3.2 Food matrix related factors influencing survival of microorganism in the gut

3.3 Dose-response relationship between exposure and probability of outcome

Risk Assessment

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Hazard Characterization

Various disease outcomes associated with the factor are identified

Two approaches used to estimate the disease burden:

- Exposure based approach

- Assessment of the exposure of the study population to the risk factor is made
- **Dose-response relationship** for the given hazard is defined
- Exposure and dose-response are combined to produce **estimates of outcome**

- Outcome-based approach

- **Disease outcome data** are obtained
- The **fraction attributable** to the **risk factor** of interest is **estimated**

From: McEwens, Rec Sci tech Off. Int. Epiz., 31 (1)

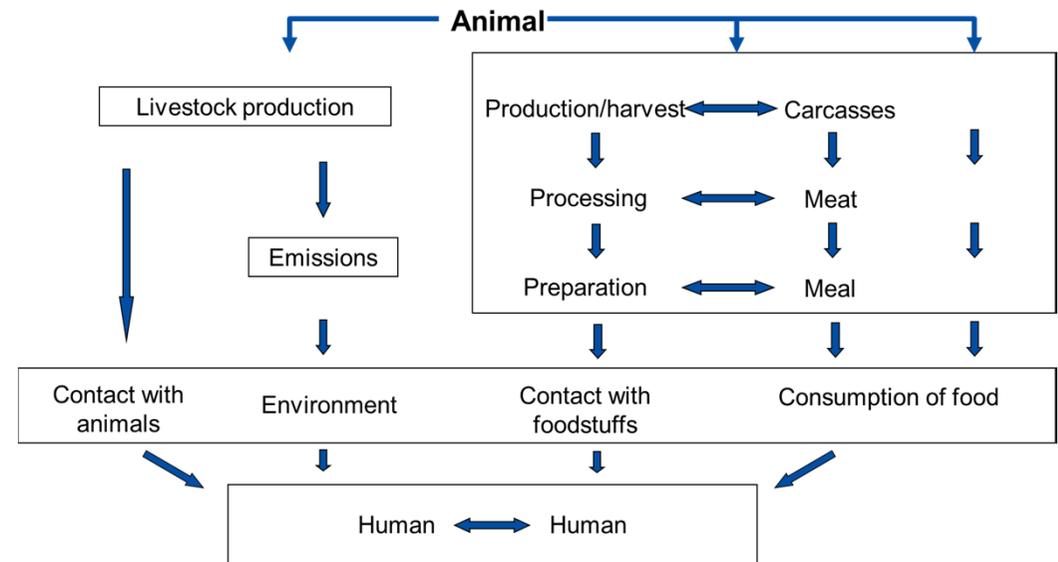
Exposure assessment

Risk Assessment

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The fundamental activities in exposure assessment:

- (a) clear depiction or drawing of the **exposure pathway**
- (b) detailing the necessary **data requirements**
- (c) **summarising the data.**



Adapted from: Codex Alimentarius, CAC/GL 77-2011

Risk Assessment

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Exposure Assessment

Antimicrobial resistant microorganism (AMRM) /
Antimicrobial resistance determinant (AMRD)

Three major players

Selection of resistant
bacteria in **primary**
production/
pre-harvest



Transmission of
bacteria to meat
during slaughter and
processing

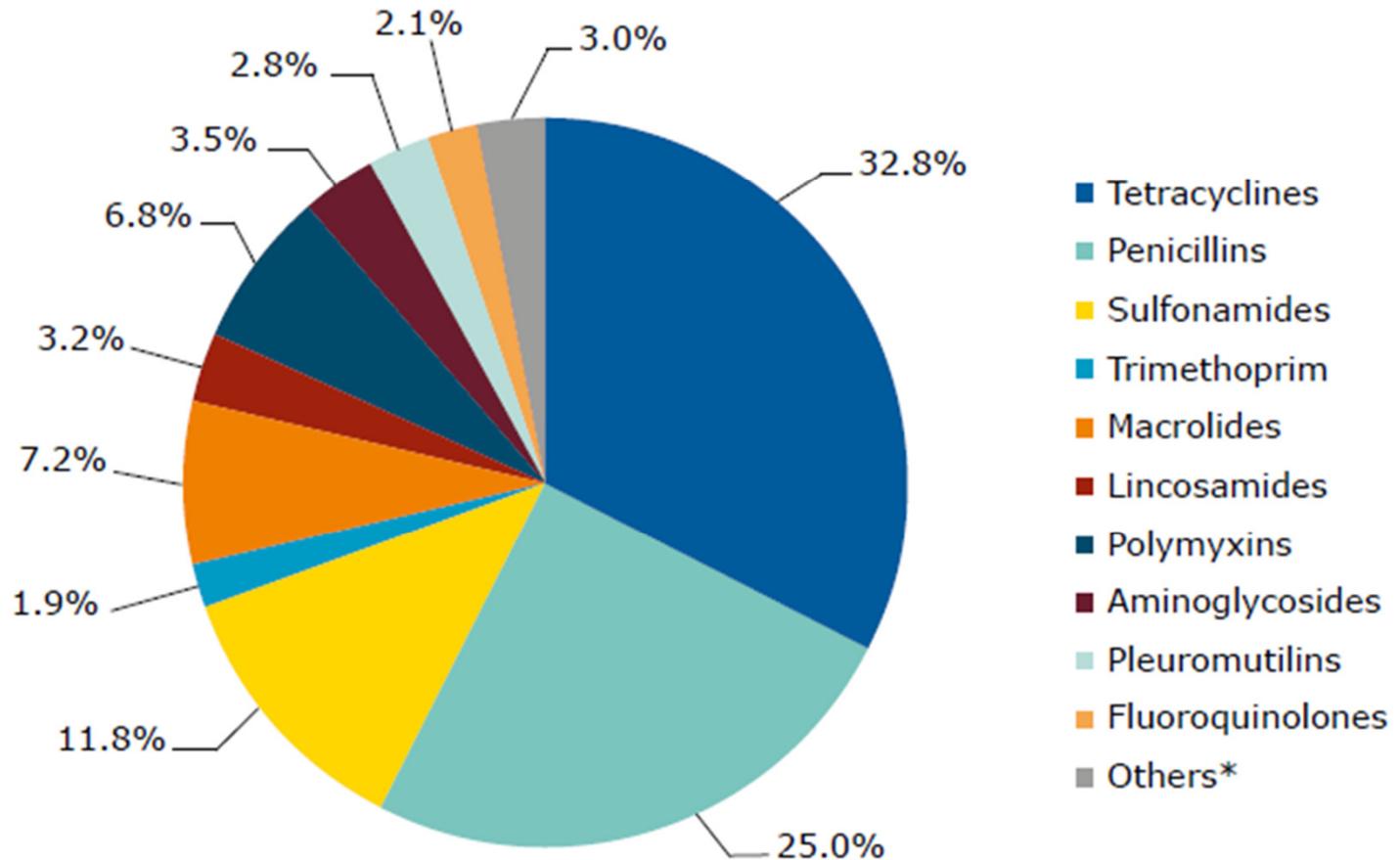


Handling and **preparation** of
food in public or household
environment



Sources of information: Antimicrobials sold in the EU 2015 (EMA 2017)

Sales of antimicrobial agents by antimicrobial class as percentage of the total sales for food-producing species, in mg/PCU, aggregated by 30 European countries, for 2015



But: where, when and for how long were these drugs used?

- Sales data reflect overall use but have limited analytical value
- Exposure of animals needs to be measured on: species or production type level
 - ➡ Number of treatments highly depend on production level/stage
- **Amount** of substance alone is a **poor measure**.

Risk Assessment

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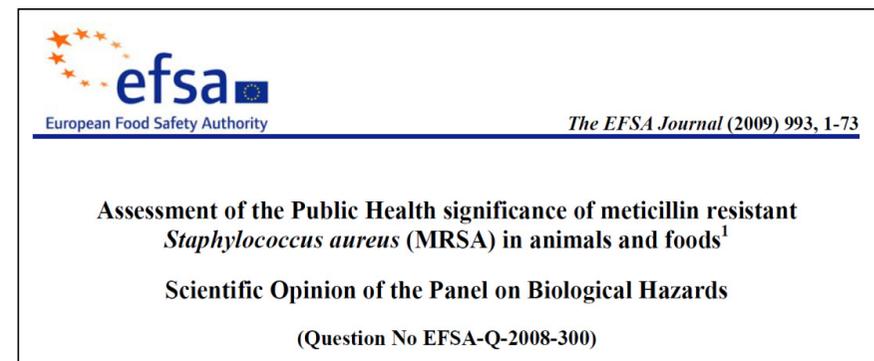
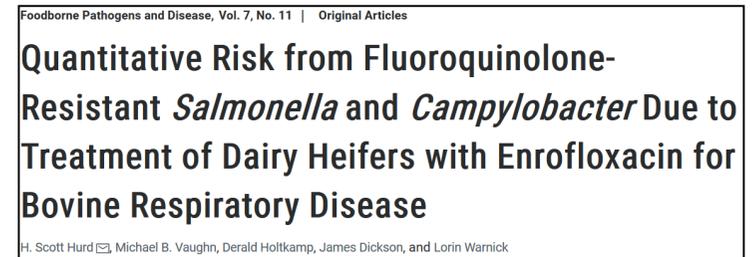
Risk Characterization

Risk characterization considers the key findings from

- hazard identification,
- hazard characterization
- exposure assessment

to estimate the risk.

The **form** and the **outputs** will **vary** from assessment to assessment as a function of the risk management **request!**



Risk characterisation

Risk Assessment

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Qualitative risk assessment - example

Additional risk		Exposure assessment		
		Negligible	Moderate	High
Hazard characterisation	Negligible			
	Mild			
	Moderate			
	Severe			

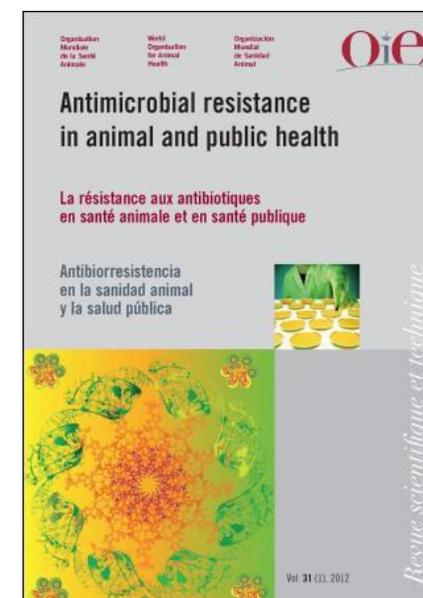
Quantitative risk assessment in AMR - challenges

- Bacterial concentrations are not constant over time
- Bacterial growth is determined by many factors
- Bacteria interact (horizontal gene transfer, competition) with varying intensity
- Resistance determinants can be carried by different bacterial species
- Knowledge of processes on presence and concentration of bacteria is still limited

More information can be found here: McEwen SA

Quantitative human health risk assessments of antimicrobial use in animals and selection of resistance: a review of publicly available reports.

Rev Sci Tech 2012 Apr;31(1):261-76



Summary

AMR risk assessment follows **general** risk assessment **principles**

Codex alimentarius guideline can and should be used

Major challenges

- **Complexity** of **biology**
 - Horizontal gene transfer within/between species
 - Cross and co-resistance
 - Bacterial growth
- AMR is related to **human** and **veterinary medicine**
 - Veterinary / food chain share needs to be determined
- Complex **exposure patterns**
 - Environment / Contact to animals / Contact to humans / Food
- **Shortage** on quantitative **data**

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Thank you for your attention

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