



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Guideline on the assessment of the risk to public health from AMR due to use of an antimicrobial VMP in food-producing animals –

## **Pragmatic consequence assessment**

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Focus group meeting, 19 Sep 2018, London

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An agency of the European Union

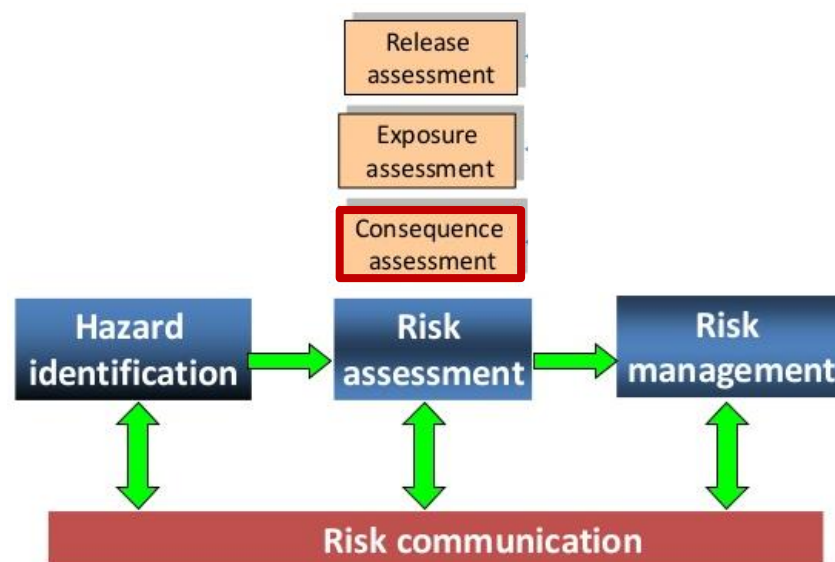




# Data requirements:

## 4. Consequence assessment

This step addresses the potential consequences of exposure of humans to each of the hazard(s) in the EU and the severity and probability of the consequences occurring.





# Consequence assessment: data requirements and guidance.

## A. Relative importance of the antimicrobial to human medicine

= **Source:** WHO categorisation / ESAC database

## B. Dose-response relationships (where available)

## C. Consequences of AMR in human infections

= **Sources:** The EU Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents and Food-borne Outbreaks; European Surveillance System (TESSy), Scientific Opinions from BIOHAZ



## Consequence assessment: data requirements and guidance.

A discussion should be provided: the overall conclusion on the potential adverse health effects of exposure of humans to the hazard(s) + the severity and probability of those consequences.

### Proposed categories to be used:

- **Very low:** The antimicrobial is of very low importance in terms of the frequency of use to treat a disease for which alternatives are commonly available.
- **Low:** The antimicrobial is of low to medium importance in terms of the frequency of use to treat a disease for which the outcomes are more serious.
- **Medium:** The antimicrobial is of medium to high importance in terms of the frequency of use to treat a disease for which the outcomes are more serious with impact on the individual and on healthcare services.
- **High:** The antimicrobial is a last resort treatment (or one of few alternatives) for a disease for which the outcome of treatment failure is very severe.



# Consequence assessment: Pragmatic approach

Acknowledging the extent of the gaps in the data needed to perform the consequence assessment, an option is proposed for a simplified consequence assessment that would be based on the **AMEG categorization** for the antimicrobials substance and the **extent of use** of the AM class in human medicine.



# Pragmatic approach

## AMEG categorisation



**Importance for human medicine**



**Probability of resistance transfer**



# Pragmatic approach

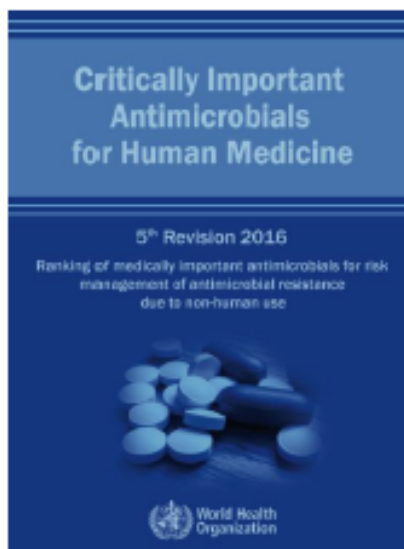
## AMEG categorisation



Importance for human medicine



Probability of resistance transfer



### First categorization of antimicrobials by classes

- **Criterion 1:** The antimicrobial class is the sole, or one of the limited available therapeutics to treat serious bacterial infections.
- **Criterion 2:** The antimicrobial class is used to treat infections caused by either (1) bacteria that may be transmitted to humans from non-human sources, or (2) bacteria that may acquire resistance genes from non-human sources.

= *Critically important (C1 + C2)*

= *Highly important (C1 or C2)*

= *Important*



# Pragmatic approach

## AMEG categorisation



Importance for human medicine

Probability of resistance transfer

Antimicrobial class	Vertical transmission of resistance gene(s) <sup>a</sup>	Mobile genetic element-mediated transfer of resistance <sup>b</sup>	Co-selection of resistance <sup>c</sup>	Potential for transmission of resistance through zoonotic and commensal food-borne bacteria <sup>d</sup>	Evidence of similarity of resistance: genes / mobile genetic elements / resistant bacteria <sup>e</sup>	Overall probability of resistance transfer
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Classes of antimicrobials for which there are substances authorised for use in veterinary medicine





# Pragmatic approach

## AMEG categorisation



Importance for human medicine

Probability of resistance transfer

The AMEG proposes to classify antimicrobials from the WHO CIA list in three different categories:

- Category 1 as antimicrobials used in veterinary medicine where the risk for public health is estimated as low or limited,
- Category 2 as antimicrobials used in veterinary medicine where the risk for public health is estimated higher and
- Category 3 as antimicrobials not approved for use in veterinary medicine.



New mandate given to AMEG to revise the categorisation



# Pragmatic approach

## Extent of use

### Consumption of antibacterials for systemic use

DDD per 1000 inhabitants per day

Based on data provided courtesy of ESAC-Net

Antibacterial class	ATC code	Consumption (DDD per 1000 inhabitants per day)	Categorisation (as provided by CVMP)*
Tetracyclines, incl. glycylicyclines	J01AA	60.30	M
Amphenicols	J01BA	0.08	VL
Penicillins with extended spectrum	J01CA	121.22	H
Beta-lactamase sensitive penicillins	J01CE	24.68	M
Beta-lactamase resistant penicillins	J01CF	12.57	L
Combinations of penicillins, incl. beta-lactamase inhibitors	J01CR	153.38	H
1 <sup>st</sup> - and 2 <sup>nd</sup> -generation cephalosporins	J01DB, J01DC	55.27	M
3 <sup>rd</sup> - and 4 <sup>th</sup> -generation cephalosporins	J01DD, J01DE	13.55	L
Monobactams	J01DF	0.04	VL
Carbapenems	J01DH	1.83	L
Sulfonamides and trimethoprim, incl. combinations	J01EA to J01EE	17.58	L
Macrolides	J01FA	74.99	M
Lincosamides	J01FF	8.79	L
Streptogramins	J01FG	0.89	VL
Aminoglycoside antibacterials	J01GA, J01GB	2.58	L
Quinolone antibacterials	J01MA, J01MB	55.92	M
Glycopeptide antibacterials	J01XA	1.03	L
Polymyxins	J01XB	0.72	VL
Steroid antibacterials	J01XC	0.25	VL
Imidazole derivatives	J01XD	2.03	L
Nitrofurantoin derivatives	J01XE	18.17	L

\*VL (very low), <1.0; L (low), 1.0 to <20.0; M (medium), 20.0 to 100, H (high), >100 DDD per 1000 inhabitants per day.



# Pragmatic approach

## AMEG categorisation + Extent of use

The ranking for the consequence is then derived according to the matrix:

AMEG category	Extent of use in human medicine			
	Very low	LOW	MEDIUM	HIGH
3	High	High	High	High
2	High	High	High	High
2/1	Low	Medium	Medium	High
1	Very low	Low	Low	Medium



This table will be subject to revision and finalised after the [AMEG scientific advice](#) is completed.



# Thank you for your attention

## Further information

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