



“Microbial Biocontrol Agents
Professional Group Talks”

Antibiotic Resistance in Agricultural Applications: What's the Struggle?



ABIM 2018 - Basel

22/10/2018 / Dr. Amelie Deredjian, Dr. Leah Zorrilla





Antibiotic resistance: “a serious challenge in the EU and globally”

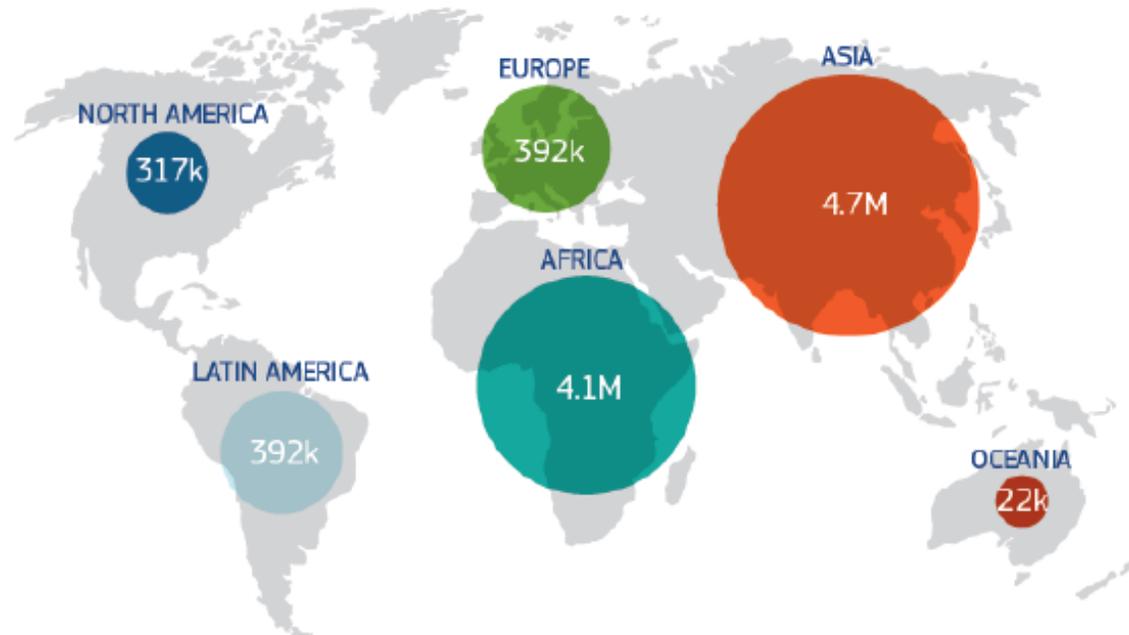
A European One Health Action Plan against Antimicrobial Resistance (AMR)

AMR is responsible for:

- 25 000 deaths per year in the EU
- 700 000 deaths per year globally

2050 projection:

- Billions of deaths globally
- May cause more deaths than cancers



Projection for number of annual deaths attributable to AMR by 2050, (source: O'Neill AMR review¹, May 2016)



Antibiotic resistance: “a serious challenge in the EU and globally”

A European One Health Action Plan against Antimicrobial Resistance (AMR)

On 29 June 2017, the Commission adopted the **EU One Health Action Plan against AMR** to preserve the possibility of effective treatment of infections in humans and animals

Actions linked to AMR in the environment still limited *but growing interest*

3) intensifying EU efforts worldwide to shape the global agenda on AMR

Clear objectives regarding AMR in the environment:

- Better addressing the role of the environment
- Close the knowledge gaps on AMR in the environment and on how to prevent transmission

Why to investigate the role of the environment in AMR?

Antimicrobial production and antimicrobial resistance in the environment

Focus on the soil

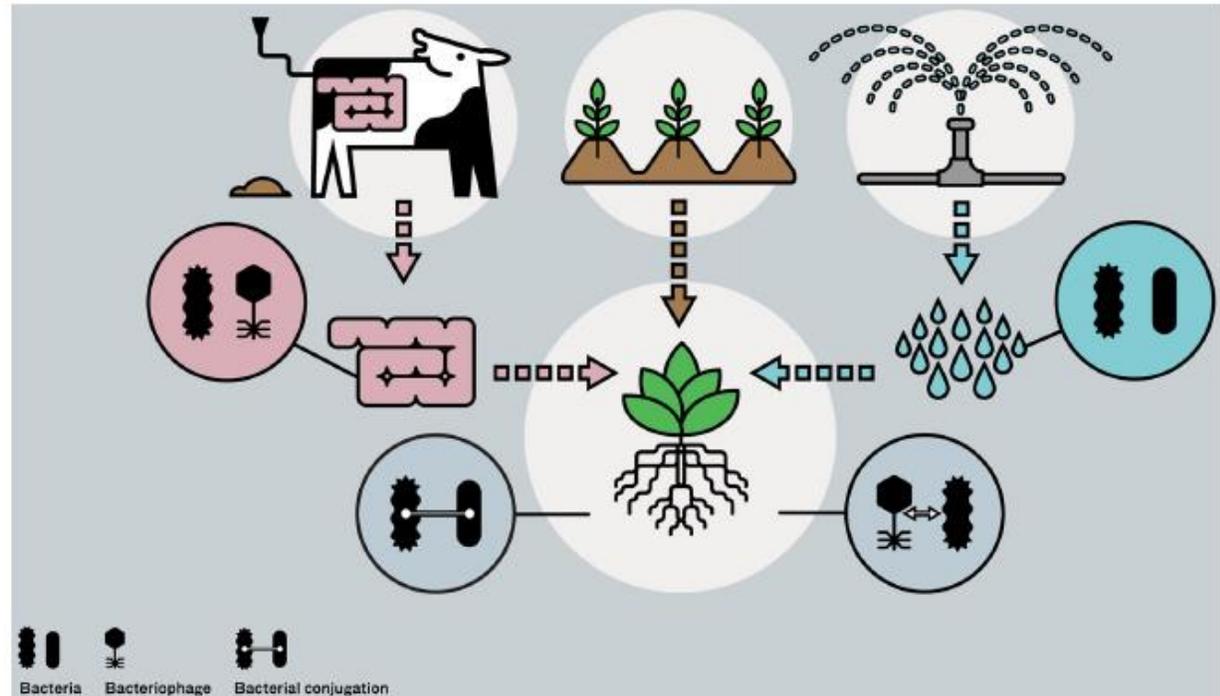
- Selective pressure is naturally present as antibiotic production confers a competitive advantage
- Specific niches like the rhizosphere can be considered as a hotspot for gene exchanges

How agricultural practice may have an impact ?

- Use of manure
- Use of wastewater / irrigation water

⇒ Increasing

- ⇒ the quantity and diversity of antimicrobials
- ⇒ the quantity and diversity of antimicrobial resistance genes / antimicrobial resistant strains





Why to investigate the role of the environment in AMR?

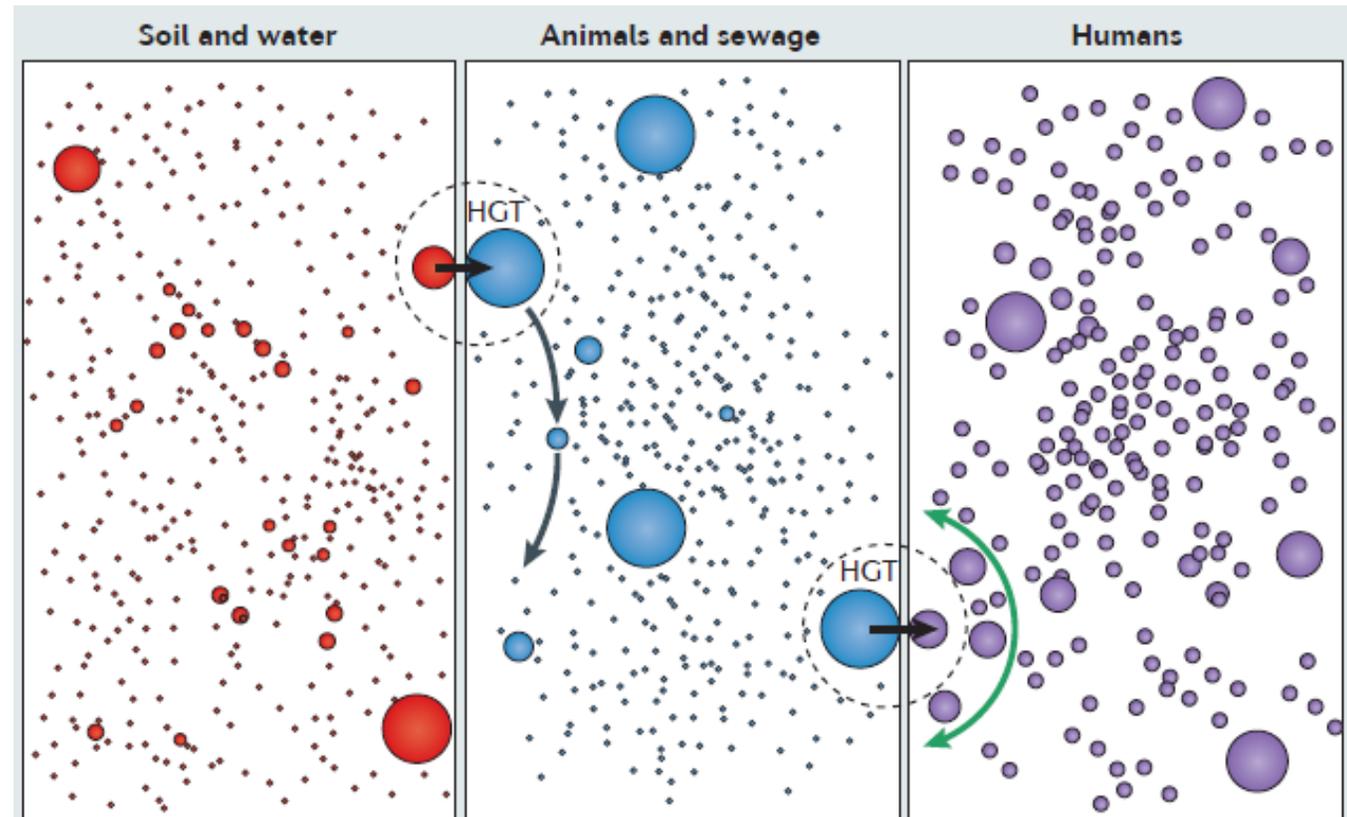
Antimicrobial production and antimicrobial resistance in the environment

What could be the impact of microbial containing products used in agriculture ?

Bring new determinants / phenotypes which are absent in the soil and could spread in strains present in the soil and then in other environments like the hospital

How can resistance genes spread from the soil/water to the hospital?

Opportunistic pathogens make the link as they are able to survive in both environments



Martinez et al., 2015



Why to investigate the role of the environment in AMR?

Antimicrobial production and antimicrobial resistance in the environment

Independently, microbial based products may have a limited impact on AMR, HOWEVER,

The risk to have antimicrobial resistance genes / phenotypes from a microbial based product spread in the soil and then in other environments **cannot be excluded nor considered as negligible...**

This is not an issue without a potential solution, but requires industry thought to find and address this solution



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.



What is the status of AMR in the PPP regulation?

Requirements to be listed on Annex 1 of 1107/2009 and low risk substance criteria

In commission Regulation (EU) No 283/2013

2.9. Antibiotics and other anti-microbial agents

Many micro-organisms produce some antibiotic substances. Interference with the use of antibiotics in human or veterinary medicine must be avoided at any stage of the development of a microbial plant protection product.

Information on the micro-organism's resistance or sensitivity to antibiotics or other anti-microbial agents must be provided, in particular the stability of the genes coding for antibiotic resistance, unless it can be justified that the micro-organism has no harmful effects on human or animal health, or that it can not transfer its resistance to antibiotics or other anti-microbial agents.

In commission Regulation (EU) No 2017/1432

- (9) Micro-organisms which are to be included in plant protection products are assessed at strain level in conformity with specific data requirements laid down in part B of the Annex to Commission Regulation (EU) No 283/2013 ⁽¹⁾. Consequently, micro-organisms should be identified and characterised at strain level also when assessed for compliance with the criteria concerning low-risk substances as toxicological properties of different strains belonging to the same species of micro-organism can vary greatly. A micro-organism may be considered to be of low-risk unless at strain level it has demonstrated multiple resistance to antimicrobials used in human or veterinary medicine.



What is the status of AMR in the PPP regulation?

Requirements to be listed on Annex 1 of 1107/2009 and low risk substance criteria

In Commission Regulation (EU) No 283/2013

2.9. Antibiotics and other anti-microbial agents

Many micro-organisms are used in human or veterinary medicine.

Information on the micro-organisms used in human or veterinary medicine should be provided to antibiotics or other anti-microbial agents.

in human or veterinary medicine.

No *SPECIFIC* guidance available to address these requirements...?



In Commission Regulation (EU) No 2017/1432

(9) Micro-organisms with specific characteristics should be assessed for compatibility with strains belonging to be of low-risk in human or veterinary medicine.

What is considered as multi-resistance?
Which antimicrobials should we consider as relevant in human or veterinary medicine?

Regulation (EU) No 2017/1432 also when considering different antimicrobials considered in human or veterinary medicine.



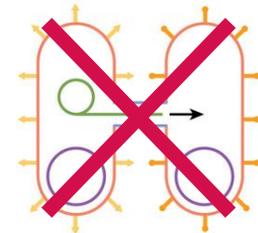
What is the status of AMR in the PPP regulation?

Requirements to be listed on Annex 1 of 1107/2009 and low risk substance criteria

Environmental strains isolated from the environment may be naturally resistant to several antibiotics

This should not be a problem to be registered as PPP / low risk substance:

- ✓ If the resistance is not clinically relevant (WHO definition, 2018)
- ✓ Or the gene encoding this resistance is not transferable to other strains
- ✓ There are still therapy options available



Antimicrobial Resistance: What is the Struggle?

North America

- No specific requirements – but must address concerns: US
- Clinically relevant ARM avoided: Canada-PMRA/CFIA

South America

- No specific requirements – but must address concerns: Brazil, Argentina
- Must inform - Chile

EU

- Required for PPP legislation
- Currently not required for Biostimulants

Asia-Pacific

- Requirements- Australia, Philippines
- No regulation- Korea, Thailand, Malaysia, India, Japan
- Controlled - Indonesia

This situation is not EU specific...

Discussions are on-going worldwide...

Some countries / regions have already set up some actions



Antimicrobial Resistance: What is the Struggle?

Addressing antimicrobial resistance could be seen as a stewardship measure rather than a requirement for approval

HOWEVER

EU Authorities will come with a proposal to address antimicrobial resistance for microbial based product in EU...
Some EU Authorities already request to apply the EFSA guidance document for microorganisms used as feed and food additives...

OPEN QUESTIONS...

Why await a guidance which could be expensive / technically challenging?
Shouldn't industry propose a guidance for evaluation ?





*Thank you for your
attention*



Questions ???



