



THE PRECAUTIONARY PRINCIPLE APPLICATION IN THE MICROBIAL BIOPESTICIDES RISK ASSESSMENT

Dr. Marisé Borja

Origin:

In the 1970s German law as the *Vorsorgeprinzip* ('foresight principle') during the preparation of legislation on air pollution.

The precautionary principle is detailed in **Article 191 of the Treaty** on the Functioning of the European Union

At the Council's request, the **European Commission adopted a Communication (2000):**

Whether or not to invoke the precautionary principle is a decision exercised where information is insufficient, inconclusive, or uncertain and where there are indications that the possible effects on the environment, or human, animal or plant health may be potentially dangerous and inconsistent with the chosen level of protection.'

Preliminary conditions

- identification of potentially adverse effects;
- evaluation of the scientific data available;
- the extent of scientific uncertainty.

The general principles of risk management

- **proportionality** between the measures taken and the chosen level of protection;
- **non-discrimination** in application of the measures;
- consistency of the measures with similar measures already taken in similar situations or using similar approaches;
- examination of the benefits and **costs of action or lack of action**;
- review of the measures in the light of scientific developments

The Commission also seeks 'to clarify a misunderstanding as regards the distinction between reliance on **the precautionary principle and the search for zero risk**, which in reality is rarely to be found'.



Hazard

Source or a situation with **the potential for harm** in terms of human injury or ill-health, damage to the environment, or a combination of these

Risk

The **chance** of something happening that will have a negative effect. The level of risk reflects:

- the likelihood of the unwanted event
- the potential consequences of the unwanted event.

Risk = Probability x Damage.

None of the articles of the European Journal of Risk Regulation was related to Biopesticides

Controls are the measures put in place to decrease the likelihood or consequences

- prevent the unwanted event or reduce the loss of control of the hazard
- reduce the effects

- **Precaution and innovation**

When regulation which concentrates solely on avoiding risk and removing scientific uncertainty it, **stifles innovation**.

Impact on innovation should be considered

- **Precaution and innovation in the European Union**

In general

- Misunderstanding of the precautionary principle (Delayed approvals reflect inaction....)
- Bad execution of 1107/2009:
 - Same regulation as chemical pesticides (same experts, ...)
 - The evaluation deadlines are not respected

Specifically for biological products

- Open scientific challenges (Sensitization, compatibility....)
- Lack of bespoke guidance (i.e. consider host range)

- It is not the same a proven risk than a potential statement

(RD 1311/2012, Anexo VIII)

En los espacios utilizados por el público en general, zonas deportivas, espacios utilizados por grupos vulnerables y espacios de uso privado, solamente pueden ser aplicados productos en los que en su etiqueta no figuren determinadas frases de riesgo (Ejemplo: Posibilidad de sensibilización en contacto con la piel (R43) o por inhalación (R42))

Artículo 48. Condicionamientos para los usos no profesionales.

1. Los usuarios no profesionales podrán realizar tratamientos en los siguientes ámbitos y con los siguientes tipos de productos:

a) En jardines domésticos de exterior y huertos familiares, con productos expresamente autorizados para uso no profesional en estos ámbitos, conforme a los requisitos especificados en el anexo VIII.

b) En la jardinería doméstica de interior, con productos envasados como aerosol o en otros tipos de envase concebidos expresamente para la aplicación directa de su contenido, conforme a los requisitos especificados en el anexo VIII.

ENV/JM/MONO(2017)8

16-Mar-2017

REPORT OF THE 7TH BIOPESTICIDES STEERING GROUP SEMINAR ON SENSITISATION POTENTIAL OF MICRO-ORGANISMS

Discussion so far: During the EFSA expert PRAPeR M3 meeting in June 2009 it was agreed that the currently existing warning phrase regarding the potential for sensitisation for microbials is: "Contains X% strain Y. Micro-organisms may have the potential to provoke sensitising reactions". It does not mean that they are sensitisers but they may have the potential. However, this has been interpreted differently by different EU member states. This was also discussed at the OECD/KEMI/EU Workshop on Microbial

EU data requirement: Regulation (EU) No 283/2013 is setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009. According to the data requirement point 5.2.1, data on sensitisation are required: "The test will provide sufficient information to assess the potential of the micro-organism to provoke sensitisation reactions by inhalation as well as with dermal exposure. A maximised test has to be performed". However, in the related foot note it is recognized: "The available methods for testing dermal sensitisation are not suitable for testing micro-organisms. Sensitisation by inhalation is most probably a greater problem compared with dermal exposure to micro-organisms but so far, there are no validated test methods. Development of these kinds of methods is therefore of great importance. Until then, all micro-organisms should be regarded as potential sensitisers...". Consequently, all micro-organisms will be labelled as potential sensitisers. Therefore, this data requirement should be regarded non-obligatory but optional, on a provisional base.

Independent of the results of sensitization studies, most respondents would accept market authorization and request product labelling with a warning phrase on sensitization potential of the relevant micro-organism. Most respondents do not or generally not exclude use by non-professionals when PPE is needed for product use.

Le point sur la Loi Labbé

4 textes | Mise à jour : janvier 2019

Thématique : Utilisation dans les espaces accueillant du public

La loi Labbé* modifiée par l'article 68 de la LTE** et la loi Pothier*** **interdit à partir du 01/01/2017 aux personnes publiques d'utiliser/faire utiliser des produits phytosanitaires pour l'entretien des espaces verts, forêts, promenades et voiries (sauf pour des raisons de sécurité ...) accessibles ou ouverts au public.**

Les **produits phytosanitaires de biocontrôle, à faibles risques et autorisés en agriculture biologique** restent cependant utilisables, ainsi que tous les autres produits de protection des plantes (macro-organismes, substances de base).

- It is not the same a proven risk than a potential statement

CHEMICALS

- **Natural substances**: exempt from the environmental criteria of persistence and bioconcentration (Annex 5.1.2).
- **Semiochemicals**: must meet all low risk criteria for chemicals (Annex II.5.1.3)

MICROBIALS

- **Microorganisms** - low risk unless the strain has demonstrated **multiple resistance to antimicrobials** used in human or veterinary medicine or has **metabolites** described as toxic
- **Baculovirus** - low risk unless a strain has demonstrated adverse effects on non-target insects

COMMISSION REGULATION (EU) 2017/1432

of 7 August 2017

amending Regulation (EC) No 1107/2009 of the European Parliament and the Council concerning the placing of plant protection products on the market as regards the criteria for the approval of low-risk active substances

Biological Properties

- Antimicrobial resistance is justified by hazard on human health and as mitigation measure

EUROPE'S FIGHT AGAINST ANTIMICROBIAL RESISTANCE

2014

WHAT IS ANTIMICROBIAL RESISTANCE (AMR)?

Antimicrobials?
 Substances used to treat a wide variety of infectious diseases in humans and animals. They:
 - kill micro-organisms
 - stop micro-organisms from growing and multiplying
 Example: antibiotics: ceftriaxone, Ciprofloxacin

Antimicrobial resistance?
 The ability of micro-organisms to with stand antimicrobial treatments.
 Example: AMR: penicillin-resistant Staphylococcus aureus, commonly present on human skin and various environments

Why is resistance growing?

- Overuse of antibiotics
- Misuse of antibiotics
- Spread through various routes

Effect of growing resistance?

- Treatment may become ineffective
- Serious risk to public health

OVERVIEW OF RESISTANCE LEVELS IN EU

Based on "European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014"

POULTRY AND FOODS

Enterococcus faecium (ppm)

| Country | Resistance to ampicillin (%) | Resistance to clindamycin (%) |
|-------------|------------------------------|-------------------------------|
| Spain | 100 | 100 |
| France | 100 | 100 |
| Italy | 100 | 100 |
| Germany | 100 | 100 |
| Netherlands | 100 | 100 |
| Poland | 100 | 100 |
| Portugal | 100 | 100 |
| Romania | 100 | 100 |
| Slovenia | 100 | 100 |
| Sweden | 100 | 100 |
| UK | 100 | 100 |

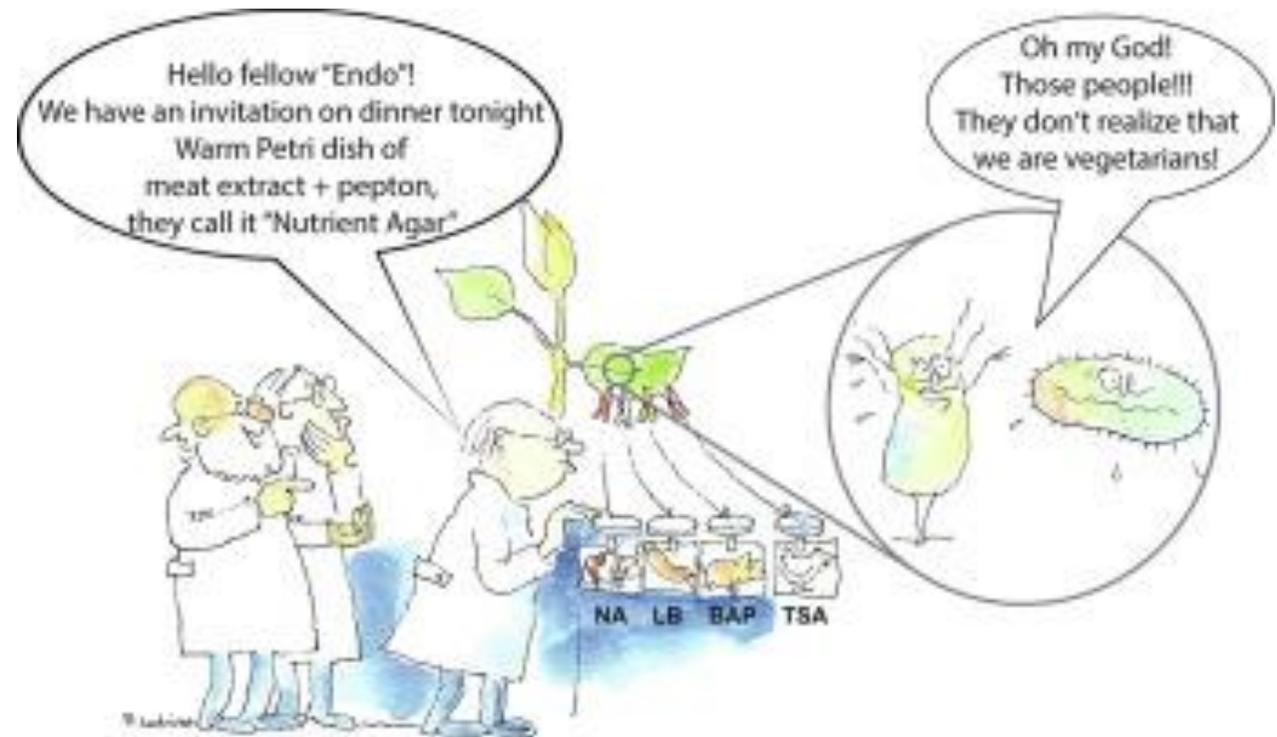
HUMANS

Enterococcus faecium (ppm)

| Country | Resistance to ampicillin (%) | Resistance to clindamycin (%) |
|-------------|------------------------------|-------------------------------|
| Spain | 100 | 100 |
| France | 100 | 100 |
| Italy | 100 | 100 |
| Germany | 100 | 100 |
| Netherlands | 100 | 100 |
| Poland | 100 | 100 |
| Portugal | 100 | 100 |
| Romania | 100 | 100 |
| Slovenia | 100 | 100 |
| Sweden | 100 | 100 |
| UK | 100 | 100 |

Biological Properties

- Metabolites, relevant known metabolites **in the production media** need to be reported
- However, metabolites produced in situ should not be considered

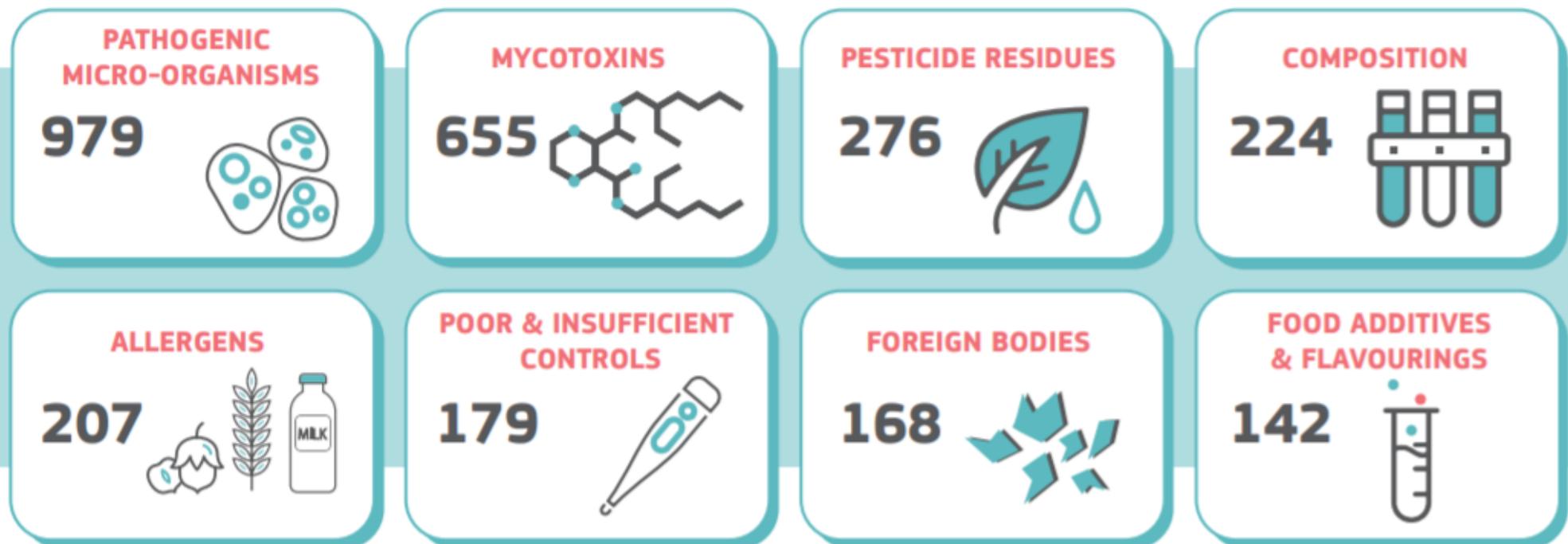


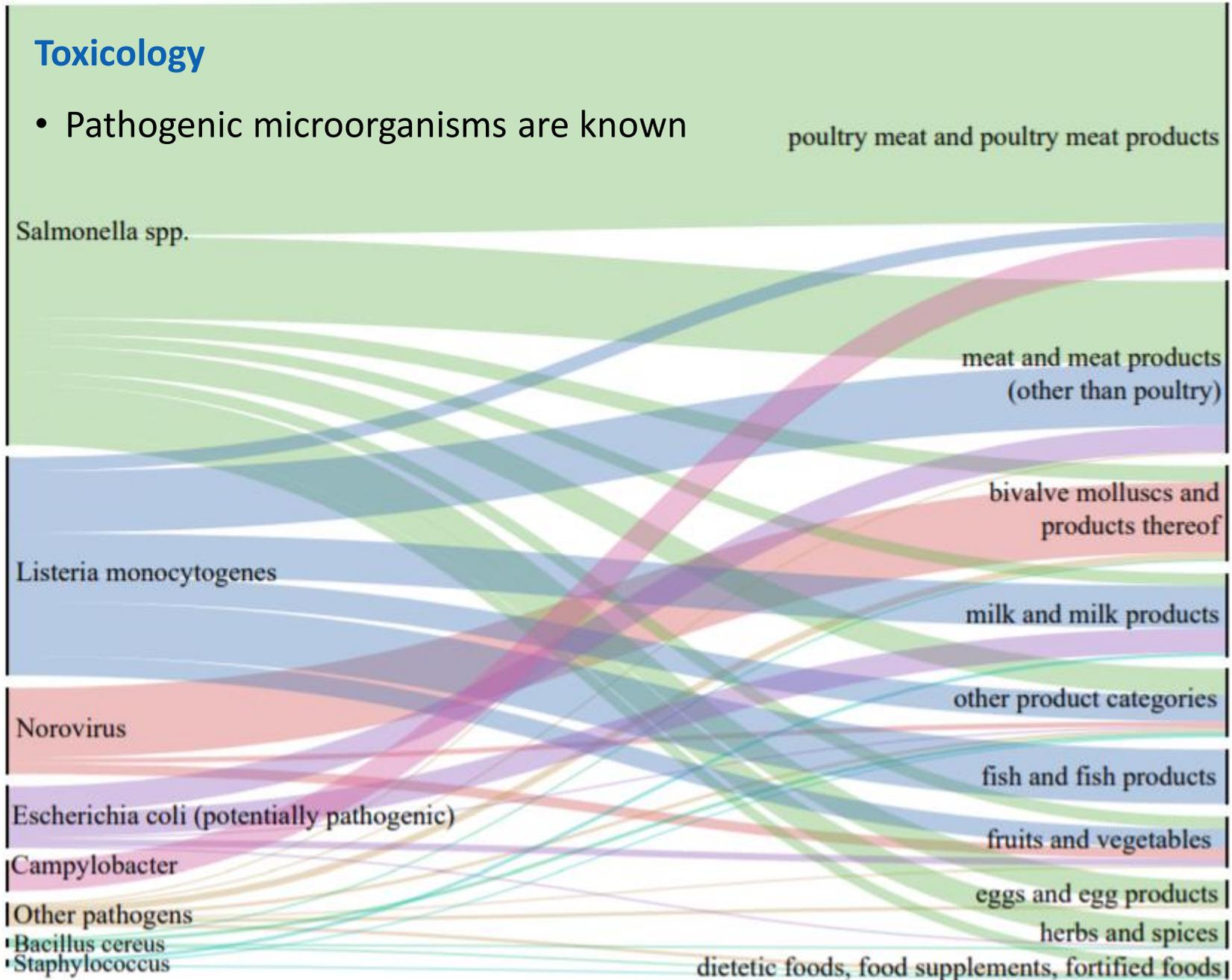
The Rapid Alert System for Food and Feed 2018 Annual Report

Microbial biopesticides have not raised alerts

Pathogen targets or mycotoxin have caused alerts

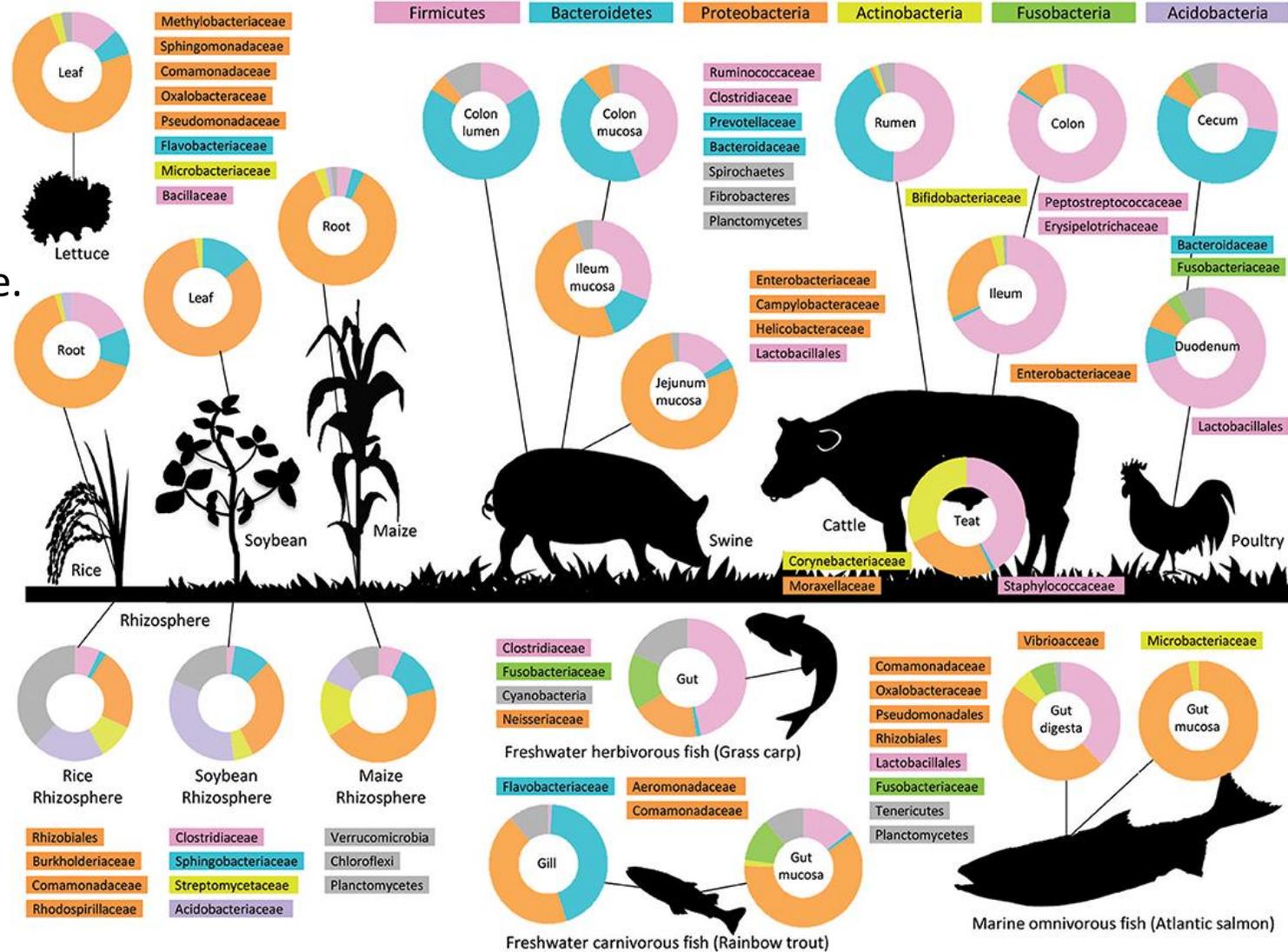
NOTIFICATIONS BY HAZARD 2018





Ecotoxicology

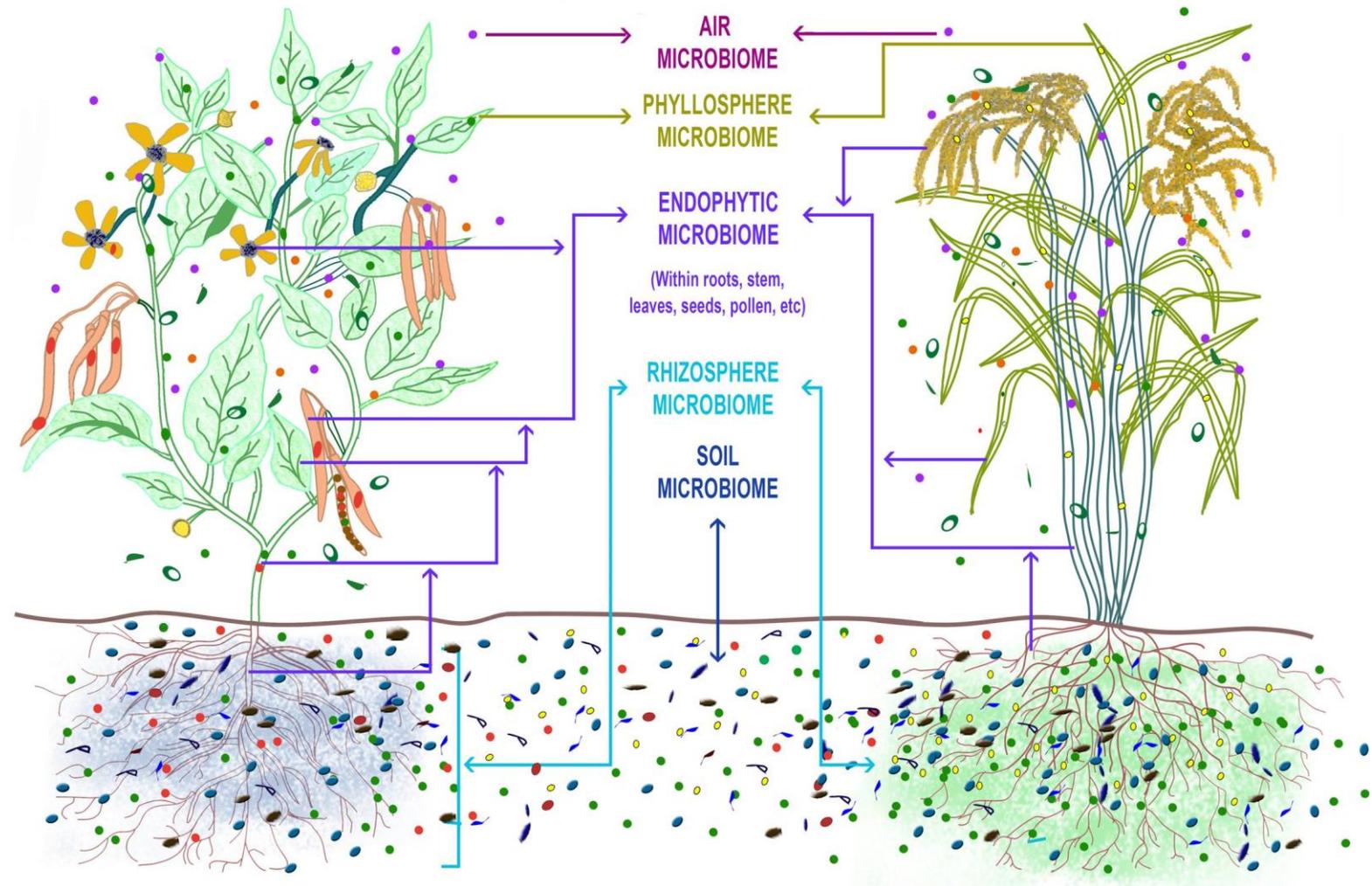
- Host range should be enough for many microorganisms (i.e. obligate parasites such as baculovirus...)



Ikeda-Ohtsubo, W., Brugman, S., Warden, C. H., Rebel, J. M. J., Folkerts, G., & Pieterse, C. M. J. (2018). *How Can We Define "Optimal Microbiota?"*: A Comparative Review of Structure and Functions of Microbiota of Animals, Fish, and Plants in Agriculture. *Frontiers in Nutrition*, 5. doi:10.3389/fnut.2018.00090

E-fate

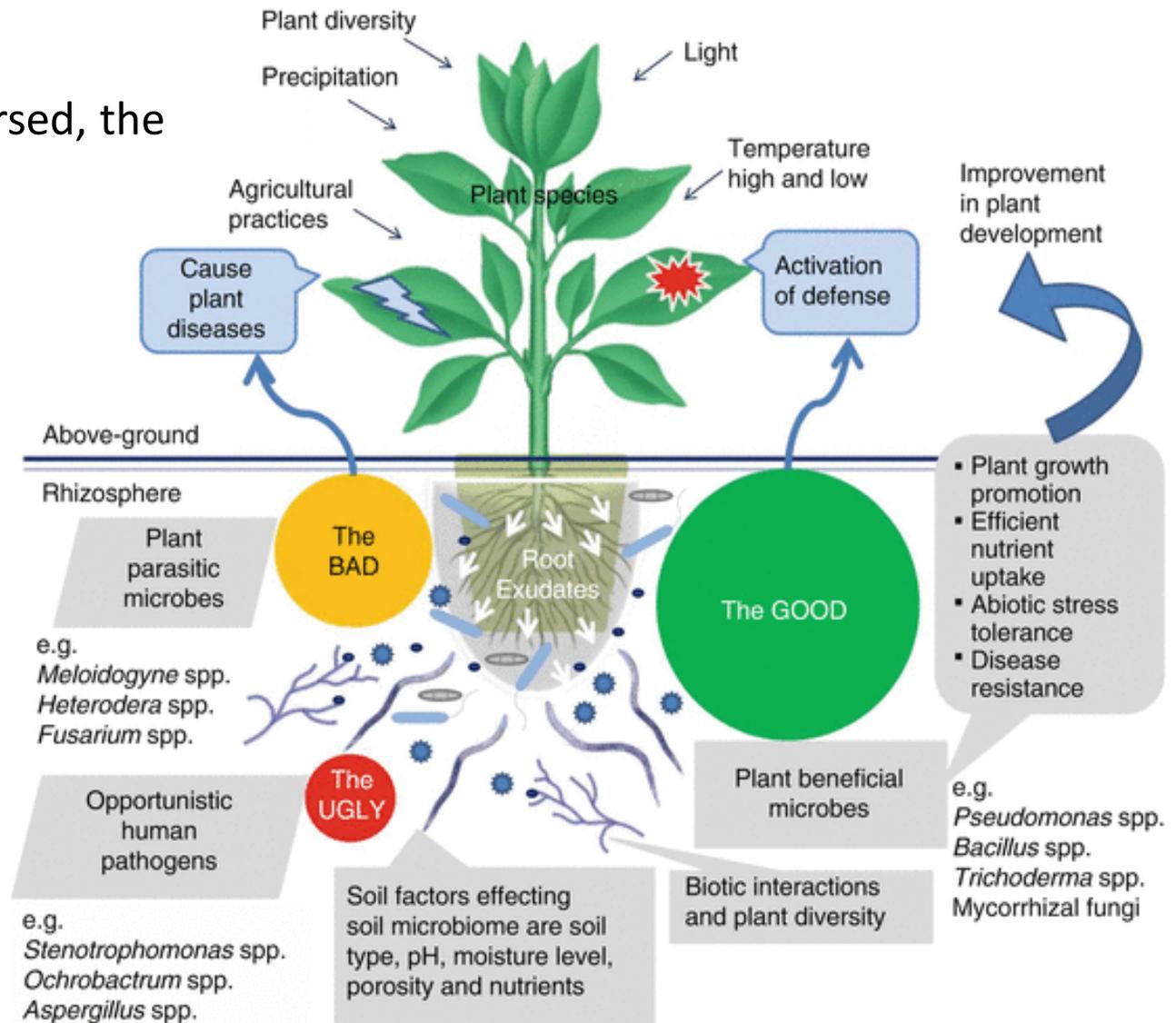
- Natural populations are driven by host plants



Gopal, M., & Gupta, A. (2016). *Microbiome Selection Could Spur Next-Generation Plant Breeding Strategies*. *Frontiers in Microbiology*, 7. doi:10.3389/fmicb.2016.01971

Ecotoxicology

- The burden of proof should be reversed, the bad and ugly are also well known



Ali M.A., Naveed M., Mustafa A., Abbas A. (2017) The Good, the Bad, and the Ugly of Rhizosphere Microbiome. In: Kumar V., Kumar M., Sharma S., Prasad R. (eds) Probiotics and Plant Health. Springer, Singapore DOI https://doi.org/10.1007/978-981-10-3473-2_11

Conclusion

- The consequences of inaction needs to be considered as well

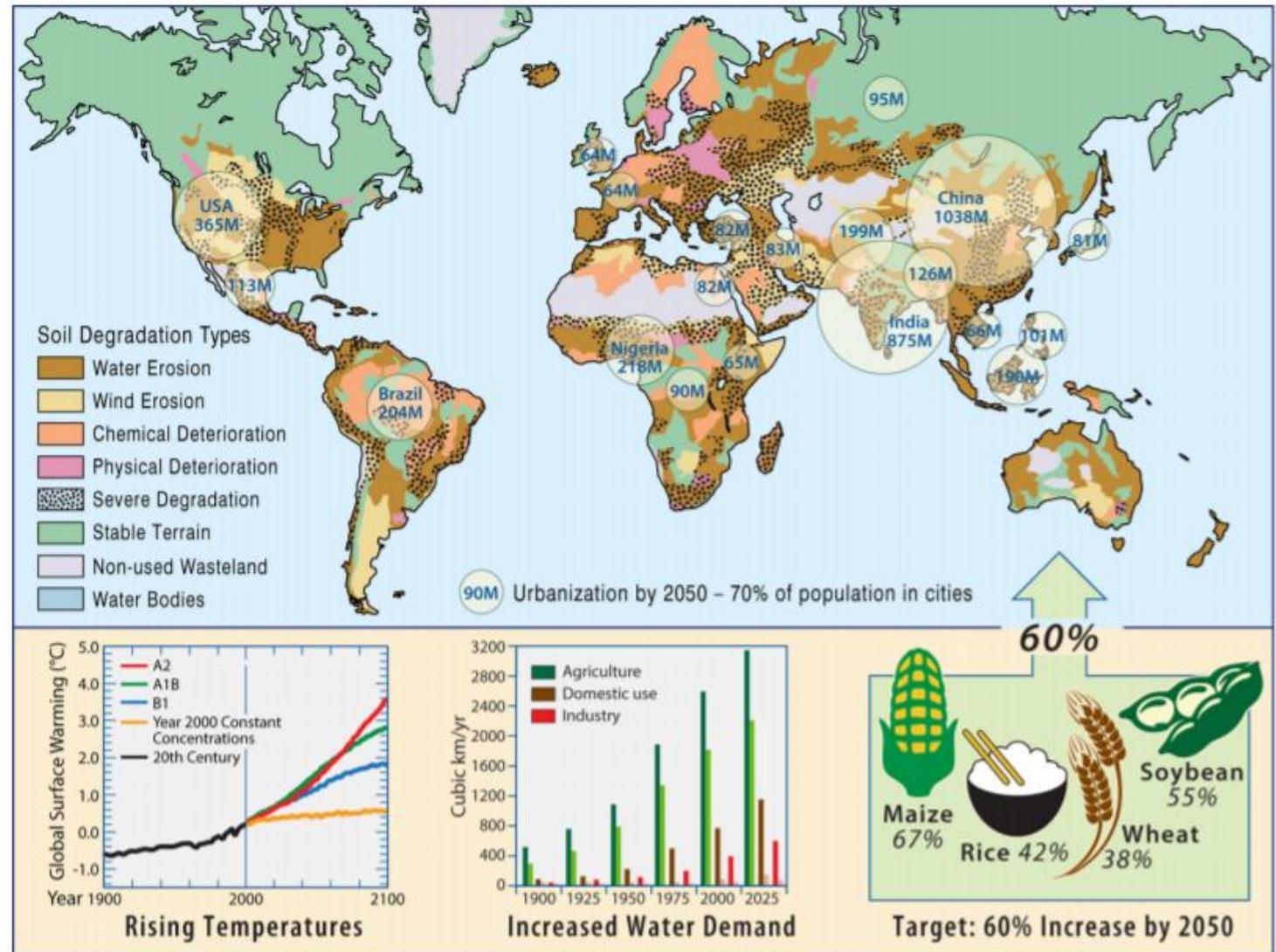


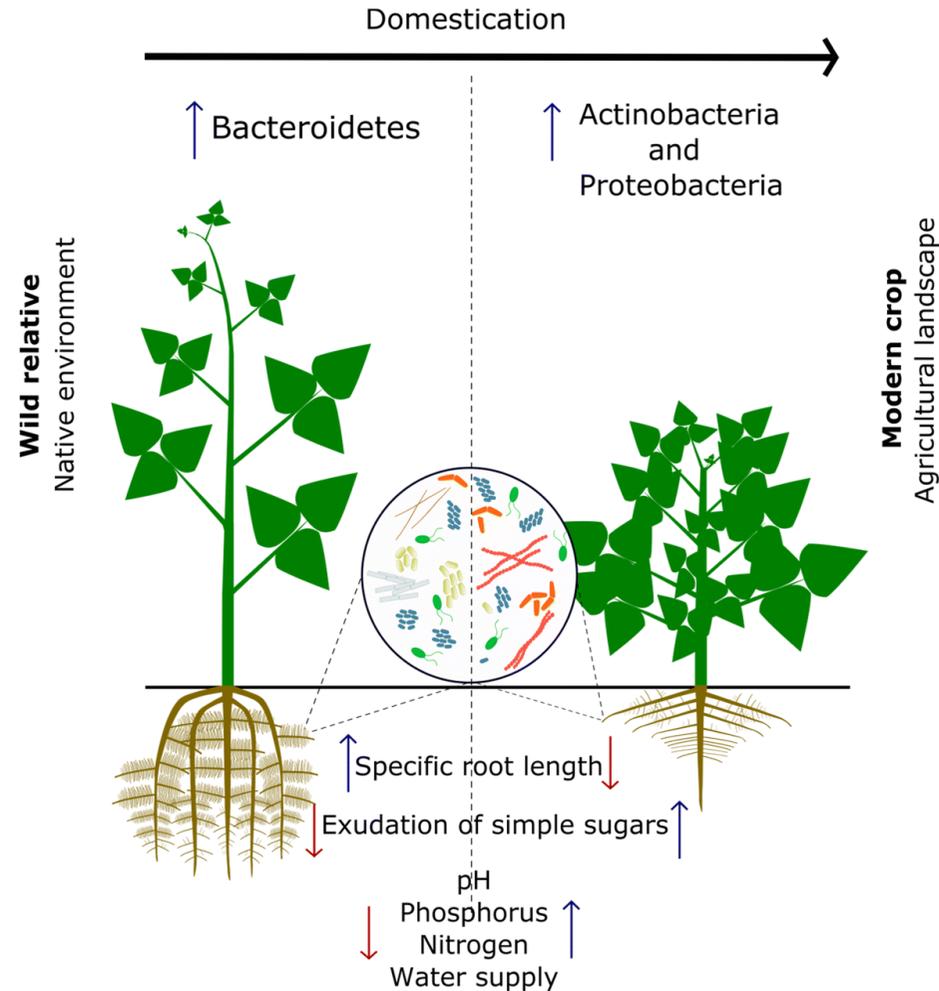
FIG 2 The microbiome and our changing Earth system. Population growth, urbanization, environmental degradation, and global climate change. Human-induced soil degradation based on data from reference 180; urban population by 2050 based on data from reference 181; global surface warming data based on data from reference 182; trends in global water extraction (dark color) and consumption (light color) by sector are based on data from reference 183; food yield increases required by 2050 are based on data from reference 184.

Blaser, M. J., Cardon, Z. G., Cho, M. K., Dangl, J. L., Donohue, T. J., Green, J. L., ... Brodie, E. L. (2016). *Toward a Predictive Understanding of Earth's Microbiomes to Address 21st Century Challenges*. *mBio*,

7(3). doi:10.1128/mbio.00714-16

Conclusion

- The adequate regulatory measures can help to implement the European Commission Circular Economy Action Plan



Pérez-Jaramillo, J. E., Carrión, V. J., de Hollander, M., & Raaijmakers, J. M. (2018). *The wild side of plant microbiomes. Microbiome*, 6(1). doi:10.1186/s40168-018-0519-z

- Pathogens are microbes, but most microbes are not!
- Abundant scientific data on potential benefits.
- Burden of the proof: adverse effects only.
- Registration of mBCA only on identity and biological properties and efficacy (Costs!!!)
- **LACK OF ACTION**, including
 - Long delayed registration timelines
 - Limited mBCA can also imply additional risks
 - Potential is not sure risk (i.e. sensitization)
 - Inadequate guidelines
 - **IS ALSO AGAINST THE PRECAUTIONARY PRINCIPLE**



THANK YOU



