Plant protection and plant health in Europe Symposium

Registration of Biorationals in practice

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Microbials
Plant-extracts
Yield-enhancer
Natural-Mimics
Macrobials
Bio-pesticides
Inoculants
basic-substance
Botanicals
Plant-strengthner
Biocontrol
Bio-stimulants
Biologicals
Biorationals
Biologically-similar
Low-risk-substances
Natural
Biologics

Agenda

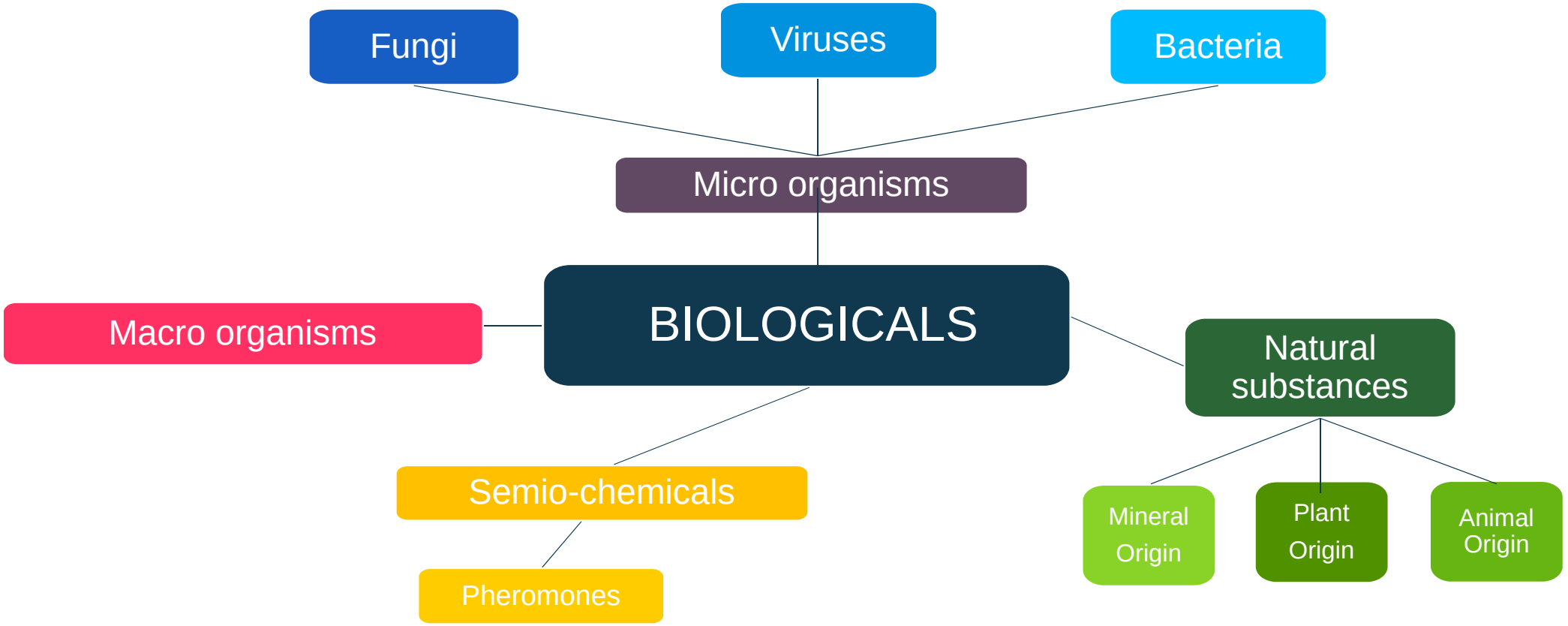
- What is a Biorational from a regulatory perspective?
- The Regulatory framework
  - What is the same ?
  - What is different ?
- The Requirements
  - What is the same ?
  - What is different ?
- Conclusion

WHAT IS A BIORATIONAL ? – SYMPOSIUM DEFINITION

Materials that are biologically-derived or, if synthetic, structurally similar and functionally identical to a biologically occurring material. Micro-organisms, plant extracts, basic substances, semiochemicals, […]

Invitation to the symposium « Plant protection and Plant health in Europe 13-14/12/2017 Braunschweig Germany

WHAT ARE BIO-CONTROL PRODUCTS IN FRANCE



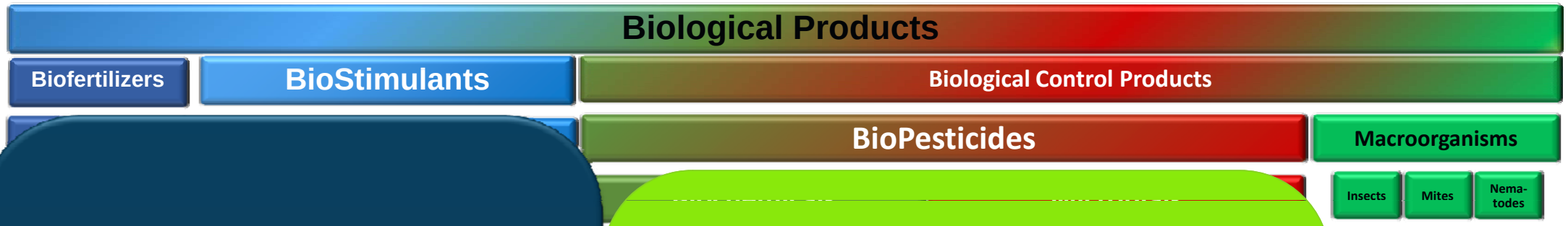
From : « Le bio-contrôle pour la protection des cultures 15 recommandations pour soutenir les technologies vertes. Synthèse du rapport au premier ministrie. Mission parlementaire confiée à Antoine Herth. 2011

WHAT ARE BIOLOGICALS – A BAYER DEFINITION

Biologicals consist of **microorganisms** such as bacteria and fungi; **beneficial macroorganisms** (e.g. predatory mites); **semiochemicals** (e.g. pheromones); or **natural compounds** (e.g. plant extracts).

The Regulatory framework for biorationals

Proposal classification of Biological products by function



Revision of 2003/2003 :

Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL laying down rules on the making available on the market of CE marked fertilising products and amending Regulations (EC) No 1069/2009 and (EC) No 1107/2009

Regulation 1107/2009

concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC

Macroorganisms

- Insects; Mites; Nematodes
- Insects followed by mites makeup the largest groups
- Unique in that the live organism in the form of eggs, larvae, pupae or adult is used.
- Most important challenge for Macros is logistics—shipping live organisms that have to have special care to survive
- Normally not classified as a Biopesticide—only as Biological Control Products

Regulatory frameworks are based on the Function of the final product

1107/2009

1. This Regulation shall apply to products, in the form in which they are supplied to the user, consisting of or containing active substances, safeners or synergists, and intended for one of the following uses:
(a) **protecting plants or plant products against all harmful organisms** or preventing the action of such organisms, unless the main purpose of these products is considered to be for reasons of hygiene rather than for the protection of plants or plant products;
(b) **influencing the life processes of plants**, such as substances influencing their growth, other than as a nutrient;
(c) preserving plant products, in so far as such substances or products are not subject to special Community provisions on preservatives;
(d) **destroying undesired plants or parts of plants**, except algae unless the products are applied on soil or water to protect plants;
(e) **checking or preventing undesired growth of plants**, except algae unless the products are applied on soil or water to protect plants.

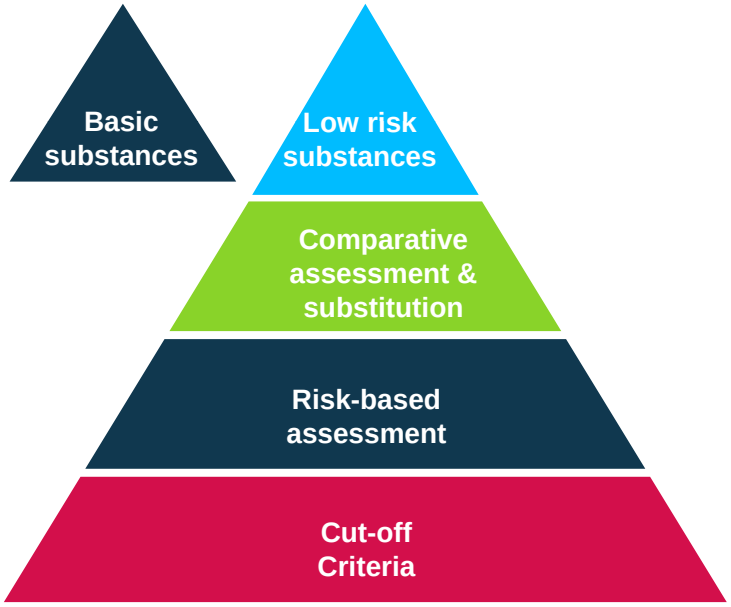
2003/2003 (revised)

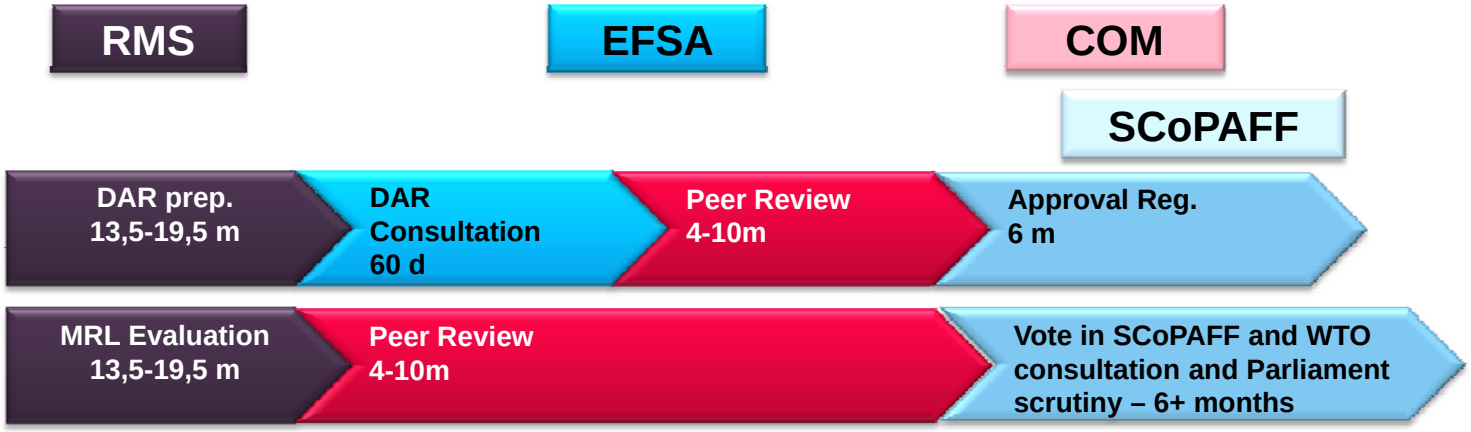
Text presented for Parliament first reading.

(1) '***plant nutrition*** product' means a substance, mixture, micro-organism or any other material, applied or intended to be applied, either on its own or mixed with another material, *on fungi or their mycosphere or* on plants *at any growth stage, including seeds, and/*or *rhizosphere*, **for the purpose of providing plants *or fungi* with nutrients or *of* improving their *physical or biological growth conditions or their general vigour, yields and quality, including by increasing the ability of the plant to take up nutrients*** *(with the exception of plant protection products covered by Regulation (EC) No 1107/2009)*;

Regulatory framework – What is the same ?

Active substance Approval



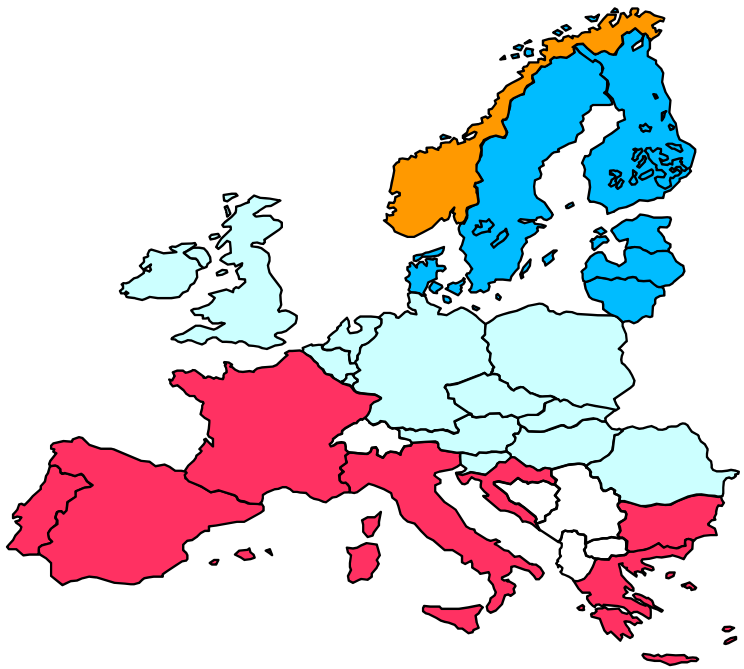


RMS: rapporteur member state
EFSA: European Food Safety Agency
COM: EU-Commission
DAR: Draft Assessment Report
MRL: maximum residue limit

Biopesticides are subject to 1107/2009 like all other PPPs.

Regulatory framework – What is the same ?

Product Authorisation



Product dossier evaluation
12 m (+ 6m for extra data)

Mutual recognition 120 d

zRMS

cRMS

Autorisation in a MS

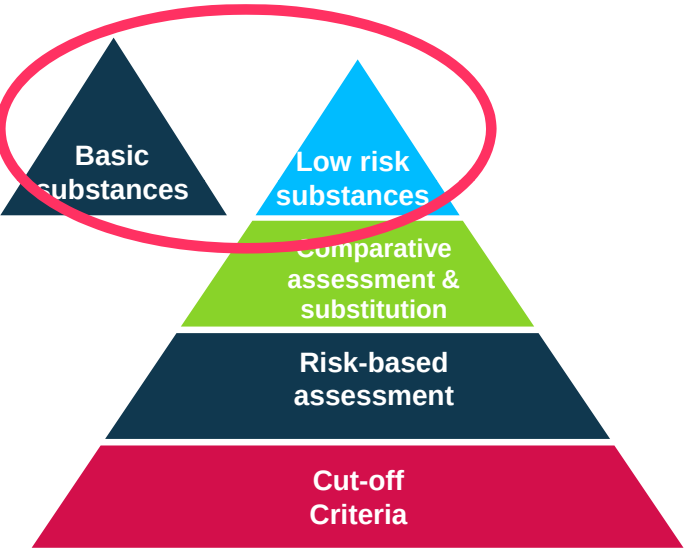
Mutual recognition 140 d

MS of another zone

Biopesticides follow the Zonal approach.

Regulatory framework - what is different ?

Active substance Approval

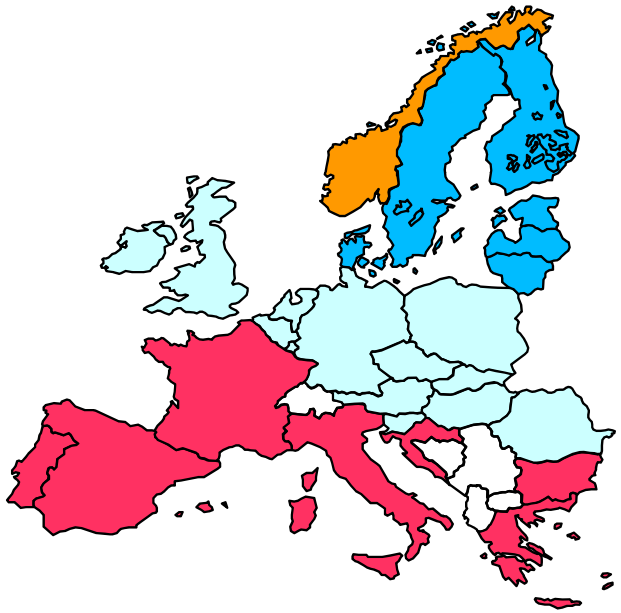


- **10 approved Low-risk substances**
  - 4 micro-organisms
  - 3 viruses
  - 1 yeast extract
- **18 approved Basic-substances**
  - Vinegar, beer
  - Mustard seed, salix spp. cortex etc…
- New Low risk criteria voted August 2017

Low-risk substances : longer approval, quicker approval of products.

Regulatory framework - what is different ?

Product Authorisation



- **Less difficult to find ZRMS and shorter “queue”**
- **Timelines better than for chemical products**
- **Inter-zonal mutual recognition works well for microbial products**

- Most of the questions during evaluation on :
  - Identity of the substance/organism
  - Contaminants and storage stability
  - Efficacy of the product

The Requirements

The Requirements – what is the same ?

COMMISSION REGULATION (EU) No 283/2013

of 1 March 2013

setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

(Text with EEA relevance)

PART A

CHEMICAL ACTIVE SUBSTANCES

PART B

MICRO-ORGANISMS INCLUDING VIRUSES

COMMISSION REGULATION (EU) No 284/2013

of 1 March 2013

setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

(Text with EEA relevance)

PART A

CHEMICAL PLANT PROTECTION PRODUCTS

PART B

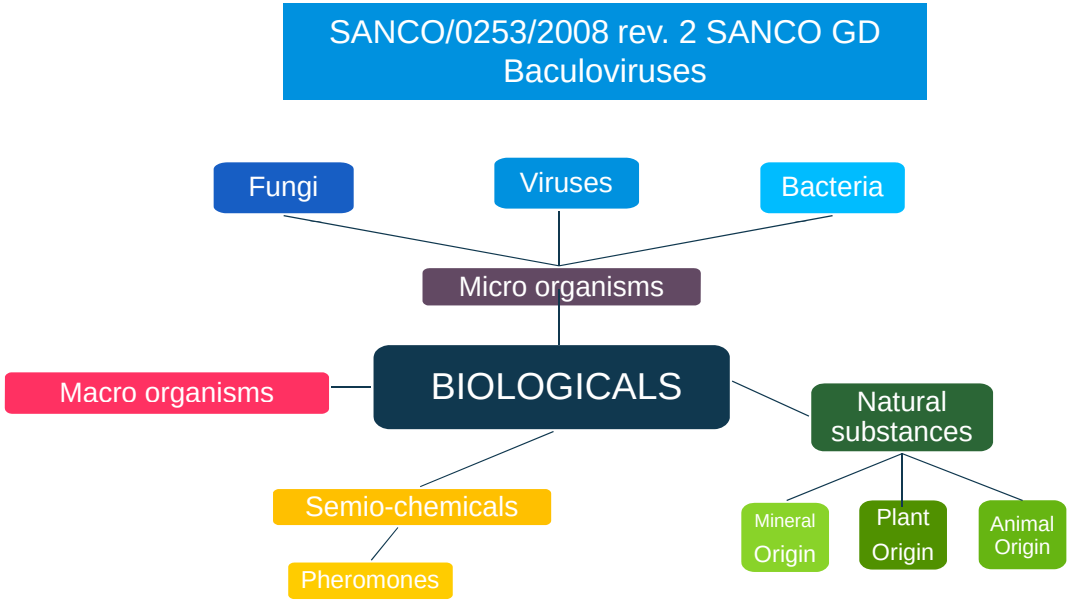
PREPARATIONS OF MICRO-ORGANISMS INCLUDING VIRUSES

In theory only specific requirements for Microbials. In practice several guidance documents provide specific data-requirements for other types of biorationals.

The Requirements – what is different ?

Guidelines

EU
- EFSA RA on microbials
- SANCO docs:
  - SANCO/12823/2012 –rev. 4 **Equivalence of technical grade a.i.**
  - SANCO/12116/2012 –rev. 0 - **microbial contaminant limits**
  - Sanco/10754/2005 rev.5 - **Taxonomic level of microorganisms**
  - SANCO/12117/2012 –rev. 0 - **Environmental safety**
  - SANCO/11188/2013 - **inclusion of active substances into Annex IV**



EU GD SANTE/12815/2014 rev. 5.2

SANCO GD SANCO/11470/2012– rev. 8 on Botanicals

The Requirements – what is different ?

A concrete example

For the a.i. (283/2013)

1.3. Name and species description, strain characterisation

(i) The micro-organism should be deposited at an internationally recognised culture collection and given an accession number and these details must be submitted.

(ii) Each micro-organism that is subject to the application shall be identified and named at the species level. The scientific name and taxonomic grouping, i.e. family, genus, species, strain, serotype, pathovar or any other denomination relevant to the micro-organism, must be stated.

For the product (284/2013)

1.4. Detailed quantitative and qualitative information on the composition of the preparation

(i) Each micro-organism that is subject to the application shall be identified and named at the species level. The micro-organism shall be deposited at a recognised culture collection and given an accession number. The scientific name must be stated, as well as the group assignment (bacteria, virus, etc.) and any other denomination relevant to the micro-organism (e.g. strain, serotype). In addition, the development phase of the micro-

(ii) For preparations the following information must be reported:

— the content of the micro-organism(s) in the plant protection product and the content of the micro-organism in the material used for manufacturing of plant protection products. These must include the maximum, minimum and nominal content of the viable and non-viable material,

— the content of co-formulants,

— the content of other components (such as by-products, condensates, culture medium, etc.) and contaminating micro-organisms, derived from production process.

The contents shall be expressed in terms as provided for in Directive 1999/45/EC of the European Parliament and of the Council (1) for chemicals and appropriate terms for micro-organisms (number of active units per volume or weight or any other manner that is relevant to the micro-organism).

The Requirements – what is different ?

A concrete example

- **Micro-organisms need to be :**
  - Identified at strain level for active ingredient approval and product authorization.
  - Quantified in the product.

The Requirements – what is different ?

A concrete example : SERENADE® ASO

Example:
Serenade® ASO

IIIM 1.7.1.1 Also indicate: scientific name and strain/serotype of MPCA, its accession number in a recognised culture collection

Strain	QST 713
Species	*Bacillus subtilis*
Genus	*Bacillus*
Family	Bacilliaceae
Order	Bacilliales
Class	Bacilli
Group	Firmicutes
Division	Bacteria

The strain QST 713 has been added to the internationally accepted Agriculture Research Culture Collection (NRRL), Illinois, USA, code number NRRL B-21661.

Why strain characterization is a critical point?

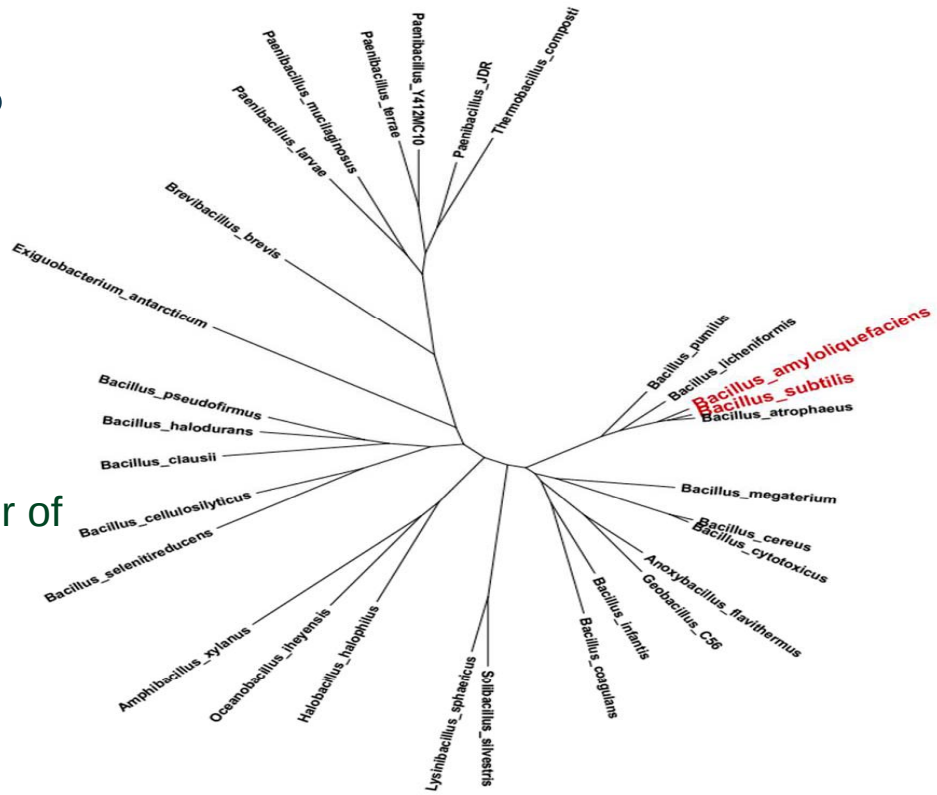
The Requirements – what is different ?

Identification of a microbial

- **Bacterial taxonomic classification is not a frozen picture.**

<u>Exemple</u>

The strain *Bacillus subtilis* QST 713 is now classified as a member of the closely related species *Bacillus amyloliquefaciens*



- **This could bring difficulties for :**
  - **other geographies,**
  - **internal databases and masterdata management**
  - **other legislations/standard based on specie name**

The Requirements – what is different ?

Quantification of a microbial

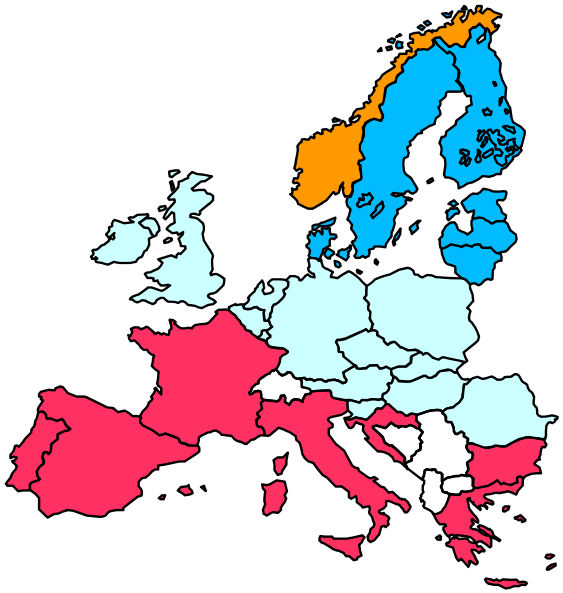
- **CFU method**
  - Best method to measure quantity of viable micro-organisms
  - But : some variability and issue with micro-organisms that tend to “cluster” on petri dishes.

- **Integrated process versus non-integrated process**
  - Certain micro-organisms cannot be easily isolated => integrated process
  - Only weight of biomass can be measured including residues and water
  - Spore weight obtained by calculation.

- **Specification based on Minimum versus Minimum and Maximum**
  - Differs from one country to the other

Requirements - what is different ?

Product Authorisation



- **Wide acceptability of public literature**
- **No/ a few higher tier studies**
- **Simple modelling calculations**

- Some technical guidance documents not adapted
  - Sensitization GD (microbial products)
  - Storage stability GD

CONCLUSION

CONCLUSION

- **Biorationals are very diverse by Nature.**
  - Same regulatory framework for all Plant Protection Products but necessity to have specificities of Biorationals to be taken into account.
    - Harmonisation of definition of Biocontrol/biorational.
    - Guidance document for specific substances/organisms.
  - A clear and precise “specification” is key.
    - Plant extracts
    - Micro-organisms
- **Biorationals can have diverse Functions.**
  - Plant Protection Products versus Biostimulants/Fertilizers

There is no regulatory “one size fits all” for Biorationals.

Thank you!