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Low Risk Substances

Complexity made Comprehensible

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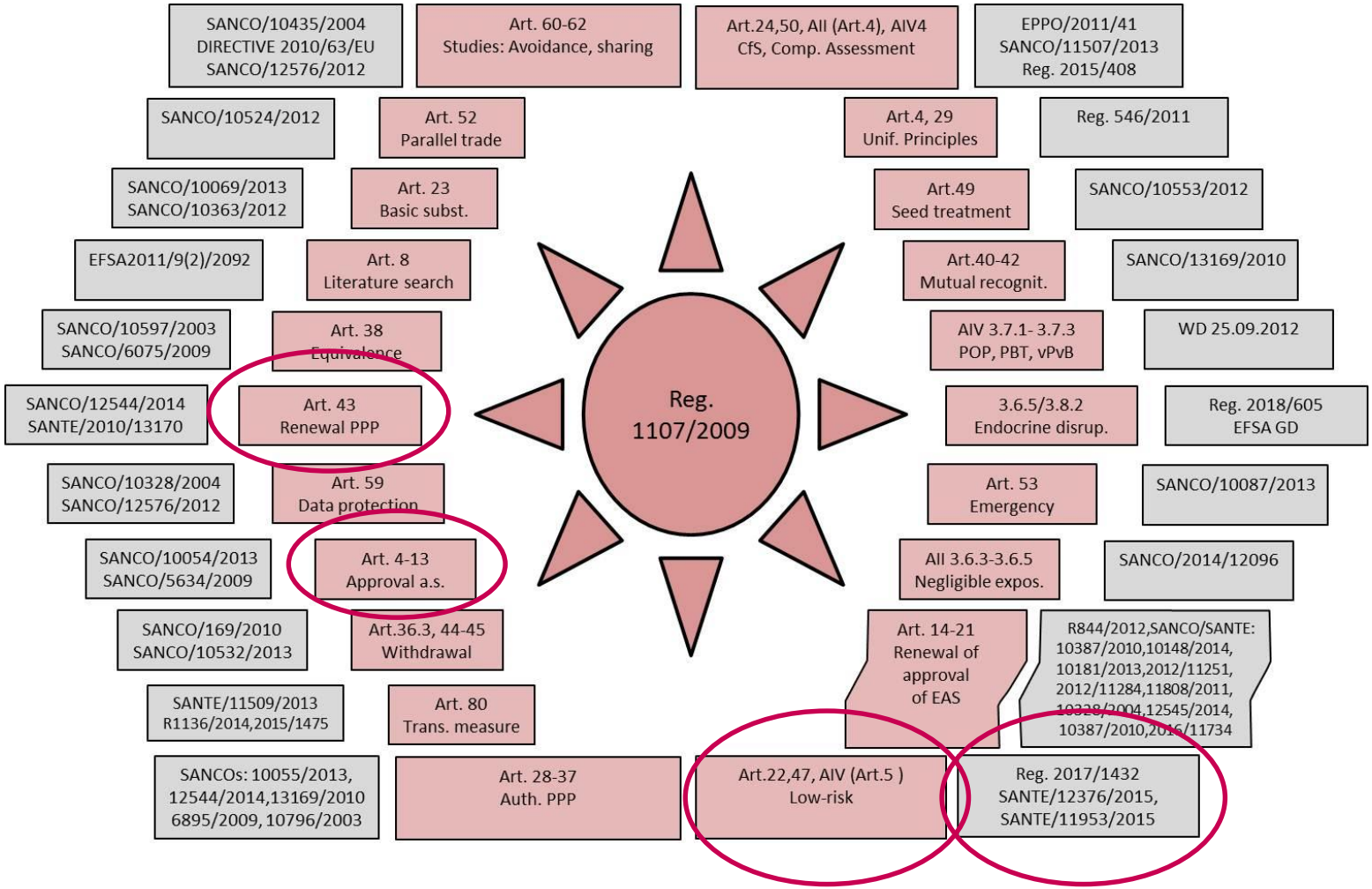
Low risk substances
Regulation 1107/2009, applicable regulations and guidelines



Low risk substances
“Biopesticide” Guidelines

SANCO/12823/2012 –rev. 4 12 December 2014: GUIDANCE DOCUMENT FOR THE ASSESSMENT OF THE EQUIVALENCE OF TECHNICAL GRADE ACTIVE INGREDIENTS FOR IDENTICAL **MICROBIAL** STRAINS OR ISOLATES APPROVED UNDER REGULATION (EC) No 1107/2009.

SANCO/12116/2012 –rev. 0 September 2012 Working Document on **Microbial** Contaminant Limits for Microbial Pest Control Products

SANCO/12117/2012 –rev. 0 September 2012 Working Document to the Environmental Safety Evaluation of **Microbial** Biocontrol Agents

SANCO/12545/2014– rev. 2 March 2016 GUIDANCE DOCUMENT FOR APPLICANTS ON PREPARING DOSSIERS FOR THE APPROVAL OR RENEWAL OF APPROVAL OF A **MICRO-ORGANISMS** INCLUDING VIRUSES ACCORDING TO REGULATION (EU) No 283/2013 AND REGULATION (EU) No 284/2013

SANTE/12815/2014 rev. 5.2 May 2016 GUIDANCE DOCUMENT ON **SEMIOCHEMICAL** ACTIVE SUBSTANCES AND PLANT PROTECTION PRODUCTS

SANCO/11470/2012– rev. 8 20 March 2014 GUIDANCE DOCUMENT ON **BOTANICAL** ACTIVE SUBSTANCES USED IN PLANT PROTECTION PRODUCTS

SANCO/0253/2008 rev. 2 22 January 2008 Guidance Document on the assessment of new isolates of **baculovirus** species already included in Annex I of Council Directive 91/414/EEC

SANCO/5272/2009 rev. 3 28 October 2010 Guidance Document on the assessment of new substances falling into the group of Straight Chain Lepidopteran **Pheromones** (SCLPs) included in Annex I of Council Directive 91/414/EEC

Sanco/10754/2005 rev.5 15 April 2005 Guideline developed within the Standing Committee on the Food Chain and Animal Health on the taxonomic level of **micro-organisms** to be included in Annex I to Directive 91/414/EEC

??? Low risk substances ≠ Biopesticide ???

Low risk substances
Approval and EFSA conclusion – Example MBCA Bacteria[1]

EFSA conclusions for bacterial strains: 12

- Average number of data gaps: 13
- Average number of issues that could not be finalised: 5
- Critical area of concern: 1

➢ **Approvals: 12**

➢ **Low risk bacterial strains: 1** (Bacillus amyloliquefaciens strain FZB24)

Data gaps:

- **literature** search on **secondary metabolites/toxins** known
- **production** of **toxins/secondary metabolites** after application (potential toxicity, RA for re-entry workers and consumers
- Production, levels **persistence**, transformation and **mobility** of **toxins/secondary metabolites**
- evidence that the strain will return to background levels in soil within a year
- information to address the risk to sewage treatment organisms
- information to address the potential infectivity and pathogenicity **aquatic invertebrates, algae, aquatic plants and adult honeybee**
- effects of **secondary metabolites/toxins** to **non-target organisms**
- risk for **non-target soil macroorganisms**

[1] Status 2018

Low risk substances

Approval and EFSA conclusion – Example MBCA Bacteria (cont.)

Issues that could not be finalised:

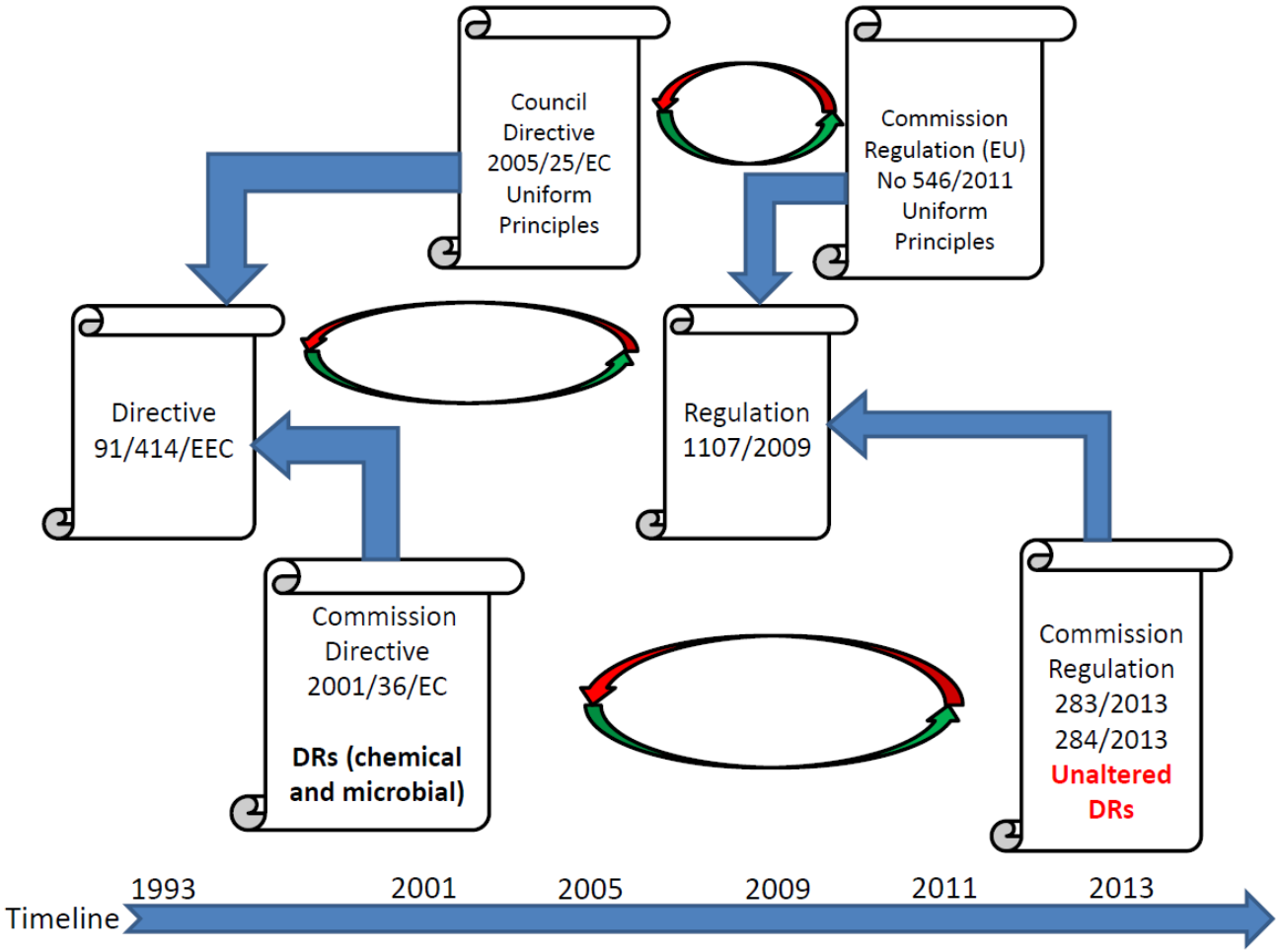
- risk assessment for the **re-entry workers and consumers** (pending further investigations of **toxins/secondary metabolites**)
- information available was insufficient to demonstrate that the strain would respect the uniform principles criterion of not being expected to **persist in soil in concentrations considerably higher than the natural background levels**
- Satisfactory information to demonstrate that, **under the conditions of use**, any **secondary metabolites/toxins** produced by the strain will not occur in the environmental compartments in concentrations considerably higher than under natural conditions was missing

➢ Potential for **transfer of genetic material**: Normally an issue that could not be finalised (10 out of 12) but sufficient information for Bacillus amyloliquefaciens strain FZB24

Critical areas of concern:

- None

Low risk substances
Data Requirements for microorganisms



Scheepmaker, J., Dutch Ministry of Health, Welfare and Sport, National Institute for Public Health and the Environment (2018): Risk assessment of secondary metabolites of beneficial micro-organisms.- Fresenius Conference June 6, Germany.

Low risk substances
Data Requirements for microorganisms
(cont.)

Primary + secondary metabolism of microorganisms (MOs)

- Primary metabolite: Relatively **few substances common in all biological systems** (polysaccharides, proteides, nucleic and fatty acids) essential for growth and development with known functions
- **Secondary metabolite**: **Tens of thousands of small molecules** of often unknown function but restricted to / specific for certain genera or species; **regulate life cycle processes** such as growth, replication, **competition** or survival at biochemical level in **minimal concentrations**

- **Scheepmaker**, J.W.A., Busschers, M., Sundh, I., Eilenberg, J. & T.M. Butt (submitted to Biocontrol): **Sense and nonsense** of the secondary metabolites data requirements for beneficial microbial biocontrol agents.

- **OECD Guidance** on secondary metabolites (under preparation)

Low risk substances
Regulation 2017/1432 – Example MBCA

Micro-organisms

1. An active substance which is a **micro-organism** may be considered as being of low-risk **unless at strain level it has demonstrated multiple resistance to anti-microbials used in human or veterinary medicine.**

? What is the definition of multiple resistance to anti-microbials ???

- Extensive guidance under preparation (per. comm. COM)

? Is any other micro-organism (without multiple resistance to anti-microbials on strain level) a low risk a.s.???

- No, see existing approvals e.g. Beauveria bassiana 147 (Date of approval 06/06/2017)
- An active substance which is a micro-organism **may be considered** …..

? What are the criteria ???

2. **Baculoviruses shall be considered as being of low-risk** unless at strain level they have demonstrated adverse effects on non-target insects.'

Low risk substances

EPPO PP 1/296: Principles of efficacy evaluation for Low-risk Plant Protection Products

"The objective of this document is to provide a framework for the minimum efficacy data requirements needed to demonstrate that a low-risk plant protection product is sufficiently effective (and crop safe) for authorization."

- *For low-risk plant protection products, a more **specialized approach** may be used compared to other plant protection products because they often have different properties and modes of action.*
- *The diversity in crop protection claims and modes of action of low-risk products is high. Some **principles and concepts** can be applied to all products, but other aspects of the efficacy evaluation and the scope of extrapolations depend strongly on the mode of action.*
- *Applicants need to provide robust **scientifically** justified argumentation to support **extrapolations** outside of EPPO PP 1/257, building on the key factors including mode of action and the proposed new extrapolations.*
- *A clear justification is always necessary and may be supported by **scientific literature and/or data**.*
- *However, non-GEP trial data may be acceptable if it is **scientifically sound** and in line with other applicable EPPO Standards.*
- *… for a number of aspects (e.g. succeeding crops) it may be possible to use **reasoned cases in lieu of actual data** (e.g. based on the mode of action, natural occurrence etc.)*
- *information may be derived from **laboratory studies, field trials or any valid relevant published paper** [Any relevant technical and/or scientific reports]*
- *Trials should follow the guidance set out in both the general and specific EPPO Standards (PP 1 series). However, it is recognized that deviations from the guidance may be required in some cases to account for the specific properties of low-risk plant protection products.*
- *… because of the risk attached to the use of plant protection products, it is necessary to decide if the benefits from the use of the plant protection product outweigh any disadvantages. **The net result of the positive and negative effects should be a sufficient overall benefit in order to justify the use of the plant protection product.***
- *Use of the product in an **IPM programme**: recommendations on how to use the product in relation to: (i) the level of pest pressure and/or the pest cycle, (ii) partnership with **other plant protection products** [e.g. alternation, or block programme (sequence), or **dose reduction of the partner plant protection product**], and/or IPM methods, when relevant.*

Low risk substances

EPPO PP 1/296: Principles of efficacy evaluation for Low-risk Plant Protection Products

- Scientific approach and justifications
- Specialized approach
- Use of MoA to extrapolate between different crops and pests,
- Use of worst case circumstances regarding product performance to extrapolate to less critical circumstances
- Further extrapolation possibilities

Low risk substances

Implications for other dossier sections

- Scientific approach and justifications e.g. in regards to identity or ecological functions
- Specialized approach e.g. baculoviruses
- Use of MoA to extrapolate between strains, species, genera, ecological functions, etc.
- Use of worst case circumstances regarding product performance to extrapolate to less critical circumstances e.g. MO secondary metabolites produced in lab/field
- Further extrapolation possibilities
- Etc.

Low risk substances
Developing species or dying breed?

- Approvals[1]
  - 492 a.s.

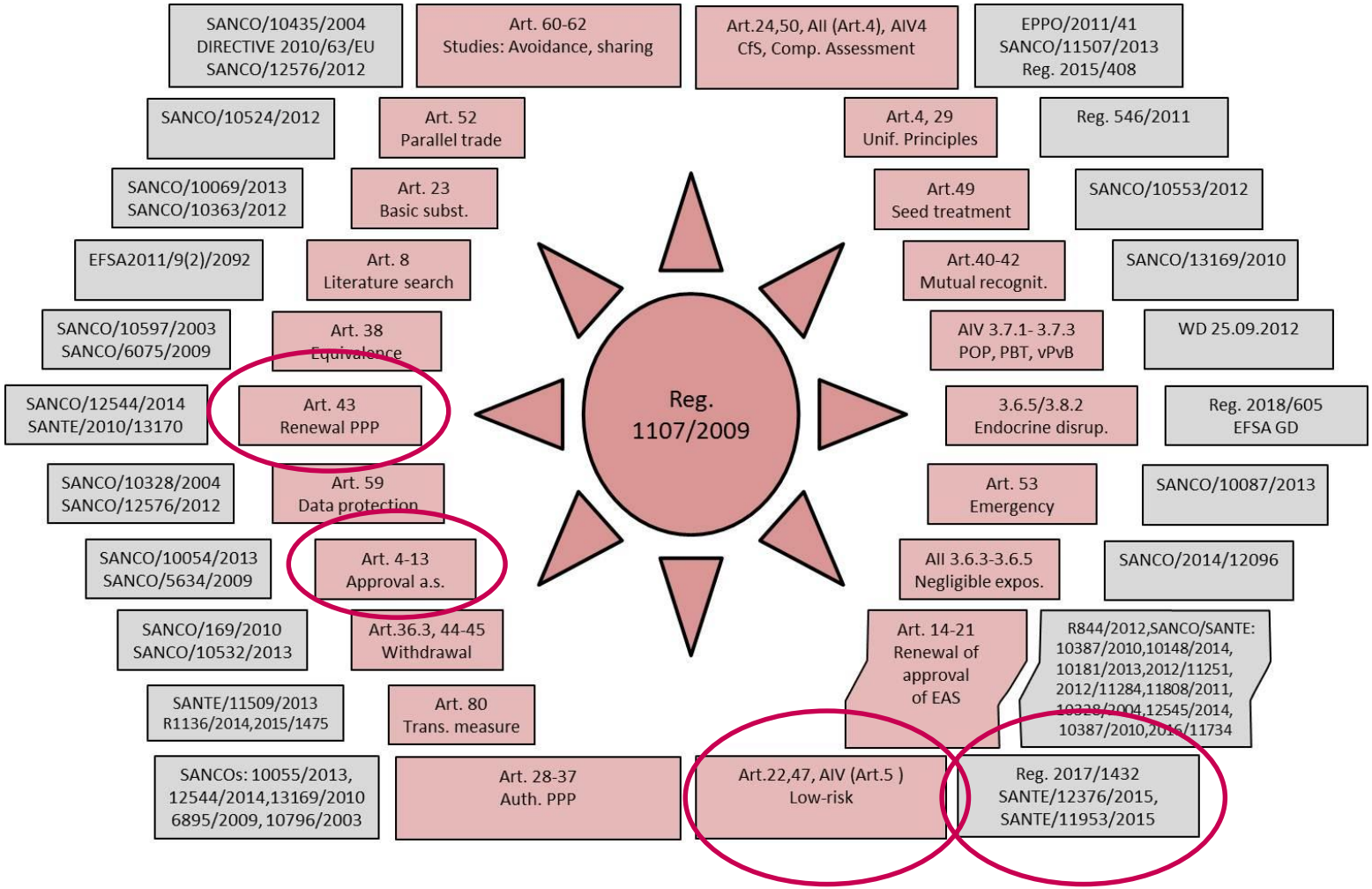
- **Low risk substances[1]**
  - 13 approvals
  - 30-?? “pending” renewals[2]

- Microorganisms[1]
  - 14 non-approved
  - 9 pending
  - 58 approved
  - **9 approved low risk**

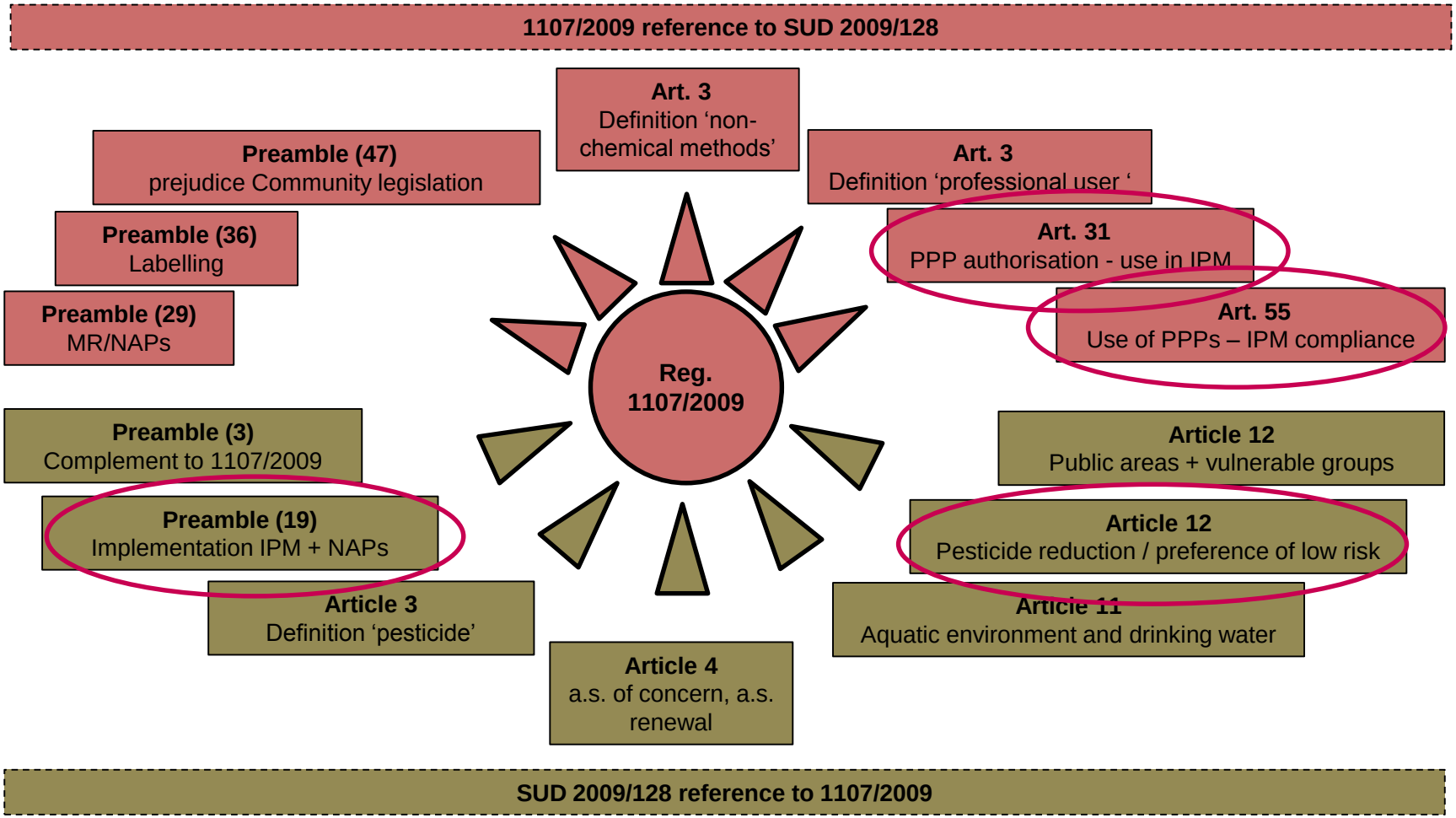
[1] EU Pesticides Database (status October 2018)
[2] SANTE-2016-10616–rev 8 of October 2017 DRAFT WORKING DOCUMENT AIR IV RENEWAL PROGRAMME

Low risk substances

Regulation 1107/2009, applicable regulations and guidelines



Low risk substances
Regulation 1107/2009 and complementary regulatory frameworks



Low risk substances
IPM - DIRECTIVE 2009/128/EC

Article 14(4): ‘Member States shall describe in their National Action Plans how they ensure that the general principles of integrated pest management as set out in Annex III are **implemented by all professional users by 1 January 2014**.

Article 4(1): Member States shall adopt **National Action Plans** to set up their quantitative objectives, targets, measures and timetables to reduce risks and impacts of pesticide use on human health and the environment and to **encourage** the development and introduction of **integrated pest management** …..

Article 4(3): By **26 November 2018**, the **Commission** shall submit to the European Parliament and to the Council a **report** on the experience gained by Member States on the implementation of national targets established in accordance with paragraph 1 in order to achieve the objectives of this Directive. It may be accompanied, if necessary, by appropriate legislative proposals

Low risk substances
IPM – dossier relevance

dRR

3.3 Information on the occurrence or possible occurrence of the development of **resistance** (KCP 6.3): …Findings on the risk of resistance by use and suitable management measures must be provided for the entire zone and if necessary, for each Member State of the zone. If monitoring proves to be necessary, it may be performed at the national or zonal level.

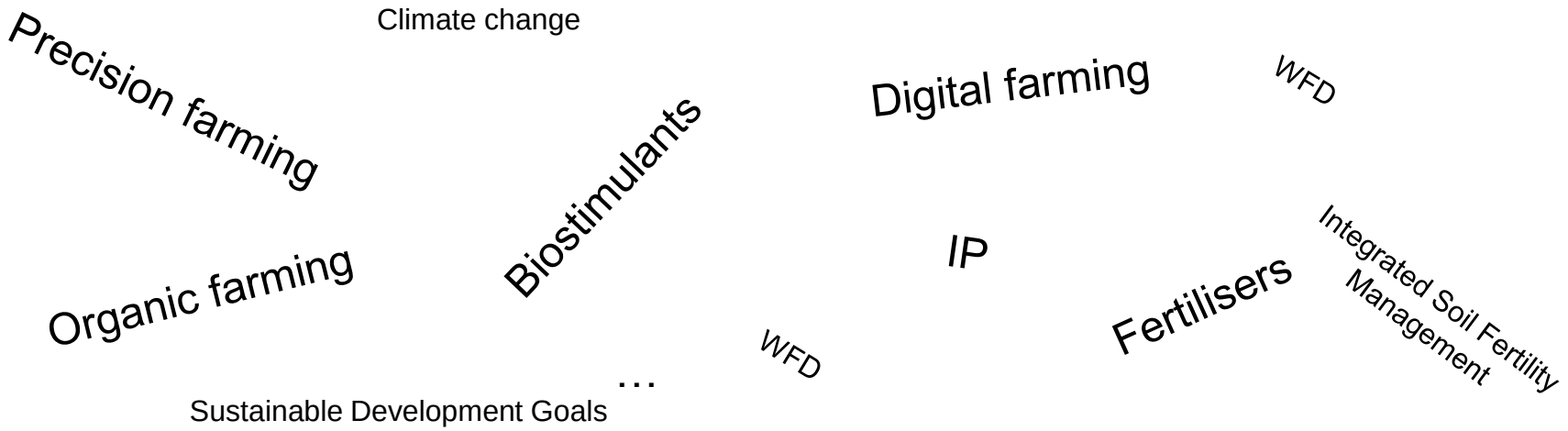
3.5.3 Effects on beneficial and other non-target organisms (KCP 6.5.3) --> Compatibility with **current management practices including IPM. If trials were carried out**, a brief description of experiments should be provided. Trials and results can be presented as described in the other parts of the dRR (efficacy, selectivity, etc.).

BAD

6.5 Contribution to risk reduction and **integrated pest management strategies** for the targeted crop or resource. …

Low risk substances
Developing this species?

- DO we need further guidance?
- What else do we need?
  - Holistic regulatory approach considering ALL regulatory frameworks
  - Scientific approach
  - Bring regulatory issues up to scientific/technical progress
  - Bring everything together for the farmers toolbox



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