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New Data Requirements for Microbials

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Regulatory Framework

Data requirements in the EU:

Commission Regulations (EU) No 283/2013 and 284/2013

Lists of data required for active substances and products

- Part A: Chemicals including natural substances and semiochemicals
- Part B: Microorganisms (e.g. bacteria, fungi, protozoa), and viruses

New Data Requirements for Microbials

EU DR for microorganisms discussed in the EU WG on Biopesticides since 2019

Draft presented in October 2021

Final version from January 2022 endorsed on 8 February 2022

Published 1.9.2022: Commission Regulations (EU) 2022/1439 and 2022/1440

Applies from 21 November 2022

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Transitional measures

Active substance approval or re-approval: old data requirements can be used for dossiers for active substance approval or re-approval submitted before 21 May 2023

Product authorisations:

If the active substance approval was under the “old” requirements:

Choice between use “old” or new requirements (from 21 November 2022 on)

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Goals for Microorganism approval

Aims at “facilitating the placing on the market of biological active substances such as micro-organisms”.

Differentiates between the living microorganism and its metabolites and specifies when Part A data requirements are applicable.

Intends to “differentiate the way to conduct the risk assessment for micro-organisms compared to the way it is being done for chemical substances.“

Emphasis on controlling antimicrobial resistance

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Identity

Definition of the active substance:

- a single strain
- “qualitatively defined combination of strains as they occur naturally or by manufacture”

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Identity

Definition of the active substance:

- a single strain
- “qualitatively defined combination of strains as they occur naturally or by manufacture”

- and one or more metabolites produced by the micro-organism that are claimed to be part of the plant protection action

- when the application of the metabolite(s) purified from the micro-organism would not cause the claimed plant protection action

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Identity / Biology

2.8. Information on metabolites of concern

Not required for a virus

List all metabolites of concern

Include “information used to identify or exclude metabolites as being of concern” in Sections on Human Health, Ecotoxicology, Residues and Fate and Behaviour

In line with metabolite guidance

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Identity / Biology

2.9. Presence of transferable antimicrobial resistance genes

Only required for bacteria

Resistance to antimicrobials

Nature of resistance genes

In line with AMR guidance

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Human Health

" ..information on the identity and biology of the microorganism (…) as well as health and medical reports may be sufficient for an assessment of the infectivity and pathogenicity potential of the microorganism".

"Further studies may be required to complete the evaluation…"

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Human Health

Separation between infectivity/pathogenicity of the MO and toxicity of metabolites

- Studies to determine the potential infectivity and pathogenicity of the micro-organism shall be performed … unless the applicant demonstrates, by following a weight of evidence approach, that no such effects are to be expected.
- Studies required for metabolites of concern where reference values cannot be set based on other information
- Short term toxicity studies are not mentioned any more

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Human Health

- For micro-organisms excluding viruses, antimicrobial agents with effectiveness against the micro-organism shall be listed – not new but more explicit now and required for the low risk status

- Assessment of Sensitization unchanged since 2002: "Until validated methods for testing dermal and respiratory sensitisation of micro-organisms become available, all micro-organisms shall be considered as potential sensitisers."
- The precautionary phrase "Microorganisms may have the potential to provoke sensitising reactions" is not mentioned.

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Residues in or on treated products, food and feed

Not required for viruses

No data required for the microorganism

Addresses only metabolites “which are a hazard for humans”

- Exposure estimation
- Studies as for Part A are required if consumers are exposed

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Environmental occurrence of the micro-organism, including fate and behaviour of metabolites of concern

- New name for the section
- Separation between microorganism and metabolites

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Environmental occurrence of the micro-organism, including fate and behaviour of metabolites of concern

Microorganism

- Predicted environmental density instead of concentration (PED)
- PED required unless absence of hazard can be stated
- Qualitative exposure assessment in case of adverse effects in studies
- Experimental data on densities only needed in case of adverse effects and no result from exposure assessment

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Environmental occurrence of the micro-organism, including fate and behaviour of metabolites of concern

Metabolites

- PEC required for hazardous metabolites
- No PEC needed for hazardous metabolites produced *in situ* but not present in the MPCA.
- Qualitative exposure assessment in case PEC is not sufficient to exclude risk
- Experimental exposure data for metabolites of concern if information above is not sufficient
- “If technically possible” information on metabolite concentration in relevant compartments shall be provided
- Study according to chemical data requirements

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Ecotoxicological Studies

- New name for the section for the a.s.
- “limit testing to what is necessary to conclude the risk assessment.”
- “Special attention .. to microbial species which are not known to occur in the relevant European environments.”
- Differentiation between infectivity/pathogenicity of the MO and toxicity of metabolites
- Study duration
- Studies should be done with organisms for which agreed testing protocols are available

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Ecotoxicological Studies

Studies are required unless

- pathogenicity/infectivity can be assessed based on the summary provided in section 1/2, or
- exposure to the micro-organism is expected to be none

- Terrestrial vertebrates include also reptiles and amphibians
- “Plants other than algae” replaced by “aquatic macrophytes” and “terrestrial plants” – studies required for herbicides
- Bee studies include “adult and larval stages”
- Non-target meso- and macro-organisms in soil replace earthworms and soil microorganisms

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Ecotoxicological Studies

Information and toxicity studies on metabolites

- Additional information required in case data submitted in Sec 2 and Sec 7 are not sufficient to exclude a risk of hazardous metabolites.
- Studies according to chemical requirements if needed
- Exposure studies are triggered by ecotoxicity data and ecotoxicity studies are triggered by exposure data - this opens the possibility to address the case by one or the other direction

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Summary

- Biology/Ecology is the central information
- Separation between toxicity and pathogenicity / infectivity
- Assessment of sensitization unchanged since 2002
- Microorganisms are not a “residue”
- Some non-target organisms changed

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Summary

- Use of conditionalities is implemented
- Provides more predictability for applicants (costs and timelines)
- Requires experience and knowledge for applicants and evaluators
- Strengthens collaboration and exchange between authorities and applicants
- Opens the use of a holistic approach instead of reductionist precautionary principle
- Encourages applications for new microbial active substances

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Proposal

- Biology/Ecology information in Sections 1/2 decides which additional data are needed for human health, residues, environment and non-target organisms
- Applicants submit full Sections 1/2
- Authorities evaluate these sections and decide which additional information is necessary
- Applicants generate information and submit Sections 3-9
- Authorities evaluate Sections 3-9 for DAR preparation


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