

# Identification of the regulatory steps and costs for registering the INBIOSOIL encapsulated biological control agent

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QuickTime™ and a  
decompressor  
are needed to see this picture.



# Biocontrol



semiochemicals

botanicals

Biocontrol can be defined as the reduction of pest populations by natural enemies and typically involves an active human role.

macroorganisms

microorganisms

# Biocontrol

pheromones

semiochemicals

botanicals

metabolites

pesticides

CO<sub>2</sub>

neem

predators

insects

fungi

bacteria

macroorganisms

microorganisms

parasitoids

nematodes

virus

pathogens

# Summary

The background of the slide is a photograph of a field of yellow flowers, possibly mustard, in the foreground. The background is softly blurred, showing rolling hills and a few trees under a pale sky.

Biocontrol

INBIOSOIL project and  
products

Data  
requirements

Areas of  
concern

Authorisation process

# INBIOSOIL Project

The INBIOSOIL (Innovative biological products for soil pest control) consortium focuses in the development of innovative biological products for the control of agricultural pests in soil.

INBIOSOIL explored the synergistic effects between entomopathogenic fungi, entomopathogenic nematodes, and semiochemicals by developing innovative co-formulations, making use of strategies derived from nature.

The experimental formulations were evaluated against key environmental performance indicators (ie. amount of active ingredient per ha, non-target effects and generate risk assessment data) as well as economic factors.

Academic groups and private sector small and medium enterprises are partnering in this project divided into 6 work packages.

# INBIOSOIL Work Packages (WP)

WP1 - Management and coordination

WP2 - Novel formulations and co-formulations for biocontrol agents

WP3 - Validation of RAFBCA-REBECA metabolite risk assessment decision scheme methods and will use molecular genetic tools to analyse direct and indirect effects of biocontrol agents in the environment and non-target organisms

WP4 - Formulations efficacy testing against soil pests in lab and field testing

WP5 - Assessment of economic aspects (environmental benefits and costs), regulatory steps and costs as well as development of business plan software

WP6 - Dissemination and communication of the INBIOSOIL project developments including leaflet and papers as well as demo trials

# INBIOSOIL Project



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# Microbial pesticide active ingredient: *Metarhizium brunneum* strain ART2825

ART2825 is a strain of entomopathogenic fungi virulent against wireworm larvae.

ART2825, BIPESCO 5 and F52 *Metarhizium brunneum* strains were previously classified as *Metarhizium anisopliae*.

Strain ART2825 was isolated from *Agriotes obscurus* infected larvae in Switzerland.

Like several other species of the *Metarhizium* genus, ART2825 may produce some toxins such as swainsonine, destruxins and cytochalasins, during certain developmental stages.



# INBIOSOIL formulated product: capsule

- Active ingredient - spores of *Metarhizium brunneum* strain ART2825
- (Source of) semiochemical - *Saccharomyces cerevisiae* (Baker's yeast) producing CO<sub>2</sub>
- Nutrient - corn starch
- Carrier - sodium alginate E401 (biodegradable biopolymer providing structure to the capsule)
- Formulation residue - calcium chloride (<1%)



# INBIOSOIL formulated product



# Regulations

A top-down view of a petri dish containing a petri dish with a dark, moist surface covered in numerous small, circular, yellowish-green mold colonies. The colonies are densely packed and vary in size, with some showing concentric rings. The background is dark, making the mold stand out.

REGULATION (EC) No 1107/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC

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

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

# Data requirements: approach



# Data requirements for ART2825 as active ingredient

Reg. EC 1107/2009

Other similar active ingredient approved under the same regulation

Other similar active ingredient approved

Approval status of other active ingredients in the registration process

Data package associated with similar active ingredient

# Data requirements for ART2825-CO2 capsule as formulated product

Reg. EC 1107/2009

Status of each substance (substance of concern)

Function of the substance (active ingredient)

Usage scope of the formulated product

Data generated for active ingredient or formulation

# INBIOSOIL WP5.2 approach



Defining the product

Minimal or standard scenario

Scope, exposure, tiers and data requirements

Costs types (studies, desk studies, administrative, etc)

Data transportability (such as BIPESCO5/F52)

# INBIOSOIL WP5.2 results

#	Section / Study	B5/F52 with B5/F52 data	B5/F52 with other strain data	ART2825 minimal scenario	ART2825 standard scenario	Comments	Cost
1	IDENTITY OF THE MICRO-ORGANISM						
1.1	Applicant	x	-	y	y		a
1.2	Producer	x	-	y	y		a
1.3	Name and species description, strain characterisation	x	-	y	y		a
1.4	Specification of the material used for manufacturing of formulated products	x	-	y	y		a
1.4	Characterisation for addition to internationally recognised culture collection	x	-	y	y		a
1.4	Addition to internationally recognised culture collection	x	-	y	y	Accession and storage according to Rule 6.1 of the Budapest Treaty - fungi 800 € plus annual 30€ ( <a href="https://www.dsmz.de">https://www.dsmz.de</a> )	800 €
1.4.1	Content of the micro-organism	x	-	y	y	The minimum and maximum content of the micro-organism in the material used for manufacturing of formulated products, must be reported (EC 283/2013).	a
1.4.2	Identity and content of impurities, additives, contaminating micro-organisms	x	-	y	y	If possible and appropriate, identity and maximum content of all contaminating micro-organisms, expressed in the appropriate unit, must be reported (EC 283/2013). No microbial contaminants are present in the ART2825 strain used during the INBIOSOIL project (2.6.2015 communication Patel)	u

Requirements for active ingredient /  
formulation

Identification of areas of  
concern



# Areas of concern

A top-down view of a petri dish containing a dense culture of green and yellowish mold. The mold is spread across the surface of the agar, forming numerous small, fuzzy colonies. The petri dish is clear, and the mold's texture is highly detailed.

Regulation EC  
1107/2009

Persistence in the  
environment

Secondary metabolites -  
residues

Secondary metabolites - non-target  
organisms

Status of co-formulants (co-formulant, synergist or residue)

# GMO - Biocontrol authorisation in the EU

15.1.2013

EN

Official Journal of the European Union

L 9/5

## **COMMISSION IMPLEMENTING REGULATION (EU) No 17/2013**

**of 14 January 2013**

**approving the active substance *Trichoderma atroviride* strain I-1237, 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, and amending the Annex to Implementing Regulation (EU) No 540/2011**

**(Text with EEA relevance)**

# Data gaps identified by EFSA for *Trichoderma* strain I-1237 and SC1

## 9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC and where the issue is of such

EFSA Journal 2012;10(10):2706

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Peer review of the pesticide risk assessment of the active substance *Trichoderma atroviride* strain I-1237

importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

1. The production of toxins/secondary metabolites of unknown toxicity cannot be excluded. Therefore the risk assessment cannot be finalised for humans (during spray use: for operators, workers, consumers from potential residues in plants and bystanders; during paint brushing and dip-in in glasshouse: for operators, workers and consumers). Also the risk assessment cannot be finalised for the environment (for the spray use), including the assessment of potential groundwater contamination.
2. The risk to aquatic organisms and non-target arthropods from infectivity and pathogenicity cannot be finalised with the available information.
3. The risk to soil microorganisms can not be finalised with the available information.



Peer review of the pesticide risk assessment of the active substance *Trichoderma atroviride* strain SC1

## 9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011<sup>7</sup> and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as an issue that could not be finalised where the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation.

1. The production of toxins/secondary metabolites cannot be excluded. Therefore the risk assessment cannot be finalised for operators, workers, residents, bystander, consumers and the environment including the assessment of potential groundwater exposure.
2. The risk assessment to aquatic invertebrates and algae from exposure to the microorganism could not be finalised consequent to the spray application to pruning cuts in established vineyards.

EFSA Journal 2015;13(4):4092

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I-1237 EFSA opinion: October 2012

I-1237 EU approval: January 2013

SC1 EFSA opinion: April 2015

# Conclusion

The regulatory steps for obtaining regulatory approval for the ART2825-CO2 capsule in the European Union were assessed in the INBIOSOIL WP5.2 report.

Regulatory and registration uncertainties remain high even if several entomopathogenic fungi formulations are currently available for commercial use in the European Union.

Until further clarifications are provided by authorities, the uncertainties will remain too high engage in a regulatory and registration procedure.

# Thank you



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