Global Challenges for Registering Biological Products - Europe

BPIA, 7th March 2018

Dr Alison Hamer, ERM

The business of sustainability

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ERM Global Product Services

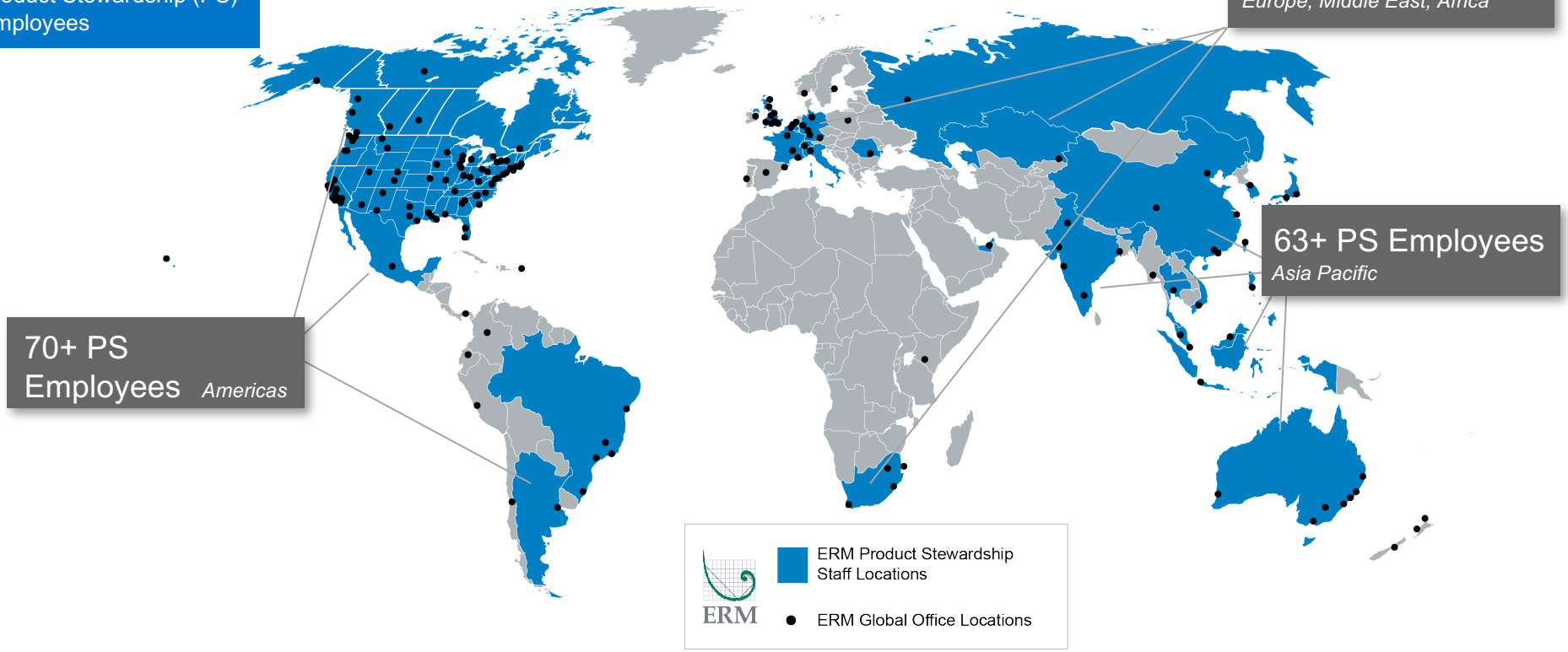
234+ Total
Product Stewardship (PS) Employees

Global Reach with Deep Regulatory and Scientific Expertise

101+ PS Employees
Europe, Middle East, Africa

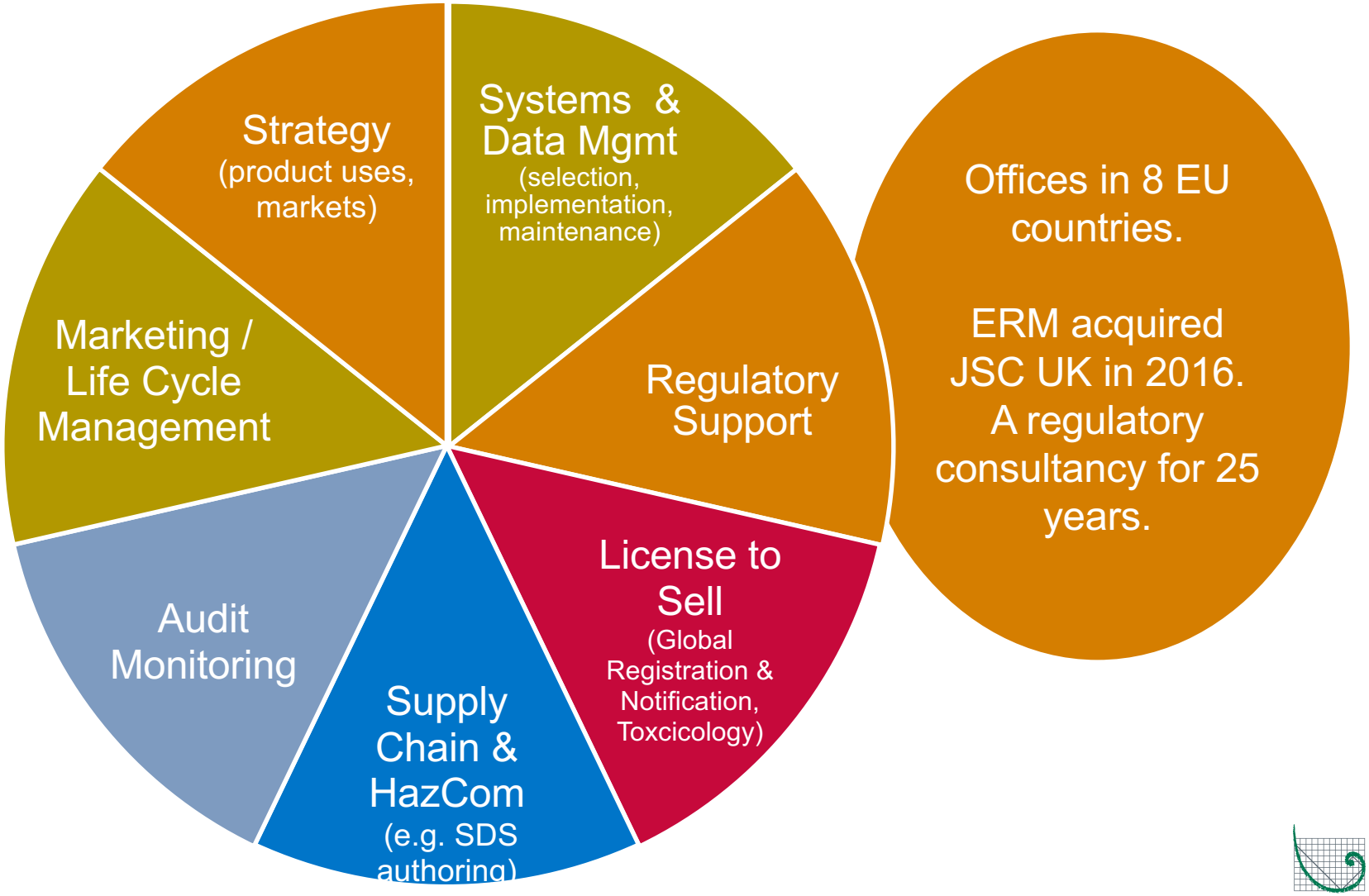
63+ PS Employees
Asia Pacific

70+ PS Employees *Americas*



Ranked Top PS Services Consultancy by EHS Leaders (Verdantix Dec 2016)

ERM's Product Safety & Stewardship Services



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Summary of presentation

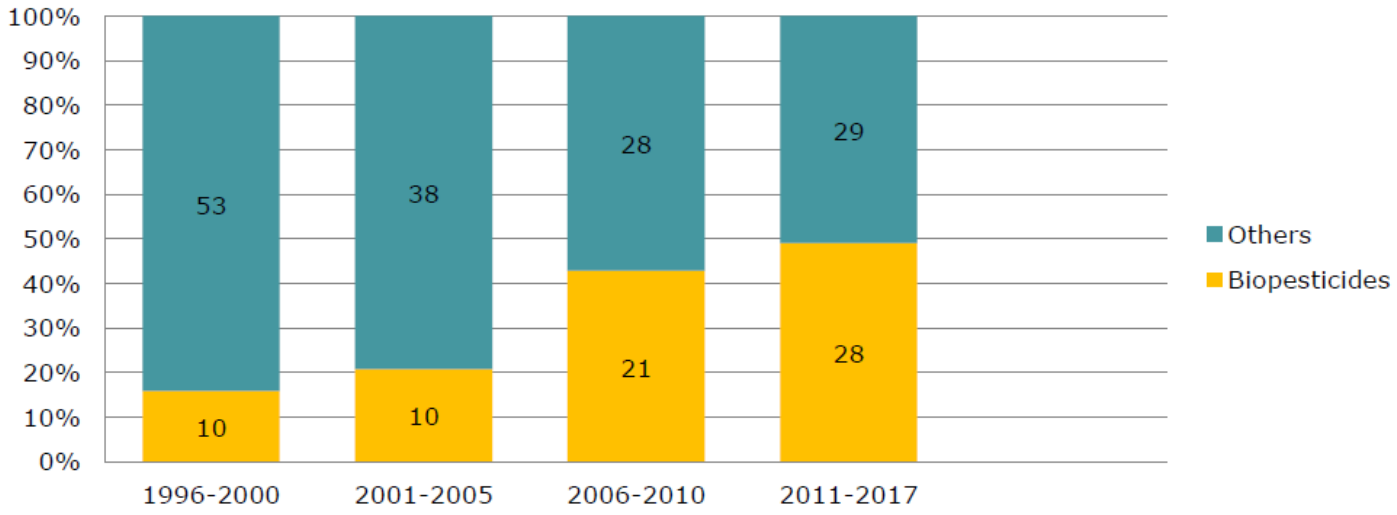
1. Hot topics related to guidelines for biologicals – Europe
2. Trends related to dossier preparation – Europe
3. Forthcoming changes

Pitton, EU Commission presentation, ABIM 2017

European Commission

More and more in new applications "biopesticides" since 1996

Application for new active substances since 1996



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1. Hot topics related to guidelines for biologicals - Europe

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Recent guidance of interest

- Recent OECD publications;
  - **Semiochemicals**, OECD Series on Pesticides No. 93 (Jan 2018)
  - **Technical equivalence** for microorganisms (in publication)
- Work ongoing on regulatory approach for **microbial secondary metabolites**
  - The OECD is finalising the working document
  - EU Commission is working on a Guidance Document
- 3rd Global Minor Uses Summit (October 2017) made a recommendation to review and publish list of **substances exempt from MRLs**, i.e. most biopesticides
- EPPO standard on low risk plant protection products: PP 1/296 (1) Principles of **efficacy evaluation for low-risk** plant protection products

"Niche Uses of Highly Specific Biocontrol Products"

- OECD Seminar, 2017, report in publication…
- Noted that the tools with arguably the safest risk profile for both human health and the environment may not be made available by the biocontrol industry because they are too specific to justify high costs related to their placing on the market
- *Examples come from **diverse groups of products**, such as semiochemicals, baculoviruses, bacteriophages or invertebrate biocontrol agents*
- The seminar presented the hurdles and issues faced and worked towards the delivery of solutions to bring biological plant protection solutions to farmers
- Recommendations were made to improve their registration

2. Trends related to dossier preparation – Europe

Trends in data sets for microbials - Toxicology

- EU Microbial Data Requirements for Human Health and Positions Taken by EFSA (David Andrew, paper for ABIM 2017)
- Extent of data should be guided by the nature of the active substance, take into account mode of action, role of metabolites, and the provision of data on the production of toxins
- Consistent concerns raised by EFSA;
  - Lack of adequate toxicity and pathogenicity data
  - Data on the potential transfer of genetic material
  - Information on the production of toxins or secondary metabolites – risk assessments could not be finalised
  - Levels of pathogenic contaminants
  - Representativeness of tested batches

Trends in data sets for microbials - Ecotoxicology

- Following review of 35 EFSA peer reviews of microbial biopesticides (Collison & Hamer, SETAC, 2017)
  - 32 included 1+ ecotoxicology data gap, average of 5/substance
  - Some **acute toxicity** studies had an extended timescale to allow sufficient time to test for infectivity
  - Some acute tests justifiably waived based on negligible exposure, only if substantiated by *good data* on **background levels**
  - **Pathogenicity and infectivity** data gaps commonly identified, OECD guidelines not yet appropriate
  - Almost all had a data gap to consider potential **secondary metabolites/ toxins** requiring revised environmental risk assessment
  - Assessment of potential **transfer of genetic material** to other organisms an area of potential concern

Recurrent technical challenges – botanicals

- Characterisation of active substances as complex mixtures – footprint or lead compound approach?
- Requirement for repeat dose toxicity studies to set regulatory reference values for use in risk assessment
- Requests for new studies may be issued by reviewers late in the process – in the phase of great time constraints
- Measurement of component concentrations in aquatic toxicity data set
- Large volume of papers and corresponding high cost to comply with EFSA literature search guidance

3. Forthcoming changes

UK exit from the EU

- UK rapporteur work reallocated
- Ongoing work to complete by March 2019
- Will UK operate to a regulatory standard similar to the EU but with own peer review? Will this mean faster processes?
- Continued engagement with OECD may result in closer linkages with other countries
- UK CRD welcomes enquiries from applicants
- Defra consultation *'Health and Harmony: the future for food, farming and the environment in a Green Brexit'* features sustainable food production and the use of biopesticides – use the opportunity to comment by 8 May 2018

REFIT

- European Commission is carrying out a ‘REFIT’ evaluation of the EU pesticide legislation
- This is in order to assess if the regulations meet the needs of citizens, businesses and public institutions in an efficient manner
- IBMA and member companies have responded to the consultation

Acknowledgements

Thank you to the stakeholders who offered advice on key topics for this presentation and for all the ongoing work on developing the regulatory framework

Key links

- IBMA http://www.ibma-global.org/en/home
- OECD biopesticides group http://www.oecd.org/chemicalsafety/pesticides-biocides/biological-pesticides.htm
- EU Commission https://ec.europa.eu/food/plant/pesticides_en
- EFSA https://www.efsa.europa.eu/en/applications/pesticides
- UK CRD http://www.hse.gov.uk/pesticides/
- 3rd Global Minor Use Summit www.gmup.org
- EPPO (https://pp1.eppo.int/standards/PP1-296-1)
- Defra consultation https://www.gov.uk/government/consultations/the-future-for-food-farming-and-the-environment

Thank you for your attention

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natural technology

Regulatory impact upon the biocontrol market development

Juan Manuel López, Chief Marketing Officer

Annual Biocontrol Industry Meeting

March 7th, 2018

bpia 2018 Spring Meeting & International Symposium

Biopesticides registration: initial questions

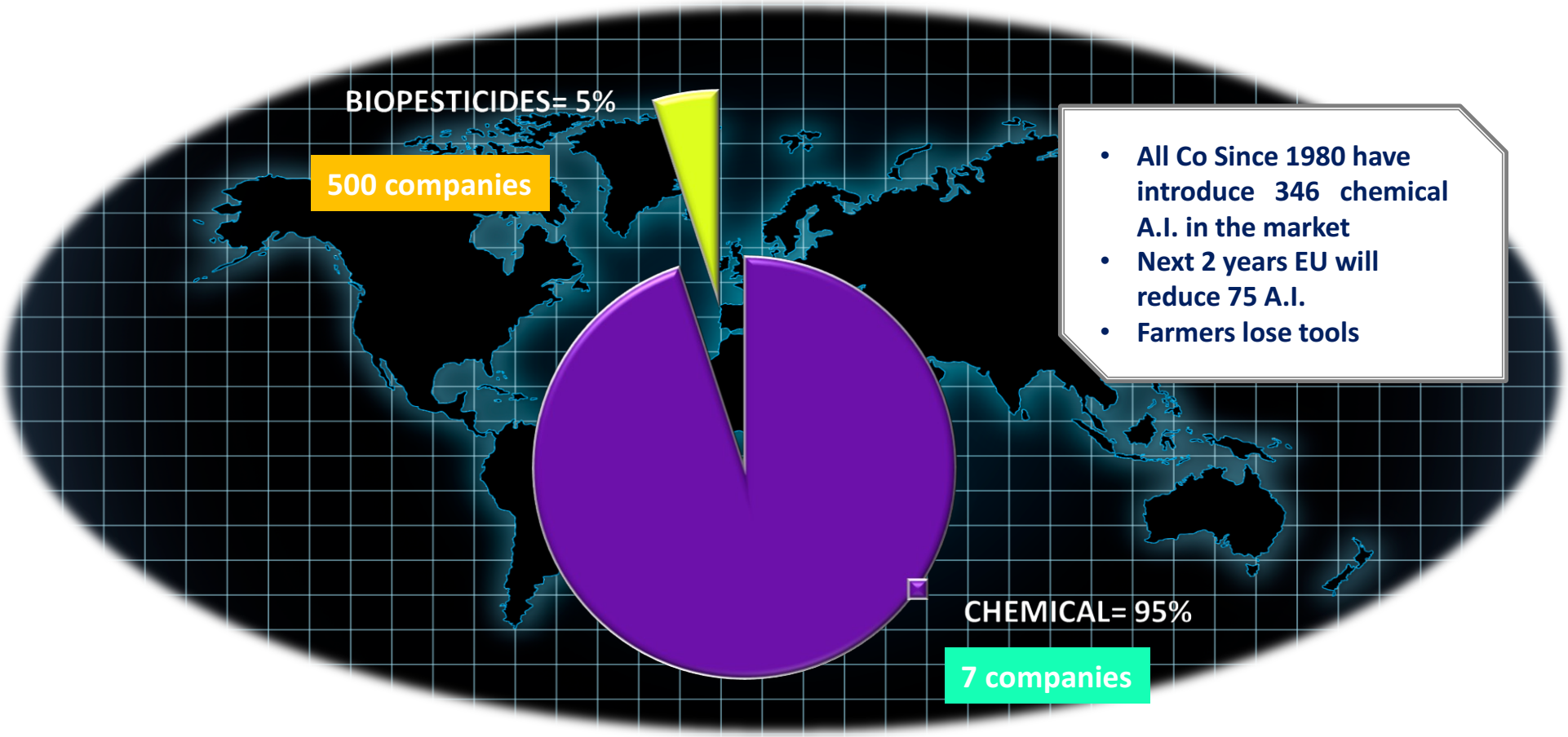
Is this a strategic decision for a medium-size company ?

Does it really worth? It is profitable?

Are all requirements **really needed?**

How much money the investment represent? When will we obtain that ROI?

Global Crop Protection Market Share: 2017



- All Co Since 1980 have introduce 346 chemical A.I. in the market
- Next 2 years EU will reduce 75 A.I.
- Farmers lose tools

Few years ago, a local registration process was enough for commercial purposes…

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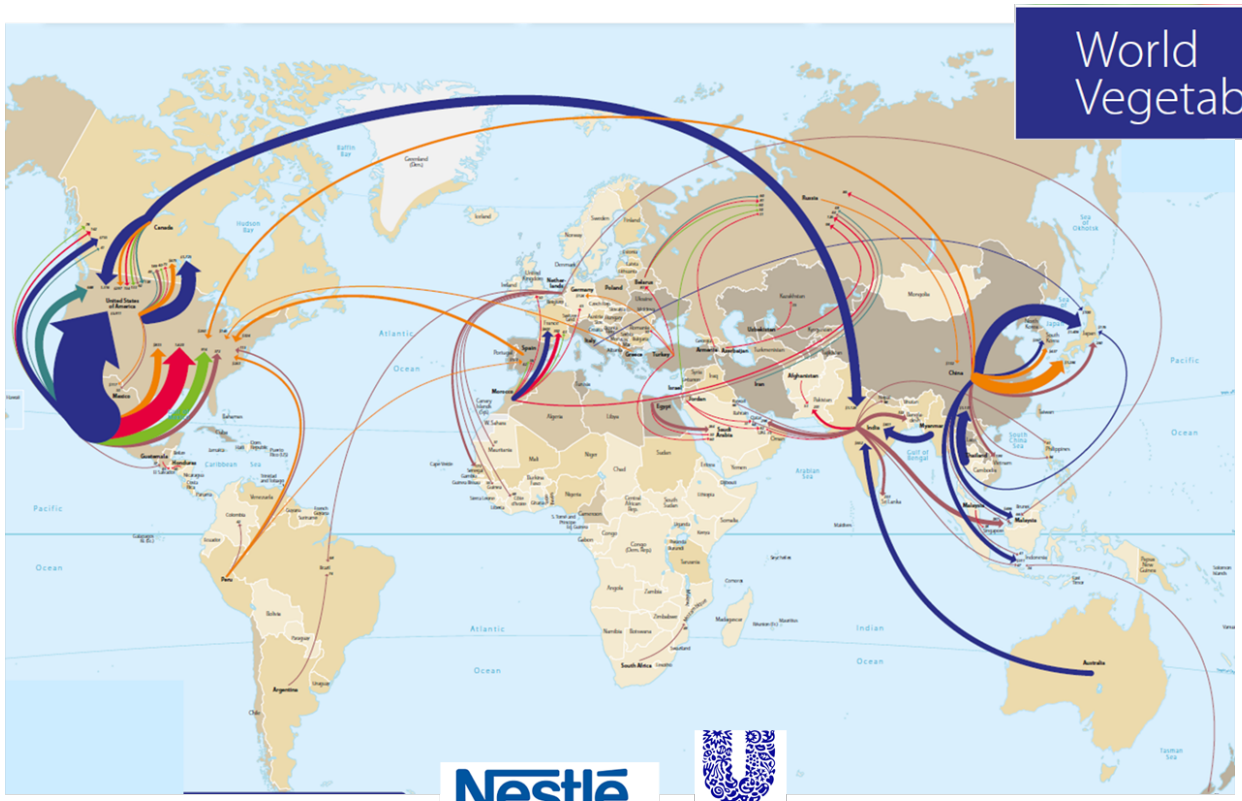
…but today, global customers imply global players and rules



15 years ago, Seipasa began the registration process

What does this process mean?

- **5 years** to obtain and formulate the quality a.i. for a global market.
- **+ 3 to 5 years** to develop dossiers and submit the register application by zone or country.
- **+ 2 to 3 years** to obtain the final registration and the final label to be approved.
- **+ 2 years** to introduce the product in the market.

12 – 15 years of investment to start getting profits

Barriers to beat

High cost of data and absolutely unpredictable

Unknown and inappropriate data requirements

Unreasonable delays

Lack of knowledge within the biocontrol industry.

High registration costs

Lack of experience in biocontrol registration

Seipasa decided to registrate plant protection products

Value investment

- **5 y** obtain and formulate the quality a.i. for a global market. **6 $M**
- **+ 3 to** to develop dossiers and submit the register application by zone or country. **3 $M***
- **+ 2 to** to obtain the final registration and the final label to be app ed. **1 $M***
- **+ 2 years** ntroduce the product in the market. **1,2 $M**

11,2 $M

* Extra cost that increase final price to products in the market

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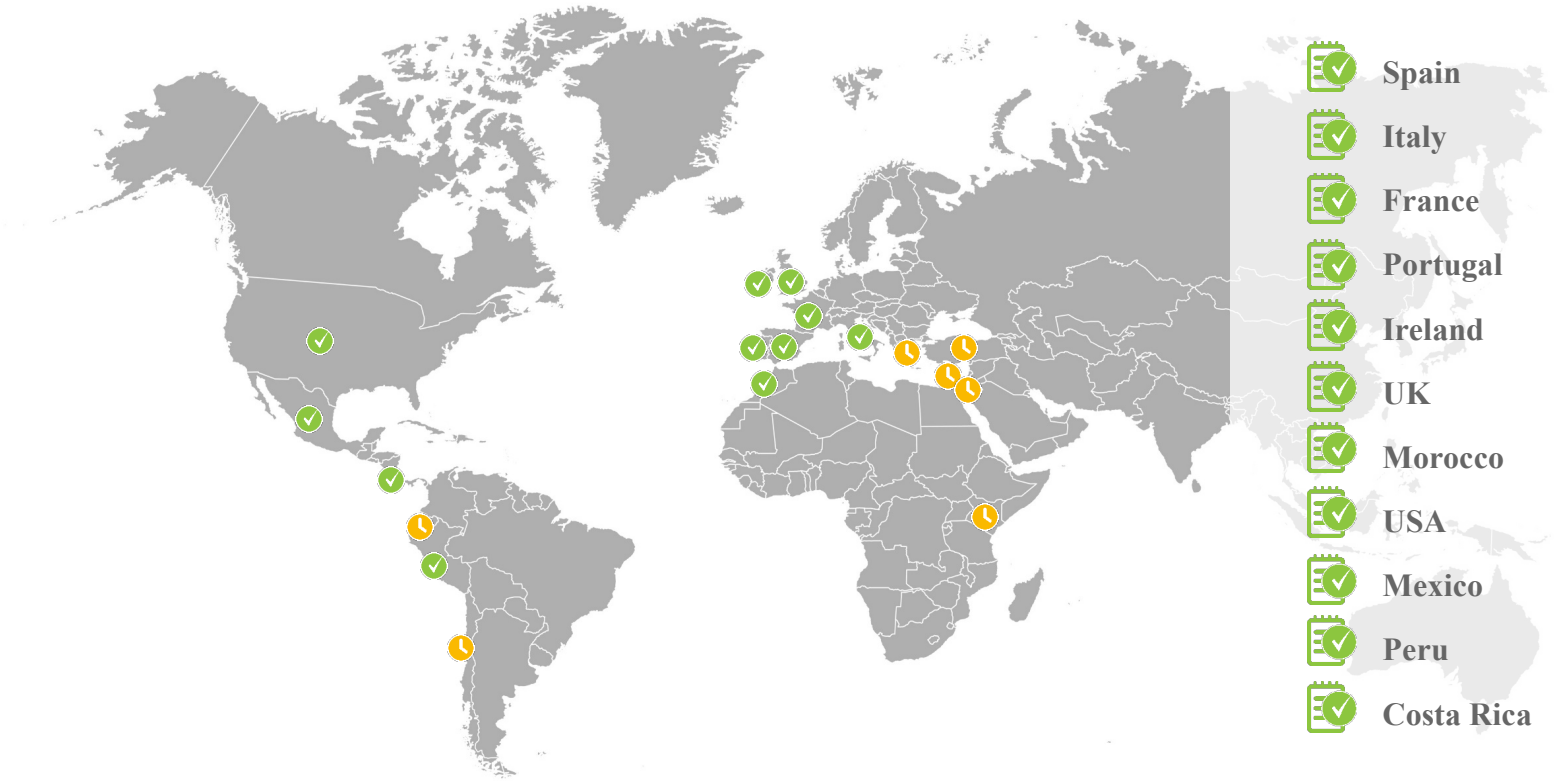
You can sum up Seipasa's global update regulatory status

Each market with different registration products and rules



Registered

- Spain
- Italy
- France
- Portugal
- Ireland
- UK
- Morocco
- USA
- Mexico
- Peru
- Costa Rica

On Process

- Turkey
- Greece
- Cyprus
- Kenya
- Israel
- Chile
- Ecuador

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Is a registration strategy profitable for a medium size company like Seipasa?

Definitely !!!!

1
Registration

=

12 %
Upon
Annual Gross Margin

BIOPESTICIDES: Open regulatory questions

Assumption: Everybody (Governments, markets, green thinkers…) is demanding biopesticides to be developed

SHOULD biopesticides have different requirements and timing in front of chemicals?

For those who are global agricultural players: Could be possible to achieve a SINGLE GLOBAL registration rule ?

If the INTEREST of these of global agricultural players is the same, why not participating in that process from a global perspective?

BIOPESTICIDES: Open regulatory questions

Assumption: Everybody (Governments, markets, green thinkers…) is demanding biopesticides to be developed

COULD THAT SINGLE GLOBAL INTEREST BE PREVAILING ?

Should you want to say YES, We do !!!

Thank you

Juan Manuel López
CMO
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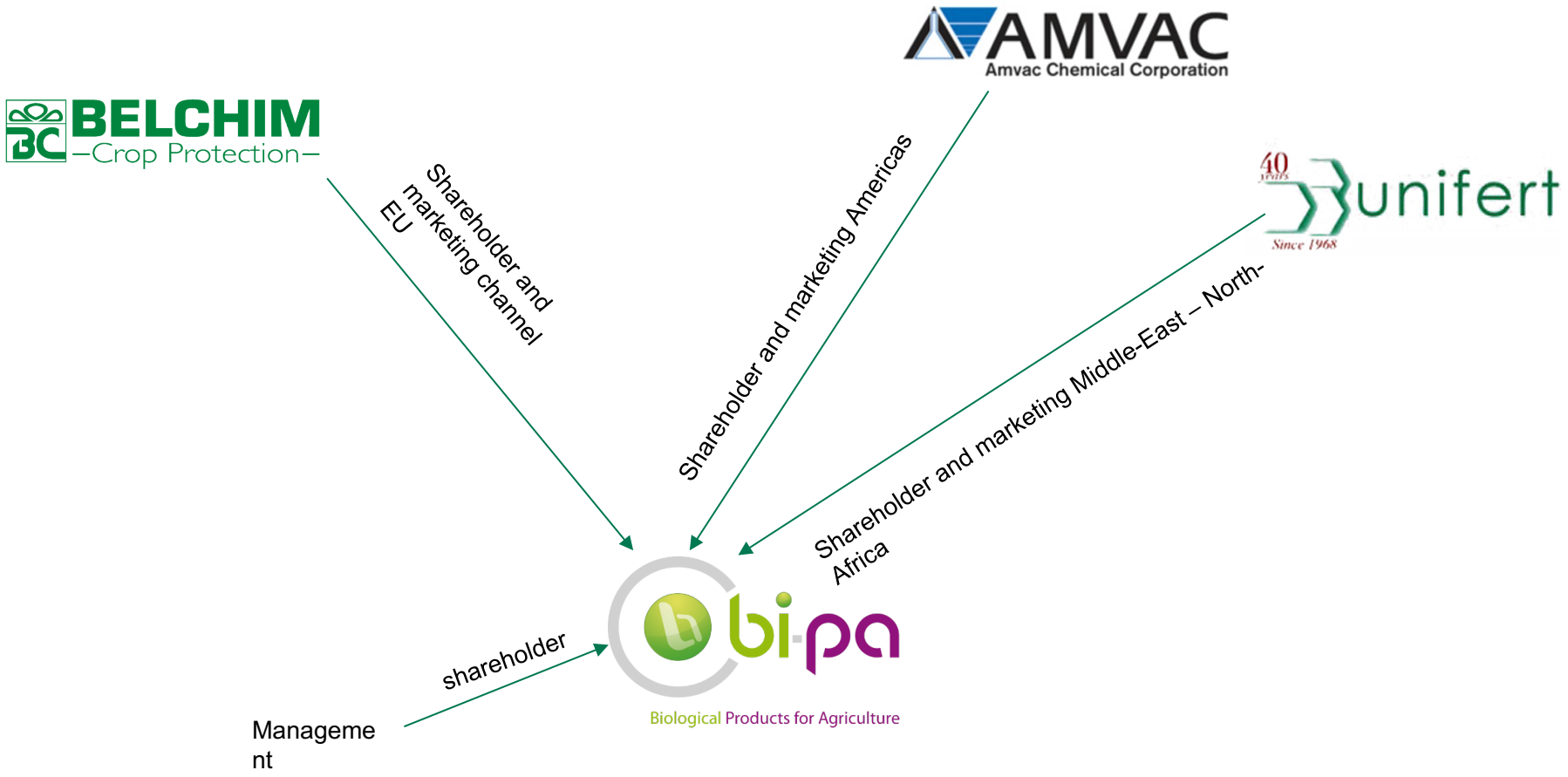
What is the impact of registration on early development and scouting?

Sandro frati

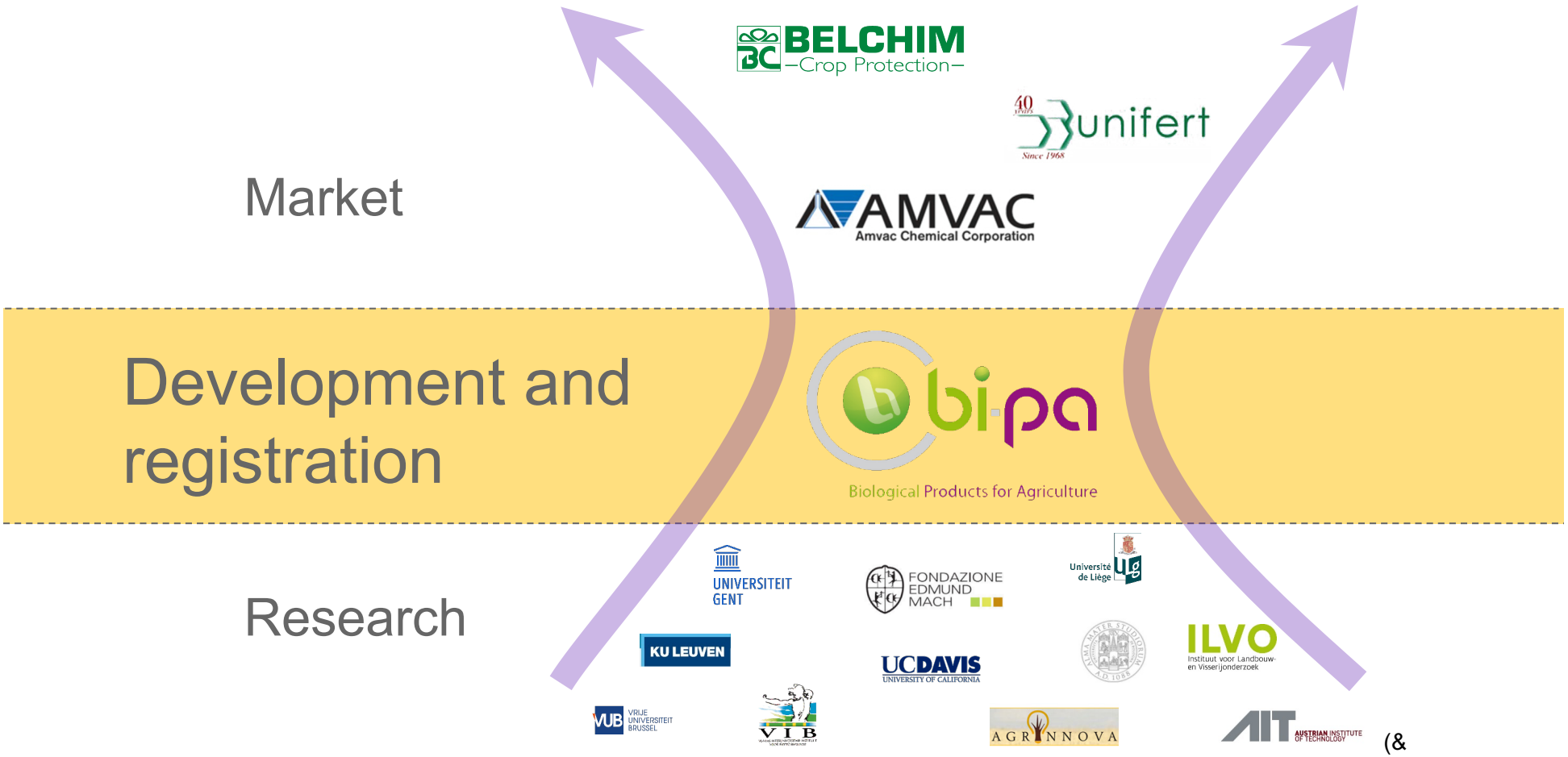
BIPA, BIOLOGICAL PRODUCTS FOR AGRICULTURE

Located in central Belgium
Focusing on development and registration of active ingredients of biological origin

OUR MARKET CHANNELS



BI-PA INTEGRATES ALL LEVELS OF THE DEVELOPMENT



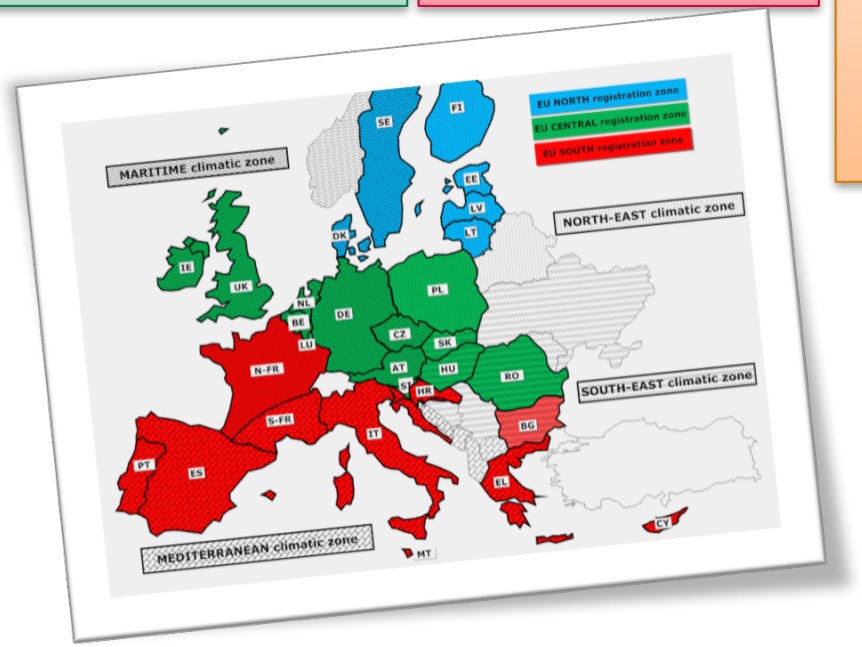
REGISTRATION IN EU, A COMPLICATED MATTER

Plant Protection Product

- Active substance
- Co-formulants

Annex III dossier

Annex II dossier

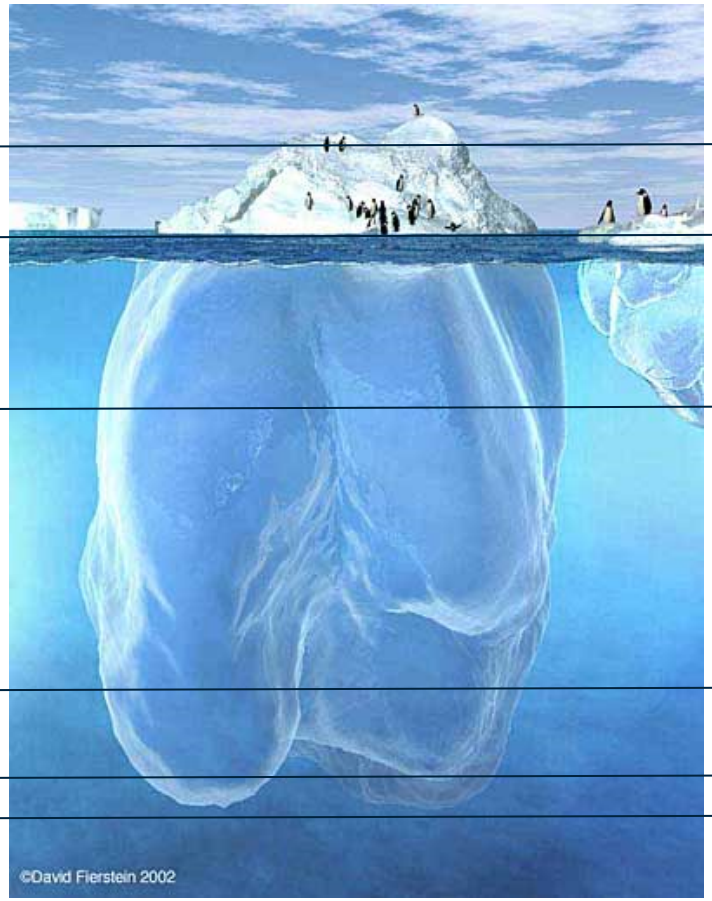


Annex II dossier:

1. Identity of the Active Substance
2. Physical and Chemical Properties of the Active Substance
3. Further Information on the Active Substance (Function, Mode of Action, Handling
4. Analytical Methods and Validation
5. Toxicological and Toxicokinetic Studies on the Active Substance
6. Metabolism and Residues Data
7. Fate and Behaviour in the Environment
8. Ecotoxicological Studies on the Active Substance
9. Proposal labelling and classification

Annex III dossier:

1. Physical, Chemical and Technical Properties of the Plant Protection
2. Product identity of the Plant Protection Product
3. Data on Application
4. Further Information on the Plant Protection Product
5. Methods of Analysis
6. Efficacy Data and Information (including Value Data) EC: IIIA 6.0 Efficacy data
7. Toxicological studies
8. Metabolism and Residues Data
9. Fate and Behaviour in the Environment
10. Ecotoxicological Studies on the Plant Protection Product
11. Further information



Δ_4 Maintenanc e

$\Delta_{3.n}$ Datacalls

Δ_3 4. Registration

3.0 Submission

3.-n Submission preparation

$\Delta_{2.n}$

2. Dossier building

$\Delta_{2.1}$

1. Start-up

Δ_1 0.0 Go/No G

Δ_0 0. PrePjt Phase

Time consuming process

Always think **registration** in every step

INTERACTION ACADEMIA – INDUSTRY – MARKET

Different institutional missions: academia is strong in discovery, science and generating knowledge

- Is the knowledge – the invention – commercially valuable? → market?
- Production and supply chain
- **Regulatory feasibility**

Registration is one of the first selection criteria in scouting

STEPWISE SCOUTING APPROACH

By considering:

- ✓ Strategic aspects
- ✓ Market analysis
- ✓ Product, biology and technology
- ✓ Financial aspects
- ✓ Safety, health and environment = **registrability**
- ✓ Marketing, commercialization and distribution

DEVELOPMENT PROCESS

Identification
- At strain level
- Effective (pathogens)

IP protection
- Patent
- Confidentialily

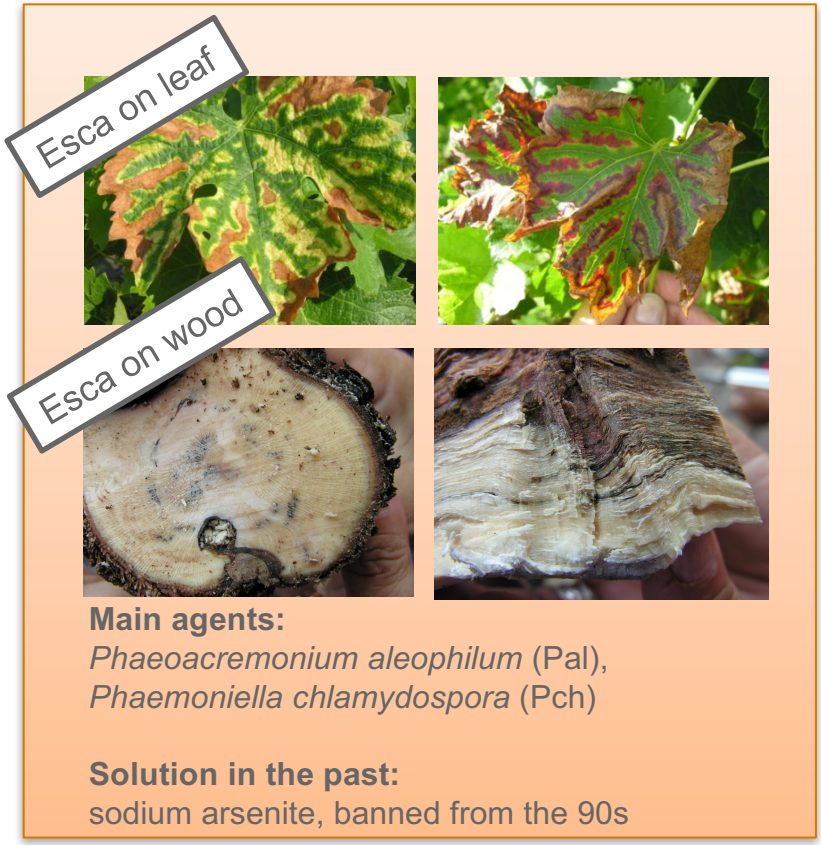
Formulation
- Shelf-life
- Increase field efficacy

Production
- Industrial scale-up
- Reducing cost of production

Registration
- Tox, ecotox, e-fate,…
- Efficacy

Market
- Integration in IPM
- Label extension

'RICHODERMA ATROVIRIDE SC1, A CASE STUDY



Main agents:
Phaeoacremonium aleophilum (Pal),
Phaemoniella chlamydospora (Pch)

Solution in the past:
sodium arsenite, banned from the 90s

- ✓ Patented strain by Fondazione Edmund Mach (Italy)
- ✓ Isolated from decayed hazelnut wood
- ✓ Very good wood colonizer
- ✓ Initial screening: interesting efficacy against several pathogens
- ✓ Data cross checking on priorities in terms of pest control (the market)
- ✓ **Registrability was ok**
- ✓ No solutions against Esca on grape
- ✓ *T.atroviride* SC1 vs. Esca = **a good match!**

Vintec

Vintec

Registration status:
✓EU: 2017 and ongoing
✓USA: in preparation

Vintec is a biocontrol agent against the main wood diseases in vine

- ✓ **Uses :** ESCA/BDA and Eutypa
- ✓ **Application: nursery + vineyard** after pruning, directly on the pruning wounds


THANK YOU!
Feel free to contact us anytime!
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