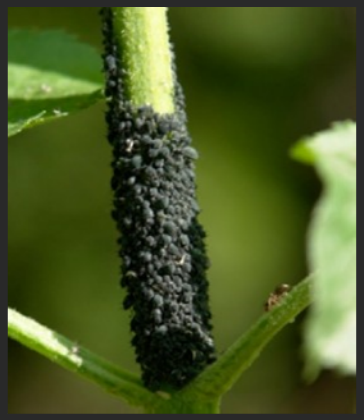
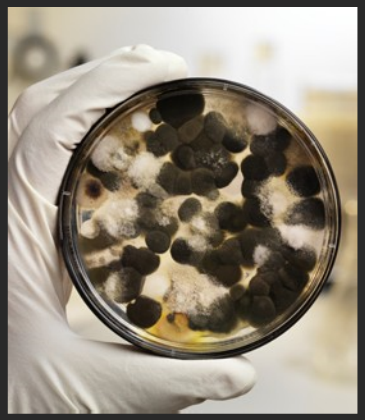
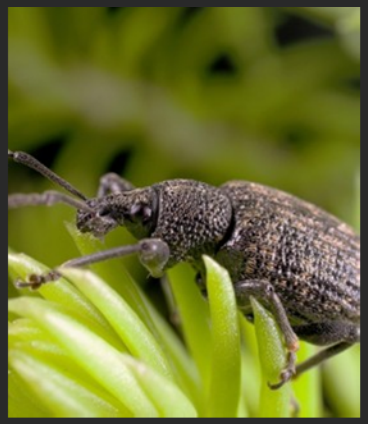





Biopesticides and development in new products

www.biorationale.co.uk

RATIONALE
BIOPESTICIDE STRATEGISTS

rgwynn@biorationale.co.uk

crops

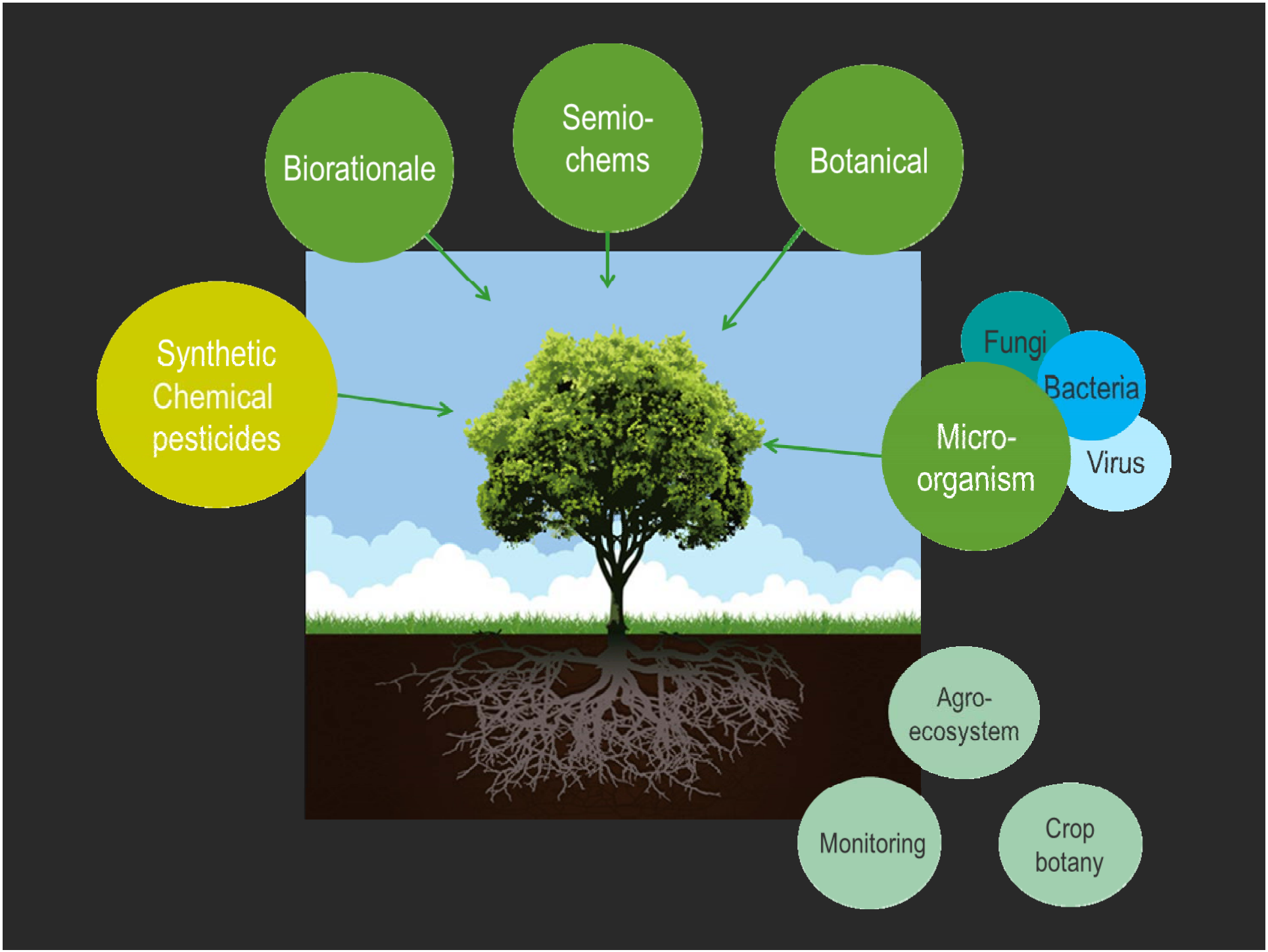
30 – 40 %
lost
before harvest

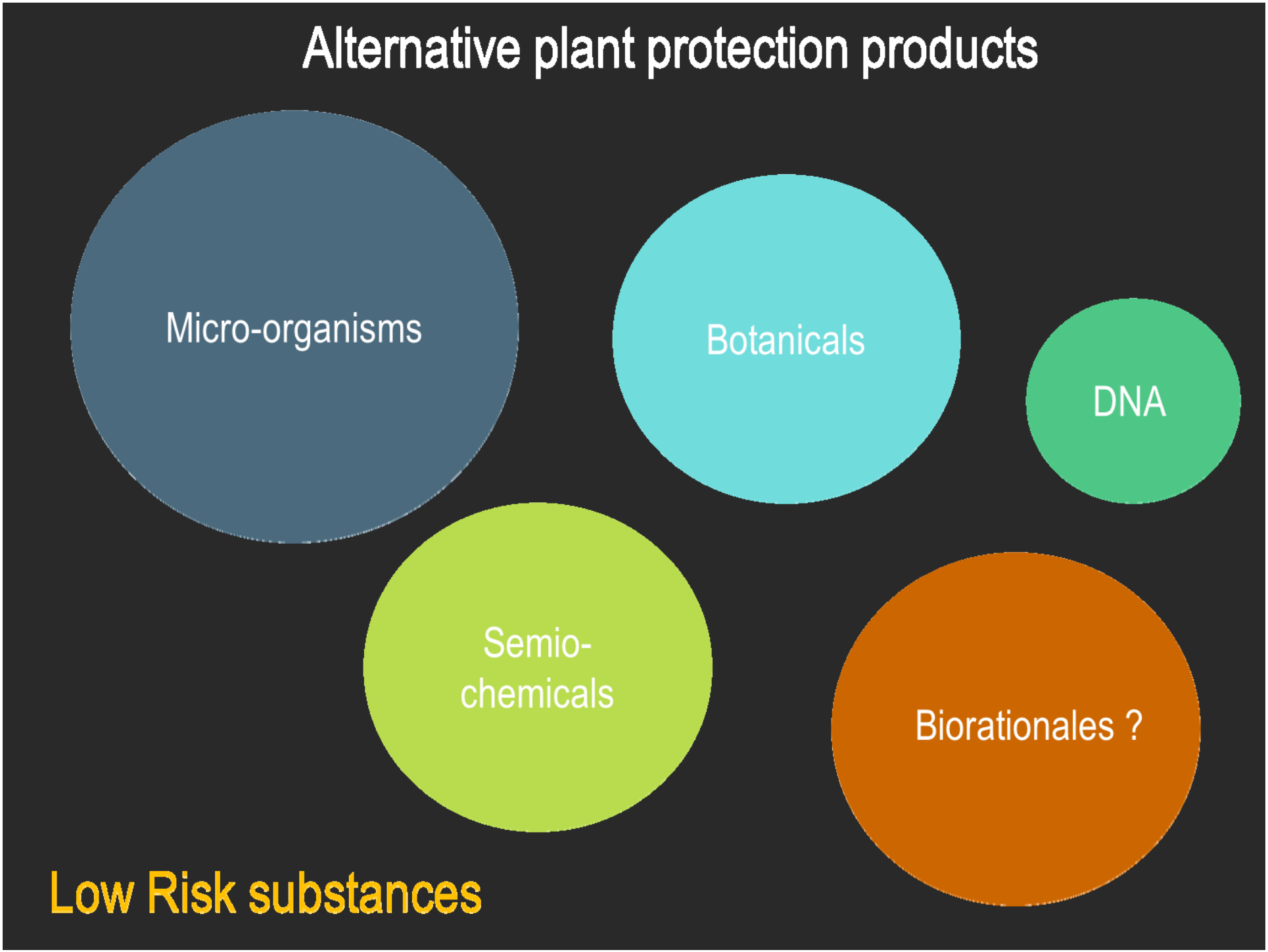
>10 %
after harvest

Food and Agriculture Organisation of the United Nations

FAO promotes biological pest control agents and IPM/IVM

“Pro-actively favouring registration of less hazardous products where such alternatives are viable and available”


Biorationale
Semio-chems
Botanical
Synthetic Chemical pesticides
Fungi
Bacteria
Virus
Micro-organism
Agro-ecosystem
Monitoring
Crop botany


Alternative plant protection products
Micro-organisms
Botanicals
DNA
Semio-
chemicals
Biorationales ?
Low Risk substances

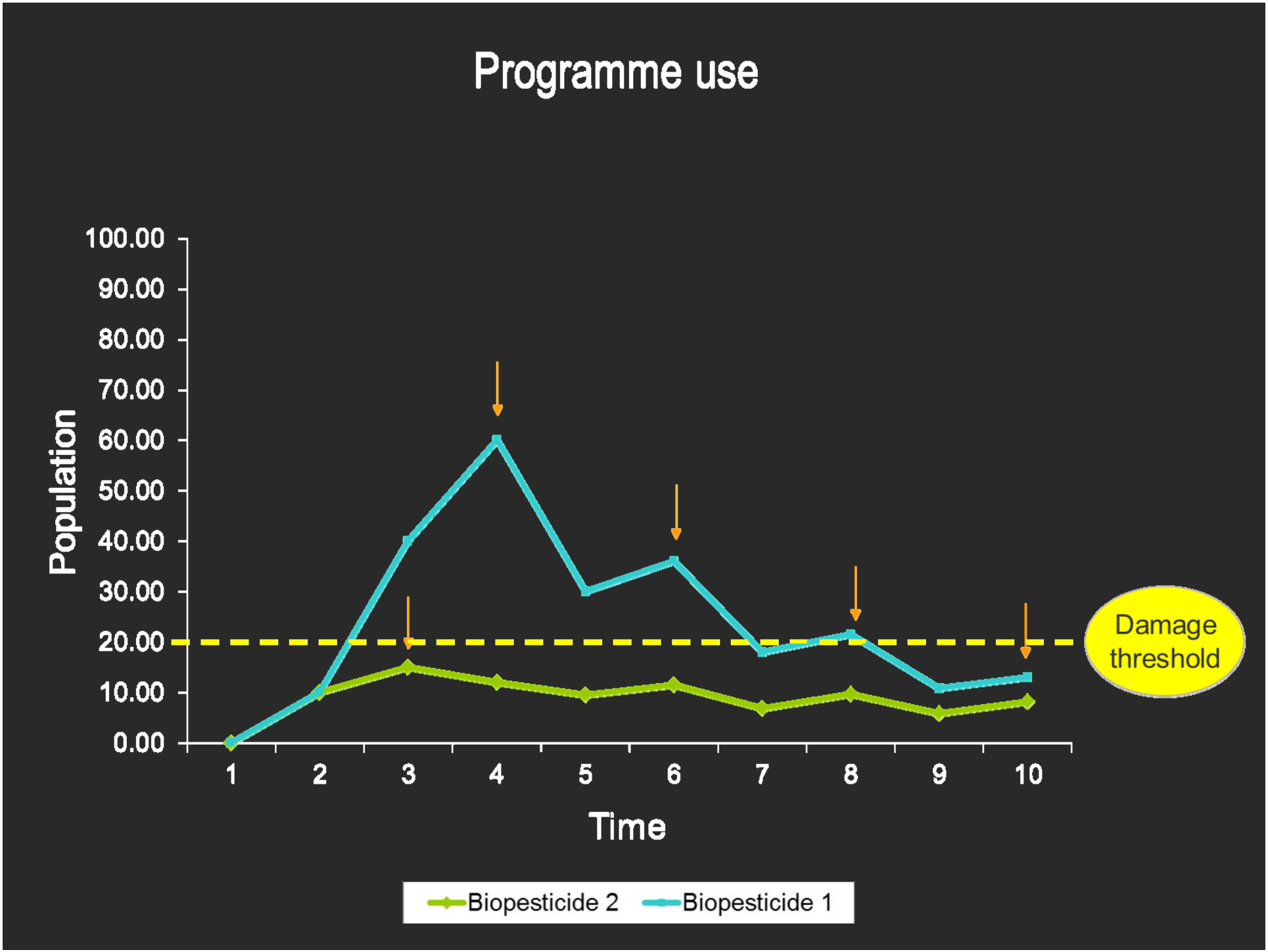
Multiple modes of action

Kill host

Competition

Stimulate plant defenses

Confer plant resistance


Programme use
Population
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
1
2
3
4
5
6
7
8
9
10
Time
Damage threshold
Biopesticide 2
Biopesticide 1

What is driving the markets

Who wants the products?

Why?

What do the products offer?

DRIVERS for farmers and growers

- Efficacy – killing target pest
- Efficacy - yield and quality improvement
- Host specificity
- Use in IPM programmes
- Useful for resistance management
- Useful for residue management
- Growers - crop management
- Worker safety
- Favourable environmental footprint
- Use in organic production

Natural forces already manage pest populations

1 cabbage aphid + 1 year = 250 million tonnes

Information and photo: courtesy of D. Chandler, Warwick Crop Centre and eplantswholesale.com.au respectively

Sustainable crop production and protection

Biology
Ecology
Population management

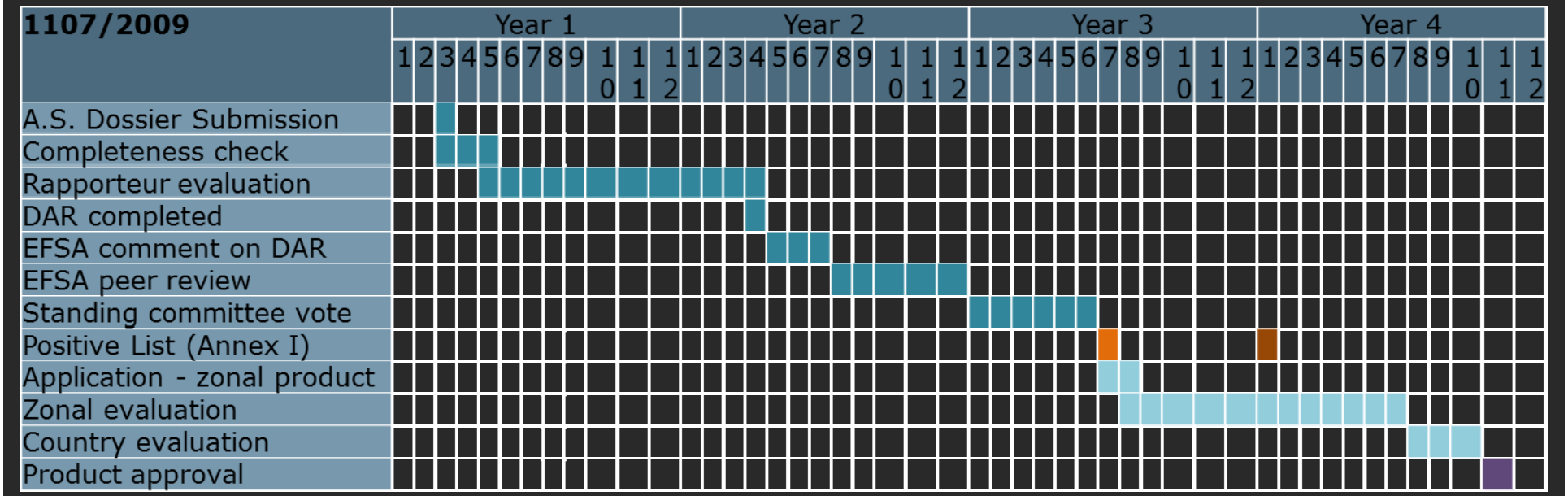
Macroorganisms

Botanicals

Semio-chemicals

Microorganisms

Plant Protection Product Registration EU - timelines



- Orange boxes indicate first the SANTE vote then it takes 6 months to be ratified
- Purple box indicates when product can be sold

- This is a broad schematic – there can be some variability depending on a.s.
- There can be some extra time added e.g. during active substance review if an expert consultation if needed

Aspects of risk

EU

Precautionary principle

USA

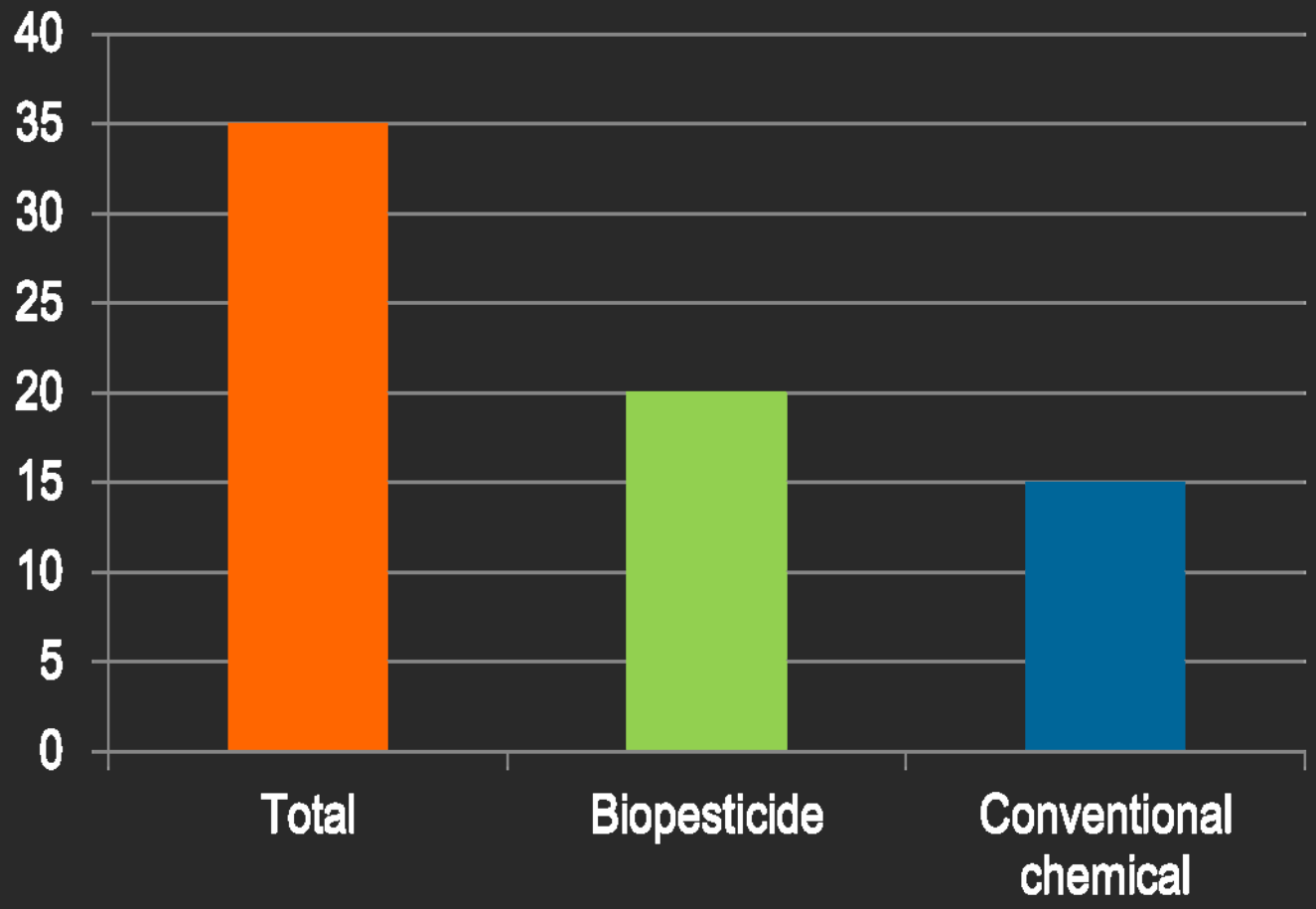
Generally Regarded As Safe (GRAS)*

EU biopesticide actives trebled to >120

2000-2015

BIOPESTICIDES

EU plant protection products – pending registration*



* October 2016

Global biopesticide market Increased over

200%

2000-2012

BIOPESTICIDES

Global market 2019

value

over

$6 billion

Increase

Examples of nematode based 'biopesticide' products

Active Substance	Product Name	Type of product	Target(s)
Steinernema feltiae	Nemasys	Entompathogenic nematode	Sciarids, leafminer, WFT
Steinernema kraussei	Nemasys L	Entompathogenic nematode	Vine weevil
Heterorhabditis megidis	Nemasys H	Entompathogenic nematode	Vine weevil
Heterorhabditis megidis	Lavanem	Entompathogenic nematode	Vine weevil
Heterorhabditis megidis	Nemasys H	Entompathogenic nematode	Grubs
Steinernema carpocasae	Nemasys C	Entompathogenic nematode	Codling moth
Steinernema carpocasae	Nemasys C	Entompathogenic nematode	*Hylobius* sp., Lepidoptera
Steinernema carpocapsae	Capsanem	Entompathogenic nematode	Lepidoptera
Phasmarhabditis hermaphrodita	Nemaslug	Slug parasitic nematode	Molluscs

Micro-organism biopesticides

Cydia pomonella granulosis virus

Pasteuria penetrans

Trichoderma harzianum

FUSARIUM OXYSPORUM

Isaria fumosoroseus

Bacillus firmus

Clonostachys rosea

Coniothyrium minitans

BACILLUS THURINGIENSIS

Bacillus subtilis

Gliocladium catenulatum

Lecanicillium lecanii

Metarhizium anisopliae

Ampelomyces quisqualis

Trichoderma asperellum

Beauveria bassiana

Microorganism bioinsecticides/nematicides examples

Active Substance	Product Name	Target(s)
Adoxophyes orana gv	Capex	Summer fruit tortrix
Bacillus firmis strain I-1582	Flocter	Free-living nematodes
Bacillus thuringiensis var. *israelensis* strain AM65-52	Vectobac 12AS	Chironomid larvae
Bacillus thuringiensis var *kurstaki* strain ABST351	DiPel DF	Lepidoptera pests
Bacillus thuringiensis var *kurstaki* strain EG2348	Lepinox Plus	Lepidoptera pests
Beauveria bassiana strain ATCC74040	Naturalis-L	Whitefly, thrips, spidermite
Cydia pomonella Granulosis Virus	Carpovirusine	Codling moth
Cydia pomonella Granulosis Virus	Cyd-X and Cyd-X Extra	Codling moth
Lecanicillium muscarium strain V-6*	Mycotal	Whitefly, thrips, scale
Metarhizium anisopliae strain F52	Met 52 Granular	Black vine weevil

What are botanicals?

From the EU Botanical Guidance document (rev. 8)

A 'botanical' active substance: obtained by subjecting plants or parts of plants to a process such as pressing, milling, crushing, distillation and/or extractions. The process may include further concentration, purification and/or blending, provided that the chemical nature of the components is not intentionally modified/altered by chemical and/or microbial processes.

The plants are live or dried plants or parts of plants, including fruits and seeds but excluding genetically modified plants.

Botanicals examples

Active Substance	Product Name	Type of product	Target(s)
Maltodextrin	Eradicoat	Biorational	Mites, aphids, whitefly
Maltodextrin	Majestik	Biorational	Mites, aphids, whitefly
Fatty Acids	Savona	Fatty Acids	Whitefly, thrips, mite, aphids
Garlic concentrate	Eagle Green Care	Botanical	Free living nematodes
Cold pressed orange oil	Prev-AM	Botanical	Insects & fungi

Pheromones - semio-chemicals

Semio-chemicals "… chemicals emitted by plants, animals, and other organisms - and synthetic analogues of such substances - that evoke a behavioural or physiological response in individuals of the same or other species"

Pheromones are semio-chemicals that modify the behaviour of other individuals of the same species

Straight-chained lepidopteran pheromones (SCLPs) … unbranched aliphatics having a chain of 9-18 carbons, containing < 3 double bonds, ending in an alcohol, acetate or aldehyde functional group. This structural definition encompasses the majority of known pheromones produced by insects in the order Lepidoptera, which includes butterflies and moths.

Control strategies using semio-chemicals

Mating disruption

- Pheromones are released to interfere with the ability of male insects to locate females of the same species,
- Disrupting mating and controlling the damage to crops inflicted by the hatching larvae.

Lure and Kill

- Again a simple concept: bring the insects to the insecticide
- Key is to attract females

Mass Trapping

- Simple Concept: trap as many insects as you can
- Key is to attract and trap females
- Kairomones becoming increasingly important

Technology innovation areas

Active substances

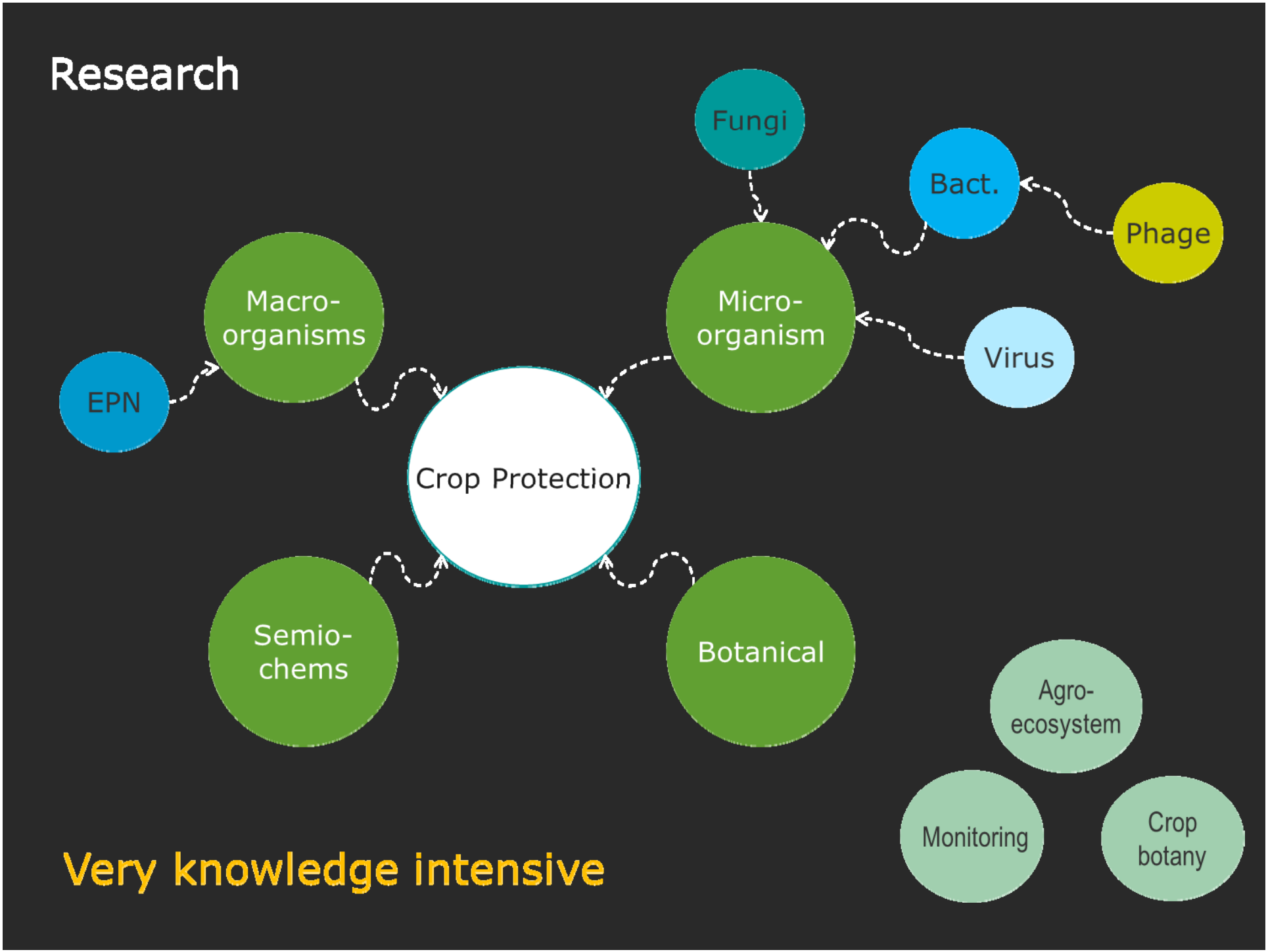
Production

Formulations

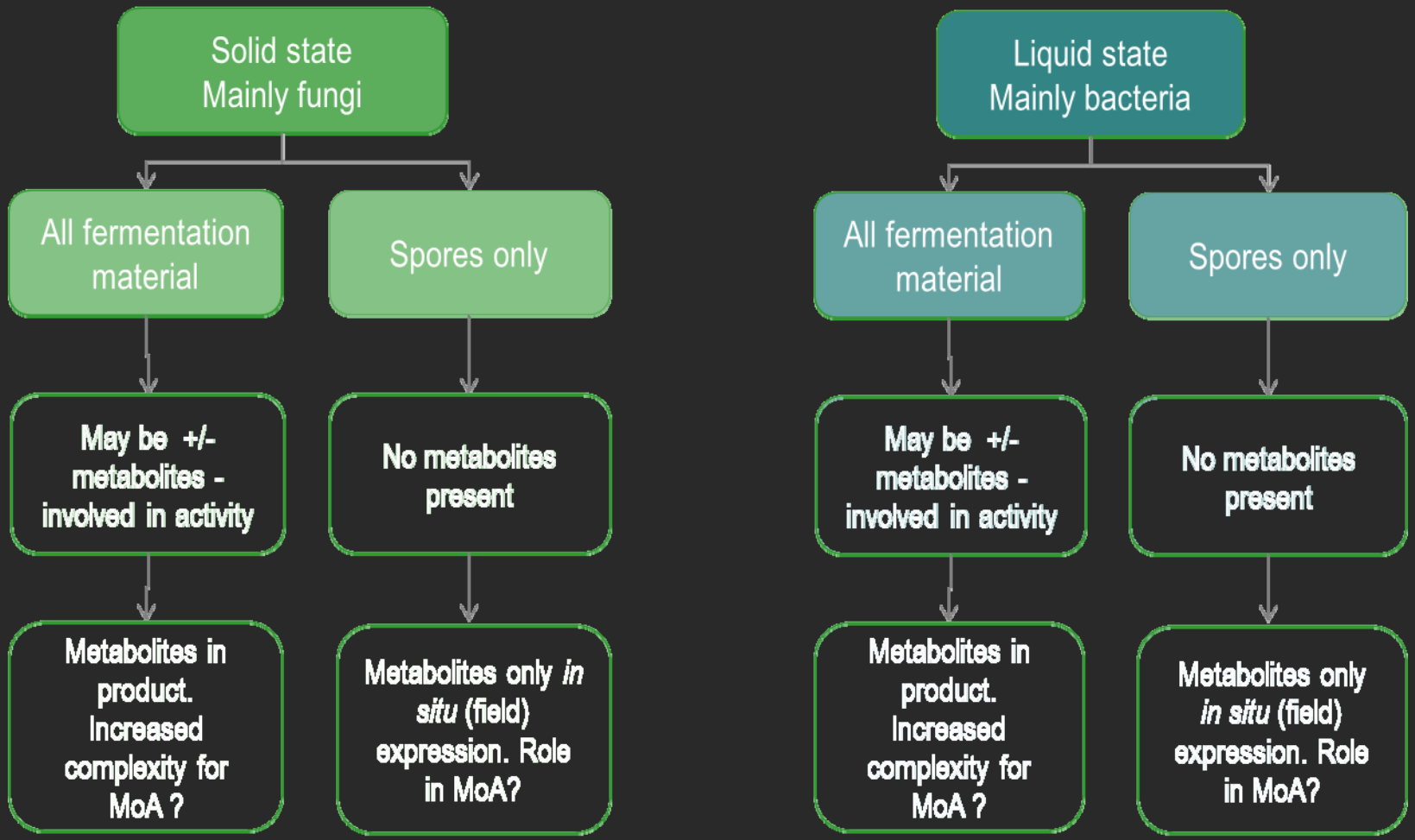
Delivery

Activity	$ Millions
Research and Development	3 - 5
Formulation	1 - 2
Development	2-3 (USA) 20 - 30 (ROW)
Registration	1 (USA) 3 - 10 (ROW)
Product launch	0.1 - 20 (over > 50 global)

EU registration – about 5 years


Research
Fungi
Bact.
Phage
Macro-
organisms
Micro-
organism
Virus
EPN
Crop Protection
Semio-
chems
Botanical
Agro-
ecosystem
Monitoring
Crop
botany
Very knowledge intensive

Microbial production systems



In vivo production

Microbial innovations

	Cells	Media	Secondary compounds
Common species	±	±	±
Product formulation - inert	±	±	±
New species	±	±	±
New MoA - endophytes	±	±	±
Split fermentation - solid	±	±	±
Split fermentation - solid + liquid	±	±	±
Split fermentation - liquid + liquid	±	±	±
Product formulation - storage	±	±	±
Product formulation - persistence on leaf	±	±	±
Product formulation - synergists	±	±	±
Co-packs - adjuvants	±	±	±
Additives	±	±	±

Technical features of active substances	$ Millions
No/low risk, no metabolites	1 - 5
Low risk + metabolite	> 5
Microbial metabolite (no micro-organism)	5-10
High risk metabolite (no micro-organism)	15-20

Biopeticide delivery

Improved delivery systems (formulation, application, *etc.*) will not save an underperforming biopesticide but...

...performance of a biopesticide, as with a chemical pesticide, may be reduced substantially by a poor delivery system.

- Tank agitation is important.
- Nozzle choice and calibration
- Nozzle wear
- Tank and sprayline cleaning...

Information courtesy of Andrew Chapple

Business innovation areas

Biocontrol producers and distributors

Knowledge transfer

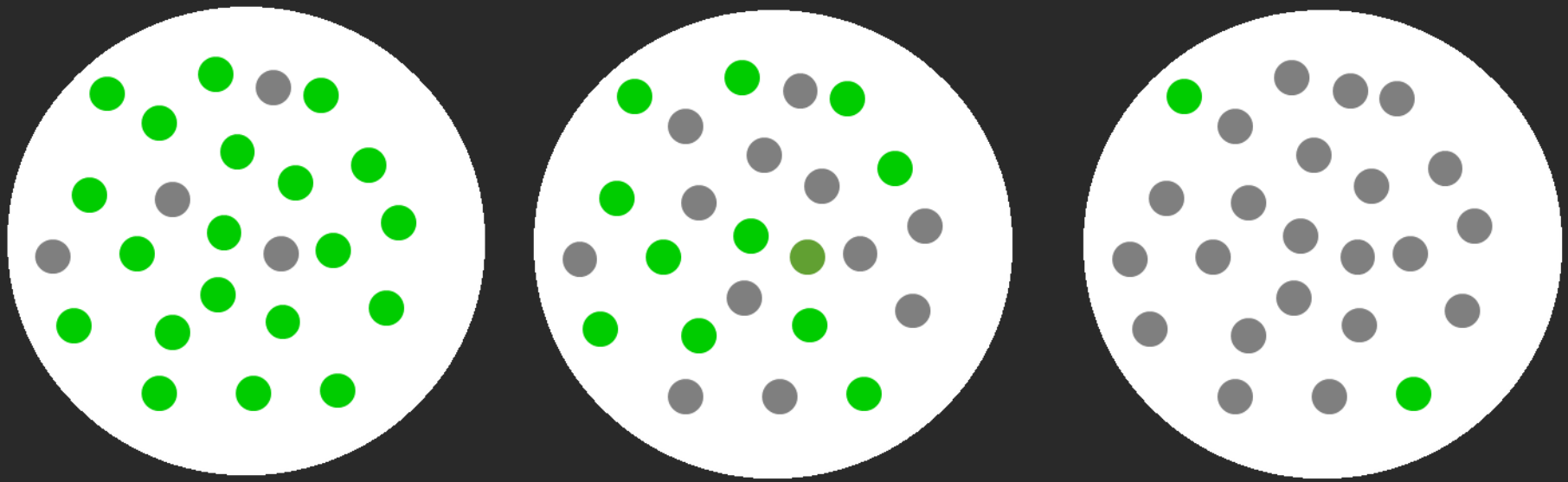
Streamlined regulation

Biopesticide industries – smarter approaches?

Start-up

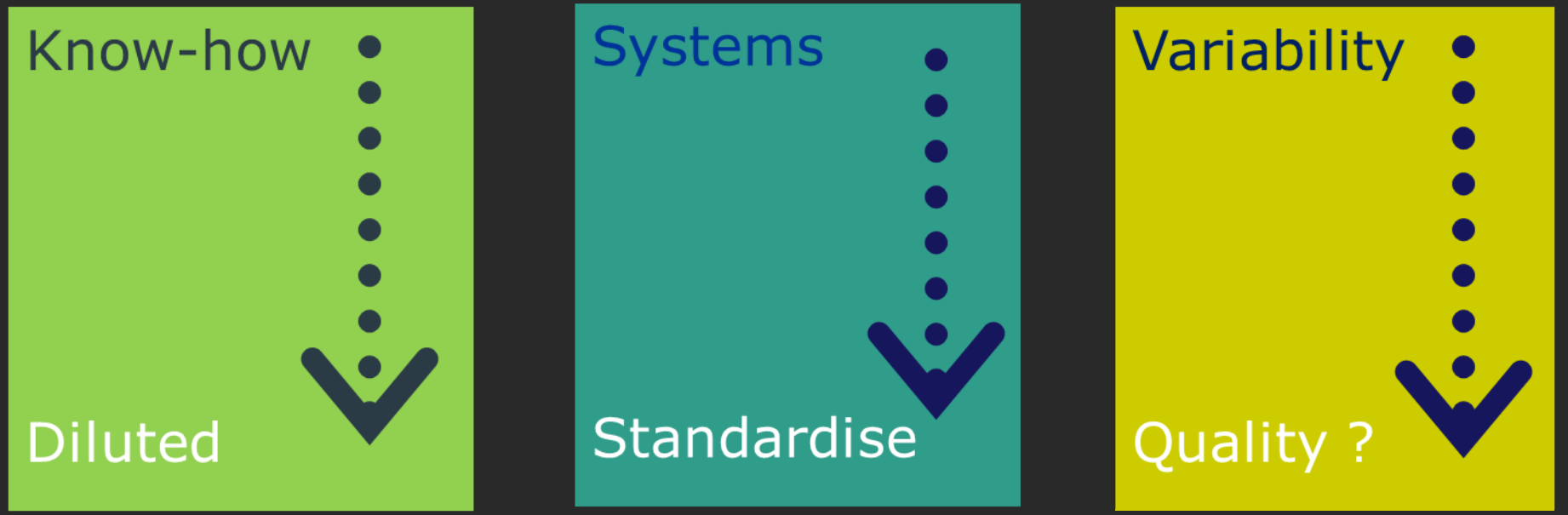
SME

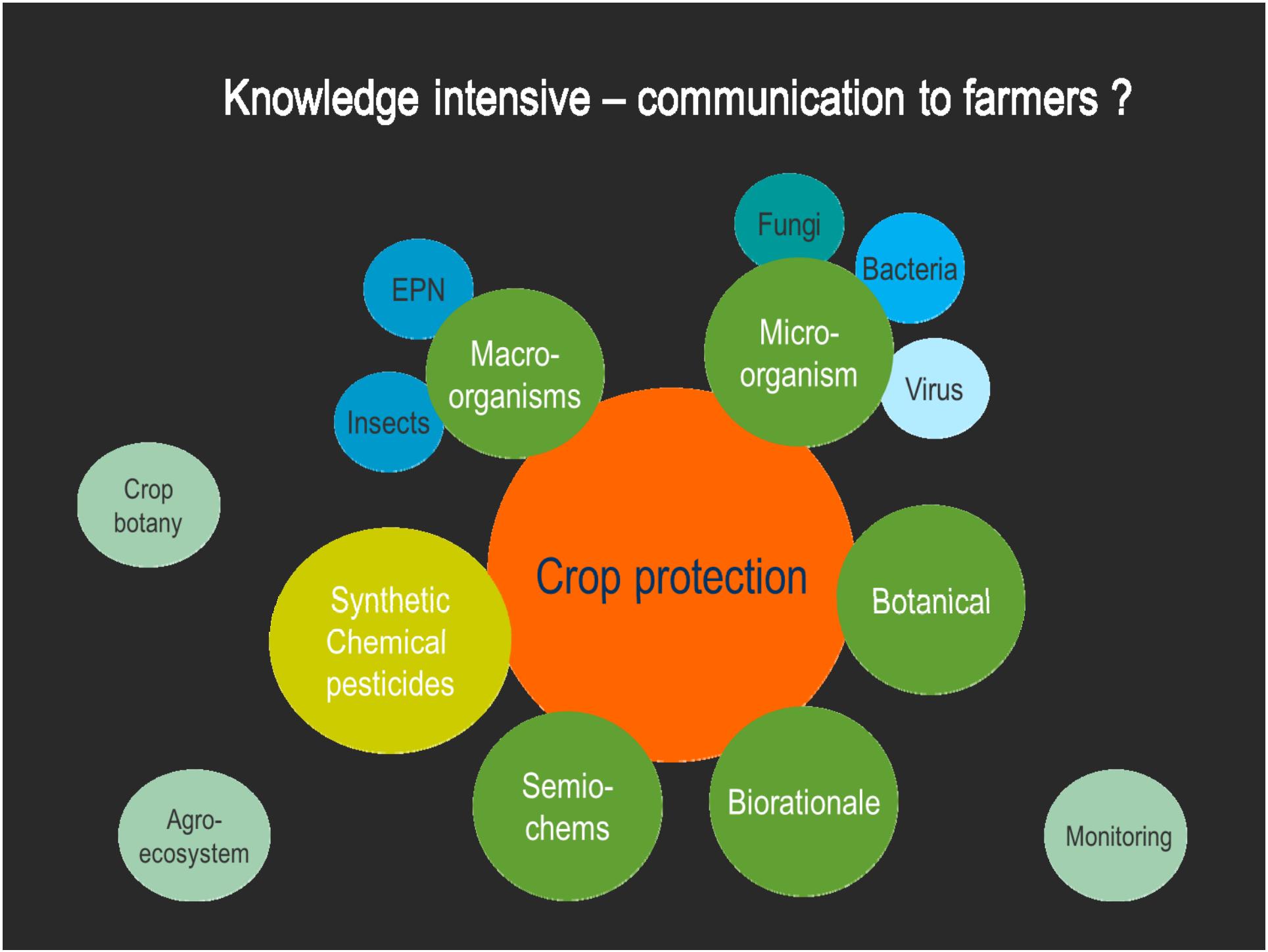
Multi-national



Very knowledge intensive

Consequences?




Knowledge intensive – communication to farmers ?
Fungi
Bacteria
EPN
Macro-
organisms
Micro-
organism
Virus
Insects
Crop
botany
Crop protection
Synthetic
Chemical
pesticides
Botanical
Semio-
chems
Biorationale
Agro-
ecosystem
Monitoring

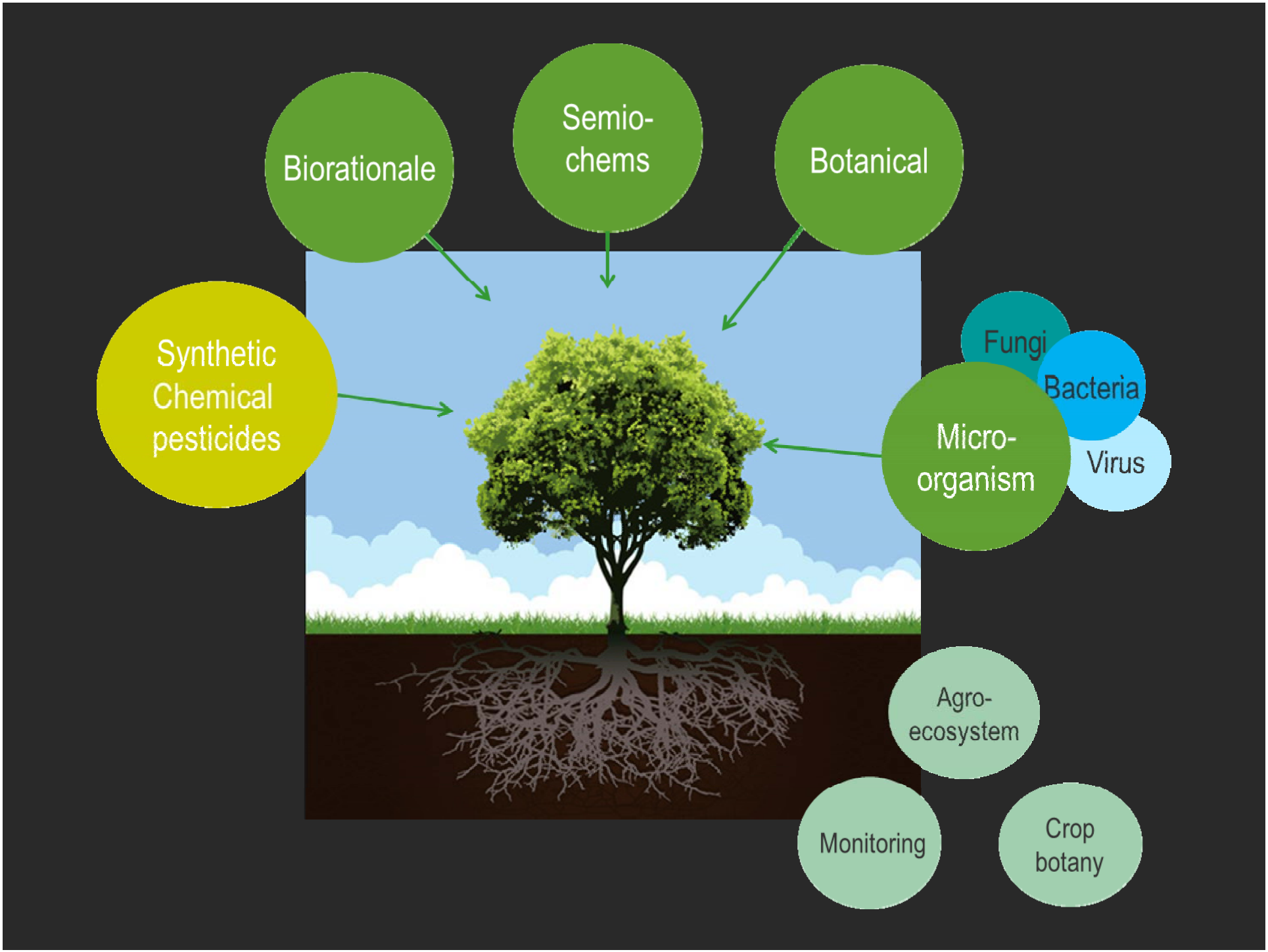
Regulatory innovation

Proportional

Relevant

Quicker

Cost effective


Biorationale
Semio-chems
Botanical
Synthetic Chemical pesticides
Fungi
Bacteria
Virus
Micro-organism
Agro-ecosystem
Monitoring
Crop botany

Recipe for success?

Employ systems biologists

Embrace variability

Good technology transfer

Maintain innovation

Directed by technology

Reflections

Research investment

Innovation

Harmonised regulation

Global grower demand

Better advocacy

Better technology transfer

Thank you for your attention

RATIONALE

BIOPESTICIDE STRATEGISTS

www.biorationale.co.uk

rgwynn@biorationale.co.uk