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1 The development, regulation and use of biopesticides for Integrated Pest Management

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15 Over the past 50 years, crop protection has relied heavily on synthetic chemical pesticides but
16 their availability is now declining as a result of new legislation and the evolution of resistance
17 in pest populations. Therefore, alternative pest management tactics are needed. Biopesticides
18 are pest management agents based on living microorganisms or natural products. They have
19 proven potential for pest management and they are being used across the world. However,
20 they are regulated by systems designed originally for chemical pesticides that have created
21 market entry barriers by imposing burdensome costs on the biopesticide industry. There are
22 also significant technical barriers to making biopesticides more effective. In the European
23 Union, a greater emphasis on Integrated Pest Management (IPM) as part of agricultural
24 policy may lead to innovations in the way that biopesticides are regulated. There are also new
25 opportunities for developing biopesticides in IPM by combining ecological science with post-
26 genomics technologies. The new biopesticide products that will result from this research will
27 bring with them new regulatory and economic challenges that must be addressed through
28 joint working between social and natural scientists, policy makers and industry.

29
30
31 **Keywords:** biopesticide, Integrated Pest Management, adoption, regulation

32 **INTRODUCTION**

33 In this paper we discuss the challenges and opportunities for Integrated Pest
34 Management (IPM) in the developed economies, with emphasis on the European Union. We
35 focus on a set of crop protection tools known as biopesticides. We are concerned in particular
36 with understanding the factors that hinder or facilitate the commercialisation and use of new
37 biopesticide products.

38 Over the next 20 years, crop production will have to increase significantly to meet the
39 needs of a rising human population. This has to be done without damaging the other public
40 goods – environment and social - that farming brings. There will be no ‘silver bullet’ solution
41 to the impending food production challenge. Rather, a series of innovations must be
42 developed to meet the different needs of farmers according to their local circumstances (see
43 for example [1]).

44 One way to increase food availability is to improve the management of pests. There
45 are estimated to be around 67,000 different crop pest species - including plant pathogens,
46 weeds, invertebrates and some vertebrate species - and together they cause about a 40%
47 reduction in the world’s crop yield [2]. Crop losses caused by pests undermine food security
48 alongside other constraints such as inclement weather, poor soils, and farmers’ limited access
49 to technical knowledge [3].

50 Since the 1960s, pest management in the industrialised countries has been based
51 around the intensive use of synthetic chemical pesticides. Alongside advances in plant
52 varieties, mechanisation, irrigation and crop nutrition, they have helped increase crop yields
53 by nearly 70% in Europe and 100% in the USA [4]. However the use of synthetic pesticides
54 is becoming significantly more difficult due to a number of interacting factors:

- 55 • The injudicious use of broad-spectrum pesticides can damage human health and the
56 environment [5, 6]. Some of the ‘older’ chemical compounds have caused serious health
57 problems in agricultural workers and others because of inadequate controls during
58 manufacture, handling and application.
- 59 • Excessive and injudicious prophylactic use of pesticides can result in management failure
60 through pest resurgence, secondary pest problems or the development of heritable
61 resistance [7]. Worldwide, over 500 species of arthropod pests have resistance to one or
62 more insecticides [8], while there are close to 200 species of herbicide resistant weeds [9].
- 63 • Pesticide products based on ‘old’ chemistry are being withdrawn because of new health
64 and safety legislation [10, 11]. However, the rate at which new, safer chemicals are being

65 made available is very low. This is caused by a fall in the discovery rate of new active
66 molecules and the increasing costs of registration [12].

- 67 • Further pressures on pesticide use arise from concerns expressed by consumers and
68 pressure groups about the safety of pesticide residues in food. These concerns are voiced
69 despite the fact that pesticides are among the most heavily regulated of all chemicals.

70

71 **INTEGRATED PEST MANAGEMENT**

72 There is an urgent requirement for alternative tactics to help make crop protection more
73 sustainable. Many experts promote Integrated Pest Management as the best way forward and
74 the European Union has placed it centrally within its 2009 Sustainable Use Directive on
75 pesticides [13]. IPM is a systems approach that combines different crop protection practices
76 with careful monitoring of pests and their natural enemies [14, 15]. The idea behind IPM is
77 that combining different practices together overcomes the shortcomings of individual
78 practices. The aim is not to eradicate pest populations but rather to manage them below
79 levels that cause economic damage. The main IPM tactics include:

- 80 • Synthetic chemical pesticides that have high levels of selectivity and are classed by
81 regulators as low risk compounds, such as synthetic insect growth regulators.
- 82 • Crop cultivars bred with total or partial pest resistance.
- 83 • Cultivation practices, such as crop rotation, intercropping or undersowing.
- 84 • Physical methods, such as mechanical weeders.
- 85 • Natural products, such as semiochemicals or biocidal plant extracts.
- 86 • Biological control with natural enemies, including: predatory insects and mites,
87 parasitoids, parasites and microbial pathogens used against invertebrate pests; microbial
88 antagonists of plant pathogens; and microbial pathogens of weeds.
- 89 • Decision support tools to inform farmers when it is economically beneficial to apply
90 pesticides and other controls. These include the calculation of economic action
91 thresholds, phenological models that forecast the timing of pest activity, and basic pest
92 scouting. These tools can be used to move pesticide use away from routine calendar
93 spraying to a supervised or targeted programme.

94 IPM can be done to different levels of sophistication. Prokopy [16] outlines four levels:
95 the basic Level One combines different tactics against one pest on one crop; whereas the
96 highest Level Four embraces all pests and crops on the farm within an overall Integrated
97 Crop Management system that involves members of the broad policy network (extension

98 services, industry, retailers, regulators) and takes account of the social, cultural and
99 ecological context of farming.

100 An analysis of 62 IPM research and development projects in 26 countries, covering over
101 5 million farm households, showed that IPM leads to substantial reductions in pesticide
102 applications [4]. Over 60% of the projects resulted in both a reduction in pesticide use
103 (average reduction 75%) and an increase in yields (average increase 40%). Approximately
104 20% of projects resulted in lowered pesticide use (average 60% reduction) with a slight loss
105 in yield (average 5% reduction) [4]. Some 15 percent of projects showed an increase of yield
106 (average 45% increase) with increased pesticide use (average 20% increase); these were
107 mainly conservation farming projects that incorporated zero tillage and therefore made
108 greater use of herbicides for weed control. The published evidence on the use of IPM by
109 farmers outside of R&D projects is somewhat thin. For outdoor crops, IPM is based around
110 targeted pesticide use, choice of cultivar and crop rotations. From a survey of 571 arable and
111 mixed farms in the UK, Bailey *et al.* [17] recorded reasonable levels of adoption of good
112 pesticide practice, including use of seed treatments (c. 70% adoption) and rotating pesticide
113 classes (c. 55% adoption), as well as good agronomic practice such as crop rotation (75%
114 adoption). However adoption of more “biologically-based” IPM tactics was low, such as
115 insect pheromones for pest monitoring (20%) and introducing arthropod predators for
116 biological control (7%).

117 In contrast, biological control plays a central role in the production of many greenhouse
118 crops. Pesticide resistance evolved in some key greenhouse pests as long ago as the 1960s,
119 prompting the development of alternative methods of management. The pressure to reduce
120 insecticide usage was reinforced by the adoption of bumblebees within greenhouses for
121 pollination. Some highly effective IPM programmes are now in place, based around the
122 biocontrol of insect and mite pests using combinations of predators, parasitoids, parasitic
123 nematodes and entomopathogens. Short persistence pesticides are used on an at-need basis if
124 they are compatible with biological control. Pest management strategies are also determined
125 through a close interaction between growers, consultants, biocontrol companies and retailers.
126 In Europe, IPM based around biological control is used on over 90% of greenhouse tomato,
127 cucumber and sweet pepper production in the Netherlands [18] and is standard practice for
128 greenhouse crops in the UK. In Almeria, Spain, the area under biocontrol-based IPM has
129 increased from just 250 ha in 2005 to around 7,000 ha in 2008, while the proportion of the
130 Dutch chrysanthemum crop grown under IPM increased from just 1% in 2002 to 80% in
131 2007 (R. GreatRex, Syngenta Bioline, pers. comm.). This use of biological control requires

132 considerable grower knowledge but it has clear benefits in terms of reliable pest control, lack
133 of phytotoxicity, a short harvest interval and better crop quality.

134

135 **BIOPESTICIDES**

136 Biopesticides are a particular group of crop protection tools used in IPM. There is no
137 formally agreed definition of a biopesticide. We define a biopesticide as a mass-produced
138 agent manufactured from a living microorganism or a natural product and sold for the control
139 of plant pests (this definition encompasses most entities classed as biopesticides within the
140 OECD countries, see for example [19]). Examples of some biopesticides are given in Table
141 1. Biopesticides fall into three different types according to the active substance: (i)
142 microorganisms; (ii) biochemicals and (iii) semiochemicals. The US Environmental
143 Protection Agency also classes some transgenes as biopesticides (see “future directions in
144 biopesticide development” later in this paper).

145 **Microbial biopesticides.** Bacteria, fungi, oomycetes, viruses and protozoa are all
146 being used for the biological control of pestiferous insects, plant pathogens and weeds. The
147 most widely used microbial biopesticide is the insect pathogenic bacterium *Bacillus*
148 *thuringiensis* (Bt) which produces a protein crystal (the Bt δ -endotoxin) during bacterial
149 spore formation that is capable of causing lysis of gut cells when consumed by susceptible
150 insects [20]. The δ -endotoxin is host specific and can cause host death within 48 hours [21,
151 22]. It does not harm vertebrates and is safe to people, beneficial organisms and the
152 environment [23]. Microbial Bt biopesticides consist of bacterial spores and δ -endotoxin
153 crystals mass-produced in fermentation tanks and formulated as a sprayable product. Bt
154 sprays are a growing tactic for pest management on fruit and vegetable crops where their high
155 level of selectivity and safety are considered desirable, and where resistance to synthetic
156 chemical insecticides is a problem [24]. Bt sprays have also been used on broad acre crops
157 such as maize, soybean and cotton, but in recent years these have been superseded by Bt
158 transgenic crop varieties.

159 Other microbial insecticides include products based on entomopathogenic
160 baculoviruses and fungi. In the USA and Europe, the *Cydia pomonella* granulovirus (CpGV)
161 is used as an inundative biopesticide against codling moth on apples. In Washington State,
162 the USA’s biggest apple producer, it is used on 13% of the apple crop [25]. In Brazil, the
163 nucleopolyhedrovirus of the soybean caterpillar *Anticarsia gemmatalis* was used on up to 4
164 million ha (approximately 35%) of the soybean crop in the mid 1990s [26]. At least 170
165 different biopesticide products based on entomopathogenic fungi have been developed for

166 use against at least five insect and acarine orders in glasshouse crops, fruit and field
167 vegetables as well as broad acre crops, with about half of all products coming from Central
168 and South America [27]. The majority of products are based on the ascomycetes *Beauveria*
169 *bassiana* or *Metarhizium anisopliae*. The largest single country of use is Brazil, where
170 commercial biopesticides based on *M. anisopliae* are used against spittlebugs on around
171 750,000 ha of sugarcane and 250,000 ha of grassland annually [28]. The fungus has also
172 been developed for the control of locust and grasshopper pests in Africa and Australia [29]
173 and is recommended by the FAO for locust management [30].

174 Microbial biopesticides used against plant pathogens include *Trichoderma harzianum*,
175 which is an antagonist of *Rhizoctonia*, *Pythium*, *Fusarium* and other soil borne pathogens
176 [31]. *Coniothyrium minitans* is a mycoparasite applied against *Sclerotinia sclerotiorum*, an
177 important disease of many agricultural and horticultural crops [32]. The K84 strain of
178 *Agrobacterium radiobacter* is used to control crown gall (*Agrobacterium tumefaciens*), while
179 specific strains of *Bacillus subtilis*, *Pseudomonas fluorescens* and *Pseudomonas aureofaciens*
180 are being used against a range of plant pathogens including damping off and soft rots [33 -
181 36]. Microbial antagonists, including yeasts, filamentous fungi and bacteria, are also used as
182 control agents of post harvest diseases, mainly against *Botrytis* and *Penicillium* in fruits and
183 vegetables [37].

184 Plant pathogens are being used as microbial herbicides. No products are currently
185 available in Europe. Two products, ‘Collego’ (*Colletotrichum gloeosporioides*) and ‘DeVine’
186 (*Phytophthora palmivora*) have been used in the USA [38]. Collego is a bioherbicide of
187 northern jointvetch in soybeans and rice that was sold from 1982 – 2003 [39]. DeVine is
188 used in Florida citrus groves against the alien invasive weed stranglervine. It provides 95% to
189 100% control for about a year after application [39,40].

190 **Biochemicals.** Plants produce a wide variety of secondary metabolites that deter
191 herbivores from feeding on them. Some of these can be used as biopesticides. They include,
192 for example, pyrethrins, which are fast-acting insecticidal compounds produced by
193 *Chrysanthemum cinerariaefolium* [41]. They have low mammalian toxicity but degrade
194 rapidly after application. This short persistence prompted the development of synthetic
195 pyrethrins (pyrethroids). The most widely used botanical compound is neem oil, an
196 insecticidal chemical extracted from seeds of *Azadirachta indica* [42].

197 Two highly active pesticides are available based on secondary metabolites
198 synthesized by soil actinomycetes. They fall within our definition of a biopesticide but they
199 have been evaluated by regulatory authorities as if they were synthetic chemical pesticides.

200 Spinosad is a mixture of two macrolide compounds from *Saccharopolyspora spinosa* [43]. It
201 has a very low mammalian toxicity and residues degrade rapidly in the field. Farmers and
202 growers used it widely following its introduction in 1997 but resistance has already
203 developed in some important pests such as western flower thrips [44]. Abamectin is a
204 macrocyclic lactone compound produced by *Streptomyces avermitilis* [45]. It is active against
205 a range of pest species but resistance has developed to it also, for example in tetranychid
206 mites [46].

207 **Semiochemicals.** A semiochemical is a chemical signal produced by one organism
208 that causes a behavioural change in an individual of the same or a different species. The most
209 widely used semiochemicals for crop protection are insect sex pheromones, some of which
210 can now be synthesized and are used for monitoring or pest control by mass trapping [47],
211 lure-and-kill systems [48] and mating disruption. Worldwide, mating disruption is used on
212 over 660,000 ha and has been particularly useful in orchard crops [49].

213 Biopesticides have a range of attractive properties that make them good components
214 of IPM. Most are selective, produce little or no toxic residue, and development costs are
215 significantly lower than those of conventional synthetic chemical pesticides [8]. Microbial
216 biopesticides can reproduce on or in close vicinity to the target pest, giving an element of
217 self-perpetuating control. Biopesticides can be applied with farmers' existing spray
218 equipment and many are suitable for local scale production. The disadvantages of
219 biopesticides include a slower rate of kill compared to conventional chemical pesticides,
220 shorter persistence in the environment, and susceptibility to unfavourable environmental
221 conditions. Because most biopesticides are not as efficacious as conventional chemical
222 pesticides, they are not suited for use as stand-alone treatments. However their selectivity and
223 safety mean that they can contribute meaningfully to incremental improvements in pest
224 control [50]. A good example is the entomopathogenic fungus *Beauveria bassiana*, which is
225 being used in combination with invertebrate predators against twospotted spider mites on
226 greenhouse crops [51]. Spider mites are routinely managed using regular releases of
227 predators, but there are often periods in the season when control breaks down. In the past,
228 growers relied on conventional pesticides as a supplementary treatment but this has become
229 ineffective because of pesticide resistance and it can have knock-on effects on other insect
230 natural enemies. *Beauveria bassiana* is effective against spider mites, has a short harvest
231 interval, and is compatible with the use of predators [51]. So it works well as an IPM
232 component and is now the recommended supplementary treatment for spider mite on
233 greenhouse crops across Europe.

234

235 **BIOPESTICIDE COMMERCIALISATION**

236 Worldwide there are about 1,400 biopesticide products being sold [52]. At present there
237 are 68 biopesticide active substances registered in the EU and 202 in the USA. The EU
238 biopesticides consist of 34 microbials, 11 biochemicals, and 23 semiochemicals [53], while
239 the USA portfolio comprises 102 microbials, 52 biochemicals and 48 semiochemicals [54].
240 To put this into context, these biopesticide products represent just 2.5% of the total pesticide
241 market [55]. Marrone [52] has estimated the biopesticides sector currently to have a five-year
242 compound annual growth rate of 16% (compared to 3% for synthetic pesticides) that is
243 expected to produce a global market of \$10 billion by 2017. However the market may need
244 to increase substantially more than this if biopesticides are to play a full role in reducing our
245 overreliance on synthetic chemical pesticides.

246 Companies will only develop biopesticide products if there is profit in doing so. Similarly
247 the decision for a farmer whether or not to adopt a novel technology can be thought of in
248 economic terms as a cost-benefit comparison of the profits to be made from using the novel
249 versus the incumbent technology. A number of features of the agricultural economy make it
250 difficult for companies to invest in developing new biopesticide products and, at the same
251 time, make it hard for farmers to decide about adopting the new technology:

- 252 • **Lack of profit from niche market products.** Many biopesticides have high levels of
253 selectivity. For example, bioinsecticides based on baculoviruses, such as the CpGV
254 mentioned previously, typically are selective for just one or a few species of insect. This
255 is of great benefit in terms of not harming other natural enemies and wildlife, but it means
256 that biopesticides are niche market products with low profit potential. To quote Gelernter
257 [56] ‘The features that made most Biological Control Products so attractive from the
258 standpoint of environmental and human safety also acted to limit the number of markets
259 in which they were effective’.
- 260 • **Fixed costs.** Because conventional chemical pesticides are used so widely, the fixed
261 costs associated with them are spread over many users and hence represent a small part of
262 the total cost of pest control. The knowledge needed by farmers to get effective control
263 with pesticides is lower than with tactics such as biocontrol [57, 58]. Potential adopters of
264 biopesticides face large fixed costs of adoption that will only decrease once the
265 technology is used more widely, thereby disadvantaging early adopters.

- 266 • **Farmers’ risk aversion.** For fruit and vegetable crops, cosmetic appearance is as
267 important as yield when it comes to making a profit. The risks of producing an
268 unmarketable crop are high, forcing growers to be risk averse with respect to new,
269 untested crop protection technologies. Because conventional pesticides have been the
270 mainstay of crop protection for over 50 years, there is a wealth of experience that gives
271 farmers and growers confidence in their effectiveness. Farmers have achieved scale
272 economies in pesticide use as a result of ‘learning by doing’ – the concept that one
273 becomes more productive at a task the more it is repeated. In comparison, the more
274 limited evidence base and practical experience with biologically-based IPM technologies
275 creates uncertainty for farmers [59 - 61]. Farmers’ risk averse preferences can result in
276 sub-optimal patterns of adoption of new technologies [62]. Risk aversion is made worse if
277 farmers’ expectations of new technologies are more focused on the potential downsides
278 rather than the benefits [63].
- 279 • **IPM portfolio economies.** Different IPM tactics work together as a ‘technology bundle’
280 or portfolio. If a farmer wants to switch from using a single chemical pesticide for pest
281 control to IPM then (s)he will have to decide which combination of tactics to use. The
282 number of potential portfolios to choose from increases rapidly as more tactics are
283 included [64]: with three tactics there are a total of seven different portfolios, with four
284 tactics there are 11 different portfolios and so forth. Choosing the best portfolio in such
285 cases is extremely challenging. The only realistic option is to develop a portfolio
286 incrementally. Where a portfolio is already in place, then a farmer has to consider the
287 benefits of adopting a new IPM tactic in the light of the current portfolio. Farmers want to
288 use the minimum number of different tactics for the maximum benefit. Should the new
289 tactic be added to the existing portfolio, or should it be used to replace an incumbent
290 tactic? In some instances it is possible to replace a conventional synthetic chemical
291 pesticide with a biopesticide without disturbing the existing IPM system (as in the case of
292 using *B. bassiana* for control of spidermites in greenhouse IPM). In such a case the new
293 biopesticide technology can be adopted quickly and easily. However, IPM tactics may be
294 synergistic, such that one tactic in the portfolio results in an improved performance in
295 others [65, 66]. This is beneficial for IPM, but the interdependency of different tactics in
296 this way can make it difficult to substitute with new technologies as they become
297 available.

298 These factors mean that using conventional synthetic chemical pesticides applied on a
299 calendar basis can be difficult to replace in favour of an IPM portfolio of alternative tactics
300 including biopesticides. Chemical pest control may then become locked into the system until
301 such a time that it fails, for example if pesticide resistance becomes widespread, as in the
302 greenhouse crops industry. Pesticide ‘lock in’ also means that the adoption of new
303 technologies will be biased towards tactics that closely resemble the incumbent pesticide
304 technology. In the case of biopesticides, the products that have been most successful so far,
305 such as microbial Bt, are very similar to chemical pesticides. This ‘chemical model’ of
306 biopesticide development has encouraged companies to turn their attention away from the
307 beneficial, biologically-based characteristics of biopesticides (such as the ability of microbial
308 agents to reproduce within host populations) and instead focus on trying to use biopesticides
309 as chemical pesticide ‘clones’, resulting in unrealistic expectations of chemical-like efficacy
310 [67].

311 It is important to stress that chemical pesticides are and will remain a vital part of crop
312 protection. When used appropriately they can give excellent control with minimal adverse
313 effects. The use of chemical pesticides should therefore be promoted within an IPM
314 framework so that they are used sparingly to minimise the evolution of resistance in target
315 pest populations. However, IPM will only work if farmers have access to a range of crop
316 protection tactics together with the knowledge on how to integrate them.

317

318 **REGULATORY BARRIERS TO BIOPESTICIDE COMMERCIALISATION**

319 Biopesticides encompass a very wide range of living and non-living entities that vary
320 markedly in their basic properties, such as composition, mode of action, fate and behaviour in
321 the environment and so forth. They are grouped together by governments for the purposes of
322 regulating their authorisation and use. These regulations are in place: firstly, to protect
323 human and environmental safety; and secondly to characterize products and thereby ensure
324 that manufacturers supply biopesticides of consistent and reliable quality. The European
325 Union also requires that the efficacy of a biopesticide product is quantified and proven in
326 order to support label claims. Only authorized biopesticide products can be used legally for
327 crop protection.

328 The guidance of the OECD is that biopesticides should only be authorised if they pose
329 minimal or zero risk. For example, the OECD guidance for microbial biopesticides is that:
330 *‘the microorganism and its metabolites pose no concerns of pathogenicity or toxicity to*
331 *mammals and other non-target organisms which will likely be exposed to the microbial*

332 *product; the microorganism does not produce a known genotoxin; all additives in the*
333 *microbial manufacturing product and in end-use formulations are of low toxicity and suggest*
334 *little potential for human health or environmental hazard'* [68]. The biopesticide registration
335 data portfolio required by the regulator is normally a modified form of the one in place for
336 conventional chemical pesticides and is used by the regulator to make a risk assessment. It
337 includes information about mode of action, toxicological and eco-toxicological evaluations,
338 host range testing and so forth. This information is expensive for companies to produce and it
339 can deter them from commercialising biopesticides which are usually niche market products.
340 Therefore, the challenge for the regulator is to have an appropriate system in place for
341 biopesticides that ensures their safety and consistency but which does not inhibit
342 commercialisation. Until very recently, it is true to say that government regulators – with the
343 probable exception of the USA - were unfamiliar with biologically-based pest management
344 and were therefore slow to appreciate the need to make the regulatory process appropriate for
345 biopesticides rather than treat them in the same way as synthetic chemical pesticides.

346 The decision whether or not to authorize a biopesticide product is made on the basis
347 of expert opinion residing within the regulatory authority. When the regulators lack expertise
348 with biopesticides, they tend to delay making a decision and may request the applicant
349 provides them with more data. There is also a risk that the regulator – using the chemical
350 pesticide registration model - requests information that is not appropriate. Some regulatory
351 authorities, the UK for example, have acknowledged that basing the regulatory system for
352 biopesticides on a chemical pesticides model has been a barrier to biopesticide
353 commercialisation [69]. A key question is whether the regulator, having recognised a
354 problem, is able to do something about it. Social science theory indicates that government
355 regulators and other bureaucratic organisations are vulnerable to “goal displacement”, during
356 which they turn their focus away from achieving outcomes and instead concentrate more on
357 internal processes [70]. This can lead to systemic problems and stand in the way of
358 introducing innovations into the regulatory system. This is not to say that regulatory
359 innovation is not possible, and where there is sound evidence that a particular group of
360 biopesticides presents minimal risk the regulators have modified the data requirements. For
361 example, the OECD regard semiochemicals used for arthropod control as presenting minimal
362 hazard, with straight chain lepidopteran pheromones which form the majority of
363 semiochemical-based biopesticides being thought sufficiently safe as to justify ‘substantial
364 reductions in health and environmental data requirements’ [71]. Other innovations are also
365 being developed, which we discuss in the following sections:

366 *New EU legislation could promote biopesticide use.* The EU passed a package of
367 legislative measures in 2009 based around IPM, including the Framework Directive on the
368 Sustainable Use of Pesticides (EU DG Environment). IPM principles do not become
369 mandatory until 2014, but member states have been encouraged to use rural development
370 programmes (funded under the Common Agricultural Policy) to provide financial incentives
371 to farmers to start implementing IPM before this date. In the Commission’s view, further
372 research is still needed to develop successful crop-specific strategies for the deployment of
373 IPM and this should include multidisciplinary research. The Commission also regards it as
374 ‘crucial that Member States support the development of certified IPM advisory services
375 organised by cropping systems to bridge the gap between research and end-users and help
376 farmers for the adaptation of IPM principles to local situations.’ [72]. Although such
377 services can be provided privately and their quality guaranteed by a system of certification, it
378 may be that countries that have retained state extension services, such as Denmark, have an
379 inherent advantage in providing IPM advice in a cost effective way.

380 Alongside the Sustainable Pest Management Directive, the EU also introduced a
381 regulation which substantially amended the plant protection legislation embodied in Directive
382 91/414 [73]. This directive provided for a two-tier system of regulation involving the
383 Community and member state levels. However, it quickly became evident that mutual
384 recognition between different member states was not working, hence undermining the
385 functioning of the EU internal market and deterring the development of biopesticides and
386 other innovative products. One of the solutions advanced was to divide Europe into
387 climatically similar zones (“eco zones”) where registration in one member state would
388 facilitate registration in others in the same zone. This proposal proved controversial during
389 the passage of the legislation. It was eventually achieved with northern, central and southern
390 zones and an EU-wide one for greenhouses.

391 The new legislation gives a specific status to non-chemical and natural alternatives to
392 conventional chemical pesticides and requires them to be given priority wherever possible.
393 Biopesticides should generally qualify as low-risk active substances under the legislation.
394 Low-risk substances are granted initial approval for 15 years rather than the standard 10. A
395 reduced dossier can be submitted for low risk substances but this has to include a
396 demonstration of sufficient efficacy. One requirement for low risk substances, that is still to
397 be elaborated, is that their half-life in the soil should be less than 60 days and this may cause
398 problems for some microbial biopesticides, such as rhizosphere-competent antagonists of
399 soil-borne plant pathogens.

400 The new European legislation does not give the biopesticides industry all that it may
401 have hoped for, but it does give biopesticides legislative recognition and opens up the
402 potential for faster authorisation processes and effective mutual recognition. This will
403 require sustained work by those interested in the wider use of biopesticides. Many of the
404 details of how mutual recognition in eco zones will operate in practice remain to be resolved,
405 for example how member states will interact with one another during the process. The
406 achievement of real gains is very sensitive to the detailed implementation of the new
407 procedures. What is clear is that the considerable variations in the levels of resource
408 available to regulatory authorities in different member states will be a constraint on effective
409 delivery.

410 ***EU member state regulation.*** In the EU, having a system of mutual recognition of
411 plant protection products means that it is possible for one member state to engage in
412 regulatory innovation and gain a first mover advantage over other member states. In relation
413 to biopesticides, it is arguable that Britain has taken such a position.

414 Concern about the lack of availability of biopesticides in the UK led to the
415 introduction in June 2003 of a pilot project to facilitate their registration. Its aim was to
416 increase the availability of biopesticides by improving knowledge and raising awareness of
417 the requirements of the UK government regulator (at the time, the government regulator was
418 the Pesticides Safety Directorate (PSD) but it has subsequently become the Chemicals
419 Regulation Directorate (CRD)). In April 2006 the pilot project was turned into a fully-fledged
420 Biopesticides Scheme. Prior to the introduction of the scheme, just four products had been
421 approved between 1985 and 1997. Following the introduction of the pilot project, seven
422 products were guided to approval. In April 2007 five products were at various stages of
423 evaluation and several other companies were discussing possible applications with PSD.
424 Two products were approved in 2009 and several were at various stages of the registration
425 process.

426 In order to better operate the scheme the regulator provides specialist training on
427 biopesticides to members of its Pesticide Approvals Group and has assigned a Biopesticides
428 Champion. PSD thought it desirable to involve as many people in their Pesticide Approvals
429 Group in this work as possible, rather than having a unit that only dealt with biopesticides
430 and which would probably have insufficient work. Trained staff members are able to
431 participate in pre-submission meetings with applicant biopesticide companies. Particularly if
432 they are held early in the process, they can help applicants to plan the acquisition of the data
433 they need for registration and also avoid the compilation of any material which would be

434 superfluous. A number of such meetings were observed on a non-participant basis as part of
435 our research. The meetings enabled the identification of gaps in the application dossier and
436 mutually helpful discussions of how these could be filled, for example, by using data
437 published in the scientific literature. The UK Scheme charges reduced fees for biopesticides:
438 £22,500 for microbial biopesticides, £13,000 for pheromones and £7,500 for taking either
439 through European Food Safety Authority (EFSA) procedures. Before the introduction of the
440 pilot project, there was a standard fee of £40,000 for everything termed a biopesticide. In
441 comparison, the cost of core dossier evaluation, provisional approval and EFSA review for a
442 synthetic chemical pesticide would be between £120,000 and £180,000 from March 2007.
443 CRD intends to continue to operate the Biopesticides Scheme with reduced fees.

444 The scheme has had to face a number of challenges. It has involved CRD reaching
445 out to non-traditional ‘customers’ who may be suspicious of the regulatory authority because
446 they have no experience of working with them. As a biopesticides consultant commented in
447 interview in our research, ‘Pre-submission is a key element because registration is still an
448 unknown, a lot of fear, people want me to hold their hands, introduce them to PSD.’ From a
449 CRD perspective, the biopesticides scheme was seen as a pathfinder in Europe and it could
450 make it the preferred regulation authority for such products providing it is able to maintain
451 the process of regulatory innovation.

452

453 **FUTURE DIRECTIONS**

454 Governments are likely to continue imposing strict safety criteria on conventional
455 chemical pesticides, and this will result in fewer products on the market. This will create a
456 real opportunity for biopesticide companies to help fill the gap, although there will also be
457 major challenges for biopesticide companies, most of which are SMEs with limited resources
458 for R&D, product registration and promotion. Perhaps the biggest advances in biopesticide
459 development will come through exploiting knowledge of the genomes of pests and their
460 natural enemies. Researchers are already using molecular-based technologies to reconstruct
461 the evolution of microbial natural enemies and pull apart the molecular basis for their
462 pathogenicity [74 - 76]; to understand how weeds compete with crop plants and develop
463 resistance to herbicides [77]; and to identify and characterise the receptor proteins used by
464 insects to detect semiochemicals [78]. This information will give us new insights into the
465 ecological interactions of pests and biopesticides and lead to new possibilities for improving
466 biopesticide efficacy, for example through strain improvement of microbial natural enemies

467 [79]. As the genomes of more pests become sequenced, the use of techniques such as RNA
468 interference for pest management is also likely to be put into commercial practice [80].

469 We stated earlier that biopesticide development has largely been done according to a
470 chemical pesticides model that has the unintended consequence of downplaying the
471 beneficial biological properties of biopesticides such as persistence and reproduction [67] or
472 plant growth promotion. The pesticides model still has much to offer, for example in
473 improving the formulation, packaging and application of biopesticides. However, it needs to
474 be modified in order to investigate biopesticides from more of a biological / ecological
475 perspective. For example, biologists are only just starting to realise the true intricacies of the
476 ecological interactions that occur between microbial natural enemies, pests, plants and other
477 components of agroecosystems [81]. Take entomopathogenic fungi for instance. We now
478 know that species such as *Beauveria bassiana* and *Metarhizium anisopliae*, traditionally
479 thought of solely as insect pathogens, can also function as plant endophytes, plant disease
480 antagonists, rhizosphere colonizers, and plant growth promoters [82]. This creates new and
481 exciting opportunities for exploiting them in IPM, for example by inoculating plants with
482 endophytic strains of entomopathogenic fungi to prevent infestation by insect herbivores.
483 There are opportunities also to exploit the volatile alarm signals emitted by crop plants so that
484 they recruit microbial natural enemies as bodyguards against pest attack [83 - 85] and to use
485 novel chemicals to impair the immune system of crop pests to make them more susceptible to
486 microbial biopesticides [86, 87].

487 The biopesticide products that will result from new scientific advances may stimulate
488 the adoption of different policies in different countries. We have seen this already with GM
489 crops. In the USA, Canada, China, India and Brazil, farmers have been quick to adopt
490 transgenic broad acre crops expressing Bt δ -endotoxin genes. For example, in the USA, 63%
491 of the area of maize planted, and 73% of the area of cotton, now consists of GM varieties
492 expressing Bt δ -endotoxin genes [88]. The US Environmental Protection Agency includes
493 transgenes in its categorisation of biopesticides. In Europe, by contrast, there has been
494 widespread resistance among consumers to GM crops and the EU excludes them from the
495 biopesticide regulatory process. Another complex issue surrounds the regulation of
496 biopesticides that have multiple modes of action. For example, species of the fungus
497 *Trichoderma*, which are used as biopesticides against soil borne plant pathogenic fungi, are
498 able to parasitize plant pathogenic fungi in the soil; they also produce antibiotics and fungal
499 cell wall degrading enzymes, they compete with soil borne pathogens for carbon, nitrogen
500 and other factors, and they can also promote plant growth by the production of auxin-like

501 compounds [89, 90]. Some *Trichoderma* products have been sold on the basis of their plant
502 growth promoting properties, rather than as plant protection products, and so have escaped
503 scrutiny from regulators in terms of their safety and efficacy.

504 In general, the adoption of IPM tactics is correlated with farmer education and experience
505 and the crop environment (with IPM being adopted more on horticultural crops [91]). We
506 have mentioned previously that biocontrol-based IPM has been adopted widely by the
507 greenhouse crops industry but is not used much by growers of broad acre crops. Greenhouses
508 represent intensively managed, controlled environments that are highly suitable for IPM.
509 Biocontrol adoption was undoubtedly helped by the fact that greenhouse crop production is
510 labour intensive and technically complex, and thus growers already had a high level of
511 knowledge and were used to technological innovation. How IPM and alternative technologies
512 such as biopesticides can be taken out to broad acre crops and the wider rural environment -
513 where human capital is spread thinly and where the ecological environment is far more
514 complex and less stable than in a greenhouse - is an interesting question, and one where
515 public policy is likely to play an important role.

516 One proposed solution is to develop a “total system” approach to pest management in
517 which the farm environment is made resistant to the build up of crop pests, and therapeutic
518 treatments are used as a second line of defence [92]. The total systems approach is based:
519 firstly, on managing the agro-ecosystem to promote pest regulating services from naturally
520 occurring biological control agents, for example by providing refugia and alternative food
521 sources for natural enemies within the crop and in field margins; and secondly, on making
522 greater use of crop varieties bred with tissue-specific and damage-induced defences against
523 pests [92]. Biopesticides would have an important role as back-up treatments in this system,
524 although some biopesticides could also be used as preventative treatments, e.g. fungal
525 endophytes (see above). A big advantage of this approach would be in preventing
526 biopesticides being viewed as just another set of ‘silver bullet’ solutions for pest control, and
527 thereby avoid repeating the mistakes of the chemical pesticides era. To make IPM work in the
528 total system concept, institutional arrangements would be required that: provide a market for
529 natural pest regulation as an ecosystem service; promote biopesticides and other
530 environmentally benign technologies in agriculture; value human and natural capital in rural
531 areas; and synthesize knowledge on natural science, economics, and the social dimension of
532 agriculture and the rural environment (see for example [93]). Such a holistic system for pest
533 management would require far better integration of the existing policy network [94]. This
534 may seem like an ambitious proposition but it is becoming increasingly necessary.

535 One area that certainly warrants greater consideration for the future is the attitude of the
536 public and the food retailers to biopesticides and other alternative pest management tools.
537 There is concern among the public about pesticide residues in food but there is little public
538 debate about the use of alternative agents in IPM. In our research, we have found that the
539 major food retailers have done little to engage in discussions about making biological
540 alternatives to synthetic chemical pesticides available to farmers and growers. This is
541 unfortunate given the importance of retailer-led governance in the agricultural economy. It is
542 farmers and growers who are particularly affected by problems of pesticide resistance and the
543 withdrawal of conventional plant protection products, and yet they are ‘policy takers’ rather
544 than ‘policy makers’ and have to operate within the constraints of a stringent regulatory
545 framework while at the same time coping with the market power of the supermarkets.
546 Unfortunately, the public/mass media debate about the future of agriculture has become
547 increasingly polarized into a conflict between supporters of ‘conventional’ versus ‘organic’
548 farming rather than considering what practices should be adopted from all farming systems to
549 make crop protection more sustainable. It is our contention that biopesticides are not given
550 due attention in debates on sustainability. In this regard it is worth concluding with Pretty’s
551 (2008) comment that sustainable agriculture ‘does not mean ruling out any technologies or
552 practices on ideological grounds. If a technology works to improve productivity for farmers
553 and does not cause undue harm to the environment, then it is likely to have some
554 sustainability benefits’ [4].

555

556

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563

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818 **Short title for page headings: biopesticides for Integrated Pest Management**

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Table 1: Examples of some commercially-available biopesticides.

Category	Type	Active ingredient	Product name	Targets	Crop
Microorganism					
Bacteria	Insecticide	<i>Bacillus thuringiensis var kurstaki</i>	Dipel DF	Caterpillars	Vegetables, soft fruit, ornamentals & amenity vegetation
	Fungicide	<i>Bacillus subtilis</i> QST713	Serenade ASO	<i>Botrytis</i> spp.	Vegetables, soft fruit, herbs & ornamentals
	Nematicide	<i>Pasteuria usgae</i>	<i>Pasteuria usgae</i> BL1	Sting nematode	Turf
Fungi	Insecticide	<i>Beauveria bassiana</i>	Naturalis - L	Whitefly	Protected edible & ornamental plant production
	Fungicide	<i>Coniothyrium minitans</i>	Contans WG	<i>Sclerotinia</i> spp.	Outdoor edible and non-edible crops & protected crops
	Herbicide	<i>Chondrostereum purpureum</i>	Chontrol	cut stumps of hardwood trees & shrubs	Forestry
	Nematicide	<i>Paecilomyces lilacinus</i>	MeloCon WG	Plant parasitic nematodes in soil	Vegetables, soft fruit, citrus, ornamentals, tobacco & turf
Viruses	Insecticide	<i>Cydia pomonella</i> GV	Cyd-X	Codling moth	Apples & pears
	Anti-viral	Zucchini Yellow Mosaic Virus, weak strain	Curbit	Zucchini Yellow Mosaic Virus	Transplanted zucchini & cantaloupes, watermelons, squash
Oomycetes	Herbicide	<i>Phytophthora palmivora</i>	DeVine	<i>Morenia orderata</i>	Citrus crops
Biochemical	Insecticide	Azadirachtin	Azatin XL	Aphids, scale, thrips, whitefly, leafhoppers, weevils	Vegetables, fruits, herbs, & ornamental crops
	Fungicide	<i>Reynoutria sachalinensis</i> extract	Regalia	Powdery mildew, downy mildew, <i>Botrytis</i> , late blight, citrus canker	Protected ornamental & edible crops
	Herbicide	Citronella oil	Barrier H	Ragwort	Grassland
	Nematicide	<i>Quillaja saponaria</i>	Nema-Q	Plant parasitic nematodes	Vineyards, orchards, field crops, ornamentals & turf
	Attractant	Citronellol	Biomite	Tetranychid mites	Apples, cucurbits, grapes, hops, nuts, pears, stone fruit, nursery & ornamental crops
Semiochemical	Attractant	(E,E)-8,10-dodecadien-1-ol	Exosex CM	Codling moth	Apples & pears