Report

Expert Consultation and Risk Assessment on the Importation and Large-Scale Use of Mycopesticides against Locusts

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PART 1. INTRODUCTION

Objectives of the Expert Consultation

1. Over the last ten years a number of projects have been developing fungal microbial pesticides (mycopesticides) for the control of locusts. The fungus *Metarhizium anisopliae* var. *acridum* has been particularly promising and has received much attention. Two isolates of *M. anisopliae* var. *acridum*, formulated as two different products, have been extensively tested in Africa and Australia against various species of locusts and grasshoppers. Commercial formulations are now ready for use and may offer an alternative to chemical pesticides under certain circumstances, thereby providing multiple approaches that are the hallmark of a true integrated pest management approach. In comparison to chemical pesticides, *Metarhizium* is regarded as being of low risk to humans and livestock while having few effects on other non-target organisms. A substantial portion of the disposal problems posed by obsolete pesticide stocks in Africa are the result of chemical-based locust control programmes. The large-scale use of microbial control products against locusts and grasshoppers would substantially reduce the accumulation of obsolete stocks of toxic chemicals, which require expensive, special disposal operations that divert resources from other important activities.

2. While field trials have been conducted in more than ten African countries as well as in Australia, only the nine member countries of CILSS[1] and South Africa have (provisionally) registered the product for use against locusts. Several countries have hesitated to import such products, even for experimental purposes. Many African national regulatory bodies lack technical expertise on microbial biocontrol products, and registration guidelines for biocontrol products have not been developed in most of them. The determination of whether an active ingredient is exotic or indigenous can pose regulatory barriers to registration and use. The fact that microbial products contain living organisms frequently requires the participation of phytosanitary agencies that have no experience in pesticide registration, little history of collaboration with pesticide registration authorities, and no clearly specified role in the registration process. Such issues were discussed recently during a *Pan-African Workshop on Biopesticide Registration,* organized in February 2001 in Cotonou, Benin by VPI[2] and IITA[3].

3. The Expert Consultation was jointly organized by the Locusts and Other Migratory Pests Group and by the Pesticides Management Group of the FAO Plant Protection Service. The meeting focussed on 2 objectives:

- to to obtain opinions and guidance on aspects of importation and registration for large-scale use of mycopesticides against locusts, particularly in countries affected by the Desert Locust,
- to review present FAO guiding documents such as the Guidelines on the registration of biological pest control agents and information under the IPPC, e.g. if these documents would provide sufficient guidance to allow the registration of biological pest control agents in particular for developing countries.

The lists of participants in the Expert Consultation is provided in Annex 1. The experts listed in this annex are responsible for the content of the report.

4. In relation to the known risks associated with chemical pesticides, the Consultation was asked to address the following four issues (comments in brackets refer to the sections of the report addressing these issues):

[1] CILSS: Interstate Committee for Drought Control in the Sahel, which consists of Burkina Faso, Cape Verde, Chad, Gambia, Guinea Bissau, Mali, Mauritania, Niger and Senegal
[2] VPI: Virginia Polytechnic Institute and State University
[3] IITA: International Institute of Tropical Agriculture

- What are the risks of importing and using exotic strains of mycopesticides for Desert Locust control? (See part 3, sections 26-43).
- Are the available data for the two existing commercial mycopesticide products considered sufficient to allow a decision on their registration and large-scale use for locust control? (See Annex 5).
- Are special registration requirements, like additional efficacy tests or ecotoxicological studies on a national level, considered justified as part of the registration in locust-affected countries? (See Annex 5).
- Are there indications that the large-scale use and registration of these products should be withheld or restricted? (See section 43).

Opening

5. In her opening statement, Ms. Louise Fresco, Assistant Director General for Agriculture, warmly welcomed all participants to Rome and to FAO. She stressed FAO's concern with respect to the potential environmental and health impact of large scale locust control operations using chemical pesticides. Using microbial pesticides in certain situations could be one of the options to reduce such impact. This would be part of a wider process towards the "greening of locust control„, which FAO supports. Even though no serious Desert Locust problems are encountered at present, options need to be ready when such situations occur in the future. She therefore considered the Expert Consultation to be particularly timely.

6. The Assistant Director General noted that the institutional capacity in many locust-affected countries to evaluate microbial pest control agents is still limited. It is therefore FAO's role to provide objective and scientifically sound guidance on such pest control agents. However, FAO is not a scientific research organisation and it needs experts consultations like this one to be able to advise its member countries in an appropriate manner. After thanking all participants for having been willing to come to Rome and spend five days working with FAO, Ms. Fresco formally opened the *Expert Consultation and Risk Assessment on the Importation and Large-Scale Use of Mycopesticides against Locusts.*

Agenda and Chair

7. The draft agenda that had been distributed among participants before the meeting, was discussed and adopted (Annex 2). The working documents and the presentations made to the meeting are given in Annex 3 and 4, respectively.

8. Mr. Amadou Diarra was elected Chairperson of the Expert Consultation. Mr. Harold van der Valk and Mr. Bernhard Zelazny were nominated as rapporteurs.

Special Considerations

9. A moment of silence was observed in the memory of Dr. Chris Lomer, who unexpectedly died in October 2001. Dr. Lomer was for many years involved in the development and promotion of microbial pest control agents for locust and grasshopper control in Africa and elsewhere. He had been involved in the preparation of the Expert Consultation.

Part 2 Use of *Metarhizium* against Locusts and Grasshoppers

Recent developments in the use of *Metarhizium*

10. Presentations on two currently available locust/grasshopper mycopesticides were made to the Expert Consultation.

11. A commercial formulation (Green Guard ™) of *Metarhizium anisopliae* var. *acridum* (isolate FI 985) is now produced in Australia. It has been field tested against the Australian Plague Locust (*Chortoicetes terminifera*), the Migratory Locust (*Locusta migratoria*), the Spur-throated Locust (*Austracris guttulosa*), and the Wingless Grasshopper (*Phaulacridium vittatum*) (Milner & Hunter, submitted). In 2000/2001 Green Guard was tested on an operational scale (23 000 ha) against Australian Plague Locust. Important reasons for using the mycopesticide were the protection of the organic beef industry from pesticide residues, increased safety for operators, as well as better protection of wildlife. The mycopesticide was applied by air at 25 g/ha (10^{12} conidia/ha) on 70 different hopper band targets. Ninety percent mortality was obtained after 14 days, and no swarms resulted from the treated hopper bands, which confirmed the efficacy observed earlier in smaller scale field trials.

12. A key to the success of Green Guard in Australia was the close cooperation, during product development, between the CSIRO[4] (research), SGB[5] (production) and APLC[6] (use & research). There is presently mounting social and political pressure in Australia to increase the use of this mycopesticide in locust control. As a result, the mycopesticide will be submitted for a full registration in Australia in 2002.

13. A second presentation covered efficacy, safety, registration and marketing of the commercial product Green Muscle ™ (which contains isolate IMI 330189 of *Metarhizium anisopliae* var. *acridum*). Trial results from Africa and Europe, with a variety of locust and grasshopper species, among them Senegalese Grasshopper (*Oedaleus senegalensis*), Brown Locust (*Locusta pardalina*), Italian Grasshopper (*Calliptamus italicus)*, Variegated Grasshopper (*Zonocerus variegatus*) and Desert Locust (*Schistocerca gregaria*), were summarized. Typically, 70 – 100% mortality was obtained after 8 to 28 days. Variability in efficacy of Green Muscle was larger than in the case of Green Guard in Australia, probably because of the wider range of species and environmental conditions in which it was tested. Green Muscle is now provisionally registered for use against locusts and grasshoppers in South Africa and the CILSS countries. It will be submitted for registration in Spain in 2002. The product was purchased in 2001 in Niger for a further operational-scale test on 2000 ha.

14. At present a sufficiently large commercial supply of this type of mycopesticide is available only in Australia for the Australian isolate. In Africa, commercial availability of locust grasshopper mycopesticides are constrained by unsteady demand. Demand for them fluctuates erratically according to outbreaks of the target insects. Furthermore, markets are limited to countries in which the products are registered or for which they would be allowed for emergency use. This temporal and spatial fluctuation in demand is a major constraint to the large-scale adoption of *Metarhizium*. Possible ways of reducing such constraints would be to aim at regional or global markets targeting several locust or grasshopper species; to harmonize registration requirements thus reducing regulatory burdens; or to use a single isolate over a large area, so as to reduce the costs of registration and production.

[4] CSIRO: Commonwealth Scientific & Industrial Research Organisation
[5] SGB: Seed Grain & Biotechnology Australia Pty Ltd.
[6] APLC: Australian Plague Locust Commission

15. Also discussed were several independent research activities in the Desert Locust Central Region (nine countries around the Red Sea), which are either being carried out or are awaiting funding. This research mainly focuses on searching for and development of native isolates of entomopathogens against locusts, as well as on studies to support registration of available isolates.

Similarity of *Metarhizium* isolates

16. An important question for the importation and registration of mycopesticides is whether data for one isolate can be used for taxonomically related isolates. If this is acceptable, authorization of the use of mycopesticides could be facilitated. The question was studied by the Expert Consultation, taking the two available commercial *Metarhizium* products against locusts as examples.

17. The most recent taxonomic revision of the genus *Metarhizium* places the isolates of both the commercial products Green Guard and Green Muscle in the taxonomic group *Metarhizium anisopliae* var. *acridum* based upon molecular sequencing[7]. Most isolates that are active against locusts and grasshoppers cluster as members of the same variety, designated *acridum*. The significance of this result is that the molecular systematics of *Metarhizium*, particularly with respect to var *acridum*, reflect natural host range. Previously, several of the current *acridum* isolates were referred to as *Metarhizium flavoviride* var. *minus* or *Metarhizium anisopliae* var. *anisopliae*. While the new nomenclature is already applied by many scientists, it is formally still a proposal, and has not yet been officially adopted.

18. All presently available information suggests that the natural host range (as judged from natural infections observed in the field) of isolates belonging to *Metarhizium anisopliae* var. *acridum* is limited to locusts and grasshoppers. Even other orthopteran hosts, such as crickets, do not seem to be susceptible in nature. *M. anisopliae* var. *acridum* has so far been found only on Acridoidea in Africa, Asia, South/Central-America and Australia[7] . However, since these are relatively recent studies, it may, therefore, be possible that the *M. anisopliae* var. *acridum* is generally present in all areas where locusts or grasshoppers are found. These data support the argument that the host-range of *M. anisopliae* var. *acridum* can be assessed at the variety level.

19. A recent (unpublished) genetic study with *M. anisopliae* var. *acridum* (isolate IMI 330189) suggests that the genetic variation within repeated cultures of this isolate is comparable to that between certain of the other var. *acridum* isolates. This finding suggests that genetic distinctions between various *M. anisopliae* var. *acridum* isolates are relatively small. It supports the argument above that biological evaluations could be more generally applicable (at least for some properties) to other isolates of this taxonomic group.

20. Physiological differences in var *acridum* isolates are known. For example, data for various isolates of *M. anisopliae* show that the production of destruxins (specific toxins) may vary according to individual isolates or production processes. Certain of these destruxins do not seem to be hazardous to vertebrates, but others may be (e.g. destruxins A and B for mammals and destruxin E for fish). Potential differences in toxin production suggest that risk assessment should be carried out at the isolate level and with respect to a particular production process.

21. **The Expert Consultation concluded that it is difficult to generalise on the exchangeability of toxicity data for isolates belonging to the same taxonomic unit**. Clearly more research is needed in this area. For the time being, data from one *Metarhizium* isolate may support, but not substitute, the risk assessment of another closely related isolate within the context of established genetic relationships.

[7] Driver *et al*. (2000)

Efficacy

22. The efficacy of the isolates in both Green Muscle and Green Guard has been adequately demonstrated for operational use against grasshoppers and locusts, but the slow speed of action may be unacceptable when crops or pastures are under immediate threat. The FAO Pesticide Referee Group already considers Green Muscle as efficacious and confirmed a dose rate. Data for Green Guard were presented to the Expert Consultation and considered sufficient to show efficacy. The Expert Consultation therefore recommends that SGB submit its efficacy data to the Pesticide Referee Group for a formal evaluation.

23. Metarhizium acts slower than most chemical pesticides, and its rate of action is strongly influenced by the range in daily temperature (apart from the locust developmental stage). Therefore, the mycopesticide may not be suitable for protection of crops if locusts are directly threatening them. On the other hand, it has the potential to suppress locust or grasshopper populations for longer periods of time compared to many synthetic pesticides used presently. It was also noted that mycopesticides have stricter storage requirements than chemical pesticides in order to preserve viability. In particular, mycopesticides are sensitive to high temperatures. Given the high temperatures that can be generated in typical storage facilities in locust-affected areas, special consideration of transport and storage of mycopesticides is warranted.

Part 3 Risks of Fungal Biological Control Agents

General safety issues related to fungal biological control agents

24. A number of general safety issues were discussed related to the production and use of fungal biocontrol products. These issues derive from inherent properties of the fungus itself (e.g. toxicity, pathogenicity, or allergenicity) and factors external to the pathogen (e.g. unintentional contamination of the product with undesirable micro-organisms during production). Safety issues are categorized in Table 1. These categories are not equally important, particularly with respect to the two products reviewed by the Expert Consultation for this report.

Table 1 General safety issues related to fungal biocontrol products[8]

	Effects inherent to the pathogen (caused by fungal biocontrol agent)	**Effects due to other factors** (caused by other factors than the fungal biocontrol agent)
Direct effects	▪ Pathogenicity ▪ Toxicity/mutagenicity (due to biologically active molecules synthesized by the pathogen) ▪ Irritation ▪ Allergenicity	▪ Undesirable microbial contaminants during the production ▪ Carriers, additives and adjuvants
Indirect effects	▪ Competitive displacement of other (biocontrol) organisms ▪ Genetic instability of the fungal biocontrol agent	

25. A specific concern expressed during the Expert Consultation was the possibility of microbial pesticides causing health effects (opportunistic infections) in immunocompromised persons exposed to high doses (e.g. production workers and applicators). **It is therefore recommended that an expert assessment be carried out to evaluate the likelihood of immunocompromised persons being affected specifically through the production and use of mycopesticides**.

Risk assessment of Green Muscle and Green Guard

26. An independent risk assessment of the two commercially available mycopesticides against locusts and grasshoppers (Green Muscle™ and Green Guard™) was commissioned by FAO for the Expert Consultation. The objective of this assessment was to evaluate the status and quality of information generated to date with respect to efficacy, production quality and human or environmental risks of these products. It is hoped that the results of the assessment will contribute to national discussions on the acceptability of such mycopesticides for locust and grasshopper control. However, FAO is not a registration authority, and the risk assessment is therefore not intended to replace any national evaluation and decision processes.

27. The companies that produce the two above-mentioned products were invited to submit technical registration dossiers to FAO for the risk assessment. The assessment was subsequently carried out by an independent expert, who had not been involved in the development of these mycopesticides. This expert has experience with the evaluation of such products in the registration

[8] Table partly based on Goettel *et al.* (2001)

system of the European Union. For that reason, the evaluation methodology follows, to a large extent, the recent framework laid down in the European Union Directive regarding the use of micro-organisms as plant protection products[9]. This evaluation procedure is in many aspects similar to the ones used by the United States, Canada and Australia. It was recognized that the EU methodology may not be entirely transferable to the ecological or environmental situations encountered in certain locust affected countries. However, since it is relatively strict in its data requirements and acceptability criteria, a high degree of acceptance under the EU system would indicate that the overall risk of the use of these mycopesticides for locust control are likely to be limited.

28. The risk assessment was discussed in detail by the Expert Consultation. Several resource persons who were directly involved in the development of the two products were given the opportunity to answer questions and provide additional information. Based on the assessment made by the consultant, the Expert Consultation then drew conclusions on the following questions:

- Can the information submitted on each product be considered complete and of sufficient quality to allow an assessment of risk? If not, what data would still need to be provided?
- Do the data indicate that the human and environmental risks of these products are small enough to be acceptable to national registrars? If this is questionable, what should be specific risk issues that national registrars may need to address.

[9] EC (2001)

A number of key elements were identified for this risk assessment:

(a) the identity of the isolates - in particular their relationships with human pathogens;

(b) the biological properties of the isolates - in particular their mode of action, the biotic and abiotic factors determining the potential for persistence in the environment and for reproduction, growth, or persistence in vertebrates;

(c) the quality assurance of the production process, specifically the control of the presence of microbial contaminants;

(d) the presence of toxins and/or secondary metabolites (e.g. destruxins).

29. The general conclusions and recommendations of the Expert Consultation are given below. A summary of the risk analysis is given in Annex 5.

Conclusions for both Green Muscle and Green Guard

Production

30. Regarding the presence of viable contaminants, both isolates are produced according to high quality standards, ensuring *a priori* that such contaminants can be maintained at an acceptable level. However, it is recommended that further data are produced on the likelihood of contaminations with those human pathogens which would be able to multiply under the specific production conditions.

Human health risks

31. Considering the data available in the literature, the genus *Metarhizium* is not closely related to human, other vertebrate, or plant pathogens. The genus *Metarhizium* has only been found to affect human beings under very rare and specific circumstances. Therefore, both isolates are not considered, *a priori,* to be able to cause adverse effects in human beings.

32. Certain *Metarhizium* isolates may produce toxic metabolites (destruxins), especially in liquid culture. Referring to limited data from the literature, it appears that the Green Muscle isolate is free of destruxin A. The Green Guard isolate, on the other hand, appears to produce destruxin A and E on locust cadavers after treatment. Both companies are encouraged to produce analytical data on destruxin levels. In particular, it is necessary to confirm that the end products being distributed for use do not contain any (eco-)toxicologically significant amounts of destruxins (especially destruxin A). This means, if significant amounts of destruxins are produced, their risks to the environment needs to be assessed, e.g. the possible risk to scavengers of fungus-killed locusts.

33. Considering the low observed persistence of both isolates in the type of environments which may be treated, the modes of application of these products, and the lack of effects on vertebrates by consumption of high doses of spores of Green Muscle, there is no major concern associated with the presence of residues on food crops.

Environmental risks

34. Considering the life cycle, the host range and the principal mode of action, both isolates can be considered as acting through infection of the host insects. There is no evidence that they are able to reproduce independently in nature, and survival in the environment is low when spores are exposed to the radiation and temperature conditions prevailing in locust areas.

Specific conclusions for Green Muscle (isolate IMI 330189)

Human health risks

35. The toxicological data submitted for Green Muscle can be considered as almost complete. No acute adverse effects were observed after oral, dermal or inhalation exposure in vertebrates and, therefore, there does not appear to be a need for further chronic toxicity studies.

36. Furthermore, this isolate appears to be unable to grow at human body temperature after inhalation or intraperitoneal exposure. The clearance times of the entomopathogen from lungs and lymph nodes after inhalation, fall in the range previously observed for other fungal microbial control agents and are not a reason for specific concern. No consensus was reached on the question if there was still a need for further tests to determine the clearance time from tissues and blood after intraperitoneal exposure, as such requirements differ between the US and EU evaluation system.

37. Based on the submitted data, the technical compound can be considered as non-irritating for skin and eyes. In the absence of a negative eye irritation test on the formulation, it is recommended that Green Muscle OF should be labelled as a potential eye irritant.

38. There is a lack of conclusive data in relation to the potential for sensitizating effects. Therefore, there is a need to conduct a new adequate study with this isolate, according to the Buehler protocol. Alternatively, in the absence of a negative sensitization test, it is recommended that the commercial formulation of Green Muscle should be labelled as a potential skin sensitizer.

Environmental risks

39. Considering the data submitted for Green Muscle, this isolate has no unacceptable adverse effects on terrestrial non-target vertebrates, non target invertebrates (including beneficial arthropods), and aquatic vertebrates and invertebrates.

Specific conclusions for Green Guard (isolate FI 985)

Human health risks

40. No acute mammalian toxicological studies were provided for Green Guard. Therefore, it is recommended that acute studies be carried out with this isolate through oral, dermal, inhalation and intraperitoneal exposure routes. If skin, eye irritation, and sensitisation tests are not conducted on the formulated product, then the product may be assumed to be a potential irritant or a potential sensitizer.

41. In the absence of such toxicological studies, no final evaluation of the human health risks of Green Guard can be made.

Environmental risks

42. Considering the data submitted for Green Guard, this isolate appears not to have any adverse effects on aquatic organisms. However, there is a lack of acute studies on terrestrial non-target vertebrates. Therefore, it is recommended that such studies are carried out to assess the potential risk to birds (e.g. feeding study with infected locusts) and other appropriate vertebrates.

General conclusion and summary of recommended additional data

43. **Taking into account the above elements, the present status of the dossiers that were provided, and the generally established adverse effects of the chemical pesticides currently being used for locust control, both Green Muscle and Green Guard can be recommended based on efficacy and low environmental risk.** With respect to data on mammal testing, the dossier of Green Muscle is essentially complete and demonstrates no serious health risks. The vertebrate toxicity portion of the Green Guard dossier is insufficient to draw conclusions about potential human health risks.

It should be noted that the Expert Consultation did not attempt to draw conclusions on whether and under which conditions mycopesticides can substitute chemical pesticides during locust control operations. Such a change in control tactics would need to be decided by locust control experts based on the performance of mycopesticides during locust campaigns.

Using the EU registration system as a guide, the following additional data and tests would be recommended:

- Data on possible contamination by human pathogens.
- Data on destruxin levels, especially destruxin A.
- For Green Guard, a series of mammalian toxicity tests.

In addition, it is recommended that an expert assessment be carried out to evaluate the likelihood of immunocompromised persons being affected specifically through the production and use of mycopesticides.

Part 4 Regulations on the use of microbial pesticides

Status of biopesticide regulations

44. The status of regulations for the introduction and registration of biopesticides in various countries was reviewed by the Expert Consultation. The results of a recent survey of biological pesticide regulations in Africa[10], carried out by IITA, CGIAR-SPIPM[11], IAPSC[12] and IBCD[13], were presented and discussed. Reference was made to the OECD draft on registration requirements for microbial pesticides and the relevant directive of the European Commission(EC). Furthermore, the recently adopted microbial pesticide registration scheme of CILSS (CSP, 2001) was presented, as were the principles of similar schemes in Africa and North America. A summary of the present status of biopesticide regulations in Africa is provided in Annex 6.

45. Increasingly, registration authorities recognize that microbial pest control agents are fundamentally different from chemical pesticides, and require special consideration. Many industrialised countries have implemented specific registration procedures for such control agents, as have now also several developing countries. However, in many countries, microbial pest control agents are still evaluated and authorised following the same system as for chemical pesticides. Using the conventional registration for microbial pest control agents can pose an unnecessarily high regulatory burden to satisfy inappropriate testing requirements.

46. Based on experience that registered microbial pest control products are less hazardous than chemical pesticides, regulatory authorities in some countries have taken a non-adversial approach to the registration of these agents. While continuing to ensure that mycopesticides are safe, they also actively promote the use of these products as an alternative to chemical pesticides. Several policies have been employed to reduce registration barriers for microbial pest control agents, but maintaining a high level of protection of human health and the environment in the countries concerned:

- tiered testing requirements (limits the amount of data to be generated to the minimum necessary);
- reduced registration fees;
- pre-registration meetings between authorities and registrants (clarifies data requirements and avoids unnecessary testing);
- waivers of some tests or data;
- fast-tracking (gives the review of biopesticides a higher priority than chemical pesticides);
- exchangeability of data (recognizes common properties within certain groups of pathogens for common regulatory treatment);
- provisional or limited-use registrations (allows temporary or localised use, while awaiting further data from tests or field use monitoring).

International Plant Protection Convention

47. The International Plant Protection Convention (IPPC)[14] Secretariat outlined the scope of the IPPC and its relevance to the importation and release of biological control agents. The process and responsibilities for the importation and release of biological control agents was discussed in terms of the IPPC and the International Standard for Phytosanitary Measures (ISPM) #3: *Code of Conduct for*

[10] Lomer *et al.* (2001)
[11] CGIAR-SPIPM: Consultative Group on International Agricultural Research – System-wide Programme on Integrated Pest Management
[12] IAPSC: Inter-African Phytosanitary Council
[13] IBCD: International Biopesticide Consortium for Development
[14] FAO (1999)

the import and release of exotic biological control agents[15], and in relation to the import, registration and release of biopesticides.

48. The main objective of the IPPC is to prevent the introduction and spread of pests of plants and plant products. The IPPC is an internationally legally binding agreement deposited with FAO, and all members of the World Trade Organization (WTO) are required to adhere to the international standards developed within the IPPC standard-setting framework. Under the IPPC, individual countries retain the sovereign authority to "*prohibit or restrict the movement of biological control agents and other organisms of phytosanitary concern claimed to be beneficial*„ (IPPC Article VII paragraph 1.d). The Expert Consultation noted that the wording of this import requirement, and its location in the Convention text, appears to put biological control agents on the same level as pest organisms. As a result, biological control agents obtain an unnecessary negative connotation. While recognizing the right of individual countries to regulate the importation of biological control agents, **the Expert Consultation suggested that the IPPC may want to rephrase this specific import requirement, in a future revision of the Convention text, to ensure that the positive sides of biological control agents are underlined.**

49. Under the IPPC, ISPMs are developed on an ongoing basis and are automatically accepted within the WTO process once adopted by the Interim Commission for Phytosanitary Measures (ICPM - governing body for the IPPC). One of those already developed is ISPM #3 (*Code of Conduct for the import and release of exotic biological control agents)*. A principal objective of this Code of Conduct is to facilitate the "*safe import, export and release of biological control agents…*„. It was noted that this ISPM is likely to be reviewed within the foreseeable future, as ISPMs are automatically considered for possible revision 5 years after adoption[16].

50. ISPM #3 defines a series of data requirements that must be submitted by the importer, and assessed by the designated authority according to the pest risk analysis ISPMs[17] [18] or other appropriate ISPMs[19], prior to import of a biological control agent, or import and release. The Expert Consultation noted that much overlap exists between the data requirements for import, as defined by the Code, and data requirements for the registration of biopesticides. In many countries, though, the national authorities responsible for (bio-)pesticide registration and those in charge of phytosanitary control are different entities within the national authorities. It is therefore possible that the risk assessments and evaluations for import and for registration of a biopesticide are at least partially duplicated. Since the importation requirements have to be met first before some of the data can be collected for the registration requirements, a delay in the process may occur. **The Expert Consultation recommends that FAO brings this problem to the attention of the governments and initiates a discussion on how this duplication can be avoided and how authorities can be encouraged to develop procedures for collaboration in reviewing, registering, and importing microbial control products, thereby reducing unnecessary regulatory burdens on biopesticides**.

51. With respect to the origin of biological control agents, the Code considers organisms exotic if they are not native to a country. This is done because the Code is directed at the movement of biological control agents from one country to another. The Expert Consultation recognized that this definition, based on political boundaries, may be logical in the framework of international trade. However, it is not considered appropriate for risk assessments. Examples were given where a microbial pesticide has been registered in an entire ecological region covering several countries (e.g. in the CILSS member states); or, alternatively, it would be authorised for use in one ecological zone of a country, but not in another (e.g. in Australia). **The Expert Consultation therefore**

[15] FAO (1996)
[16] The Fourth Session of the Interim Commission for Phytosanitary Measures (11-15 March, 2002) did not place the review of ISPM #3 on the work programme for 2002.
[17] FAO (1996)
[18] FAO (2001)
[19] FAO (2002)

recommended that, for the importation and registration of microbial biocontrol agents, the terms exotic and indigenous be based on ecological or geographical characteristics.

52. The Expert Consultation also discussed the term 'exotic' in the taxonomic context, that is whether it should apply to species, varieties and subspecies or even to lower taxonomic units. No consensus was reached on this issue.

FAO guidelines on biopesticides registration

53. In 1988, FAO published its *Guidelines on the registration of biological pest control agents*. Since its publication, the registration and regulation of biological pest control agents have seen important developments in many parts of the world. The Expert Consultation therefore reviewed these guidelines and discussed the need to update or modify them, taking into account the information received on the status of such regulations world wide. It came to the following conclusions:

54. Harmonisation of data requirements and of procedures for registration was recognized as an important step to facilitate the use of biopesticides. It provides guidance and strengthens the confidence in decision making by registration authorities in particular in developing countries. Therefore, it should be encouraged by FAO. The publication of updated Guidelines may be one of the instruments to facilitate such harmonization.

55. The FAO Guidelines need updating to reflect changes in the science and in the policies of pesticide registration since they were first developed. Guidelines covering microbial pest control agents should be dealt with as a priority, as they can be updated immediately based on the recommendations of this Expert Consultation. The Guidelines covering biochemical pesticides could be updated later.

56. **With respect to revising the Guidelines, the following recommendations were made:**

(a) A tiered system of data requirements is recommended, since it provides for optimal flexibility. The tier 1 test is typically a “maximum challenge test,, with test doses as much as 100 to 1000 times higher than expected field exposure. Tier 2 tests are used to refine the conclusions of tier 1 and typically include longer term studies at doses reflecting realistic exposures. It was noted that no microbial pesticides registered in the USA, Canada and EU required testing beyond tier 1. However, the Expert Consultation considered that upper tiers need to be defined in the Guidelines.

(b) The objective of the FAO Guidelines should be to define minimum data requirements to ensure that registered microbial pest control agents are efficacious and do not pose an unacceptable risk to humans and the environment. The updated FAO Guidelines should reflect the experience gained in the development of existing, relatively simple and robust, guidelines.

(c) With respect to risk assessment in the framework of registration, the distinction between exotic, indigenous or ubiquitous organisms should not be based on political (country) boundaries, but on ecological and geographical criteria.

(d) The issue of similarity between microbial pest control agents should be addressed in the revised Guidelines, especially with respect to exchangeability of certain data (i.e. waivers of certain data on a case-by-case basis based on scientific justification and sound knowledge about similar organisms).

(e) Data on efficacy testing are considered an essential part of the Guidelines. The issue of mutual acceptance of efficacy data from similar agro-ecological zones needs to be addressed, as this may reduce the data generation by registrants. Good descriptions of the ecological conditions during the efficacy trials would be a minimum requirement for such

mutual acceptance. Guidelines on data to be collected during field trials are available and should include information needed for comparison of physical and environmental conditions. EPPO[20] and CILSS, amongst others, have developed such protocols.

(f) The issue of data waivers needs to be addressed in the Guidelines. For instance, a waiver for certain toxicity tests may be granted in a country where personal protection during production is likely to be effectively monitored by the government.

(g) The guidelines should include reference to FAO's Pesticide Specifications and the IPPC, as they now also cover microbial pest control agents. The guidelines might reference the much more comprehensive specification guidelines.

(h) The current Guidelines do not discuss the issue of experimental use permits or provisional registrations. Procedures for use of either or both of these options should be discussed.

(i) Worker safety issues are not covered in the present Guidelines. It is recommended that they are addressed in the revision.

(j) A section should be included on potential barriers to the development and registration of microbial pesticides, and practical methods of overcoming them.

(k) A section should be included on special issues to be considered by developing countries.

[20] EPPO: European and Mediterranean Plant Protection Organization

Pesticide specifications

57. For many years, FAO has been developing specifications for chemical pesticides in agriculture, to ensure their safety and efficacy and to avoid misuse and fraud. Similarly, WHO has set technical specifications for pesticides used in public health. Recently, both organizations agreed to join forces and issue joint pesticide specifications for pesticides in agriculture and public health. As a result of this cooperation, guidelines were recently developed which facilitate the development of such joint specifications for microbial pesticides. A first set of specifications is now being issued for bacterial larvicides (for public health use).

58. The Expert Consultation recognized that quality assurance of microbial pesticides is of vital importance to the successful adoption of microbial pesticides. **It therefore recommended that the FAO and WHO, though its joint Pesticide Specification Scheme, actively pursue the development of specifications for microbial pesticides.**

Data sharing and capacity building

59. The regulation of biological control agents, and particularly of microbial pesticides, requires specific expertise of phytosanitary and registration authorities. This is why many industrialised countries have specialized units within their regulatory organizations dealing with these issues. The existence of sufficient technical capacity also allows for science-based measures to be taken to reduce registration barriers.

60. **The Expert Consultation noted that the scientific and technical experience with microbial pesticides is still limited in many developing countries. Therefore, if the use of biological control agents is to be promoted, continuous technical and financial support will be needed to strengthen institutional capacities in developing countries.** It was also noted that through the acceptance of regional regulatory authorities, administrative and technical work can be reduced considerably.

61. Furthermore, **the Expert Consultation recommended that procedures for data sharing be further developed, to reduce duplicating the work involved in evaluations and make optimal use of limited funds and expertise**. In first instance, one may think of mutual access to the evaluations of registration dossiers, both between developing countries themselves, as well as between industrialized and developing countries. Another tool that may relatively rapidly improve the information available to developing countries is the elaboration of international consensus documents. Such independent scientific reviews would outline the current, internationally accepted, scientific opinion on the biology and risks of a given microbial pest control agent. An independent international organization, such as FAO and/or WHO, could be the clearing-house for the production and distribution of these consensus documents.

Part 5 Closure

62. The meeting was closed by Mr. Abderrahmane Hafraoui, Senior Officer in charge of the Locust and Other Migratory Pests Group of FAO and by Mr.Gero Vaagt, Senior Officer of the Pesticides Management Group of FAO. Both thanked all participants in the Expert Consultation for the information and advice which they provided to FAO. While clearly “the devil was in the detail,,, FAO does feel that it can continue the promotion of *Metarhizium anisopliae* var. *acridum* for locust control with increased confidence. FAO intends to make the meeting report, and a summary of the risk assessment of the two commercial formulations of *Metarhizium*, widely available to locust affected countries and other interested parties. Furthermore, FAO will take into account the more general recommendations made for improving FAO’s guidance on the registration of microbial pest control agents. In this respect, FAO expects that its *Guidelines on the registration of biological control agents* will be updated shortly, as part of a larger process of updating the *International Code of Conduct on the Distribution and Use of Pesticides*, and its accompanying technical guidelines.

After thanking everybody again for their valuable contributions Mr. Hafraoui formally closed the Expert Consultation.

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Annex 2 Agenda

Monday, 3 December 2001

- Opening
- Adoption of the agenda
- Election of the Chairperson
- Objectives of the Expert Consultation; discussion on procedures
- Background information on the use of *Metarhizium* against locusts and grasshoppers

Tuesday, 4 December 2001

- Review of general information on possible risks associated with the use of mycopesticides for insect control, comparison of such risks with those associated with the use of chemical insecticides
- Risk assessment on the use of two *Metarhizium* products against locusts and grasshoppers
- Conclusions on risks of large-scale use of *Metarhizium* against locusts and grasshoppers

Wednesday, 5 December 2001

- Status of regulations for the introduction and registration of biopesticides in locust-affected and other countries
- Conclusions on status of registration of biopesticides
- Guidelines by FAO and other organizations on the registration of biopesticides

Thursday, 6 December 2001

- Continuation on guidelines
- Conclusions on the possible need for revised FAO guidelines
- FAO Code of Conduct for the Import and Release of Exotic Biological Control Agents
- Conclusions on the possible need to modify FAO Code of conduct for microbial pesticides

Friday, 7 December 2001

- Background information on the taxonomy and distribution of *Metarhizium*, in particular *Metarhizium anisopliae* var. *acridum*
- Discussion on quarantine issues related to the import of products of *Metarhizium anisopliae* var. *acridum*
- Conclusion on quarantine issues
- Formulation of recommendations

Annex 3 Working documents

Anon (undated) Background information on the use of *Metarhizium* against locusts (selected recent abstracts).

Driver F, Milner RJ & Trueman WH (2000) A taxonomic revision of Metarhizium based on a phylogenetic analysis of rDNA sequence data. *Mycological Research* **104** (2): 134-150

EC (2001) Commission Directive 2001/36/EC of 16 May 2001 amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market. Official Journal of the European Communities L 164/1 (20 June 2001), Brussels.

FAO (1988) Guidelines on the registration of biological pest control agents. Food and Agriculture Organiszation of the United Nations, Rome, 7pp..

FAO (1996) Code of conduct for the import and release of exotic biological control agents. International Standards for Phytosanitary Measures – Part 1 – Import Regulations. Secretariat of the International Plant Protection Convention, Food and Agriculture Organization of the United Nations, Rome, 19 pp..

FAO (1999) International Plant Protection Convention. New revised text. Food and Agriculture Organization of the United Nations, Rome, 26 pp..

Goettel MS, Hajek AE, Siegel JP & Evans HC (2001) Safety of fungal biocontrol agents. pp. 347-375 *In:* Fungi as biocontrol agents. TM Butt, C Jackson & N Magan (*eds.*). CAB International, Wallingford.

Liégeois E (2001) Risk assessment of Green Muscle ™ and Green Guard ™. An analysis of registration dossiers of two commercial formulations of *Metarhizium anisopliae* var. *acridum*. FAO, Rome. For internal use only.

Lomer C, Cherry A & Langewald J (2001) Report on the joint IITA / CGIAR-SPIPM / IAPSC / IBCD survey of biological pesticide regulations in Africa. Draft version. International Institute of Tropical Agriculture, Cotonou, 47 pp.

Milner RJ & Hunter D (submitted) Recent developments with the use of fungi as biopesticides against locusts and grasshoppers in Australia. *Journal of Orthoptera Research*.

NRA (2000) Guidelines for the registration of biological agricultural products. January 2000. National Registration Authority for Agricultural and Veterinary Chemicals. Canberra, Australia.

OECD (2001) Guidance for registration requirements for microbial pesticides. Working Document. Draft April 8, 2001; updated June 23, 2001. Working Group on Pesticides. Organization for Economic Cooperation and Development, Paris.

Stolz I, Nagel P, Lomer C & Peveling R (submitted) Susceptibility of the hymenopteran parasitoids *Apoanagyrus (=Epidinocarsis) lopezi* (Encyrtidae) and *Phanerotoma* sp. (Braconidae) to the entomopathogenic fungus *Metarhizium anisopliae* var. *acridum* (Deuteromycotina: Hyphomycetes).

Strasser H, Vey A and Butt TM (2000) Are there any risks in using entomopathogenic fungi for pest control, with particular reference to the bioactive metabolites of *Metarhizium*, *Tolypocladium* and *Beauveria* species? *Biocontrol Science and Technology* **10:** 717-735

Vey A, Hoagland R & Butt TM (2001) Toxic metabolites of fungal biocontrol agents. pp. 311-340 *In:* Fungi as biocontrol agents. TM Butt, C Jacskon & N Magan (*eds.*). CAB International, Wallingford.

Annex 4. Presentations made to the Expert Consultation

Metarhizium use in Australia. **Graeme Hamilton**, Australian Plague Locust Commission, Canberra.

Use of *Metarhizium anisopliae* var. *acridum* for biocontrol of locusts and grasshoppers: safety, registration and market issues. **Matt Thomas**, NERC Centre for Population Biology at Imperial College & CABI Bioscience, Ascot.

Experience with *Metarhizium* in the Central Region. **Tsedeke Abate**, EMPRES- Central Region Programme.

Risk assessment of Green Guard and Green Muscle. **Eric Liégeois**. Ministry of Agriculture, Brussels.

Survey of biological pesticide regulations in Africa**. Chris Lomer, Andy Cherry and Jürgen Langewald**, IITA, Cotonou [*presented by Harold van der Valk*].

Status of biopesticide registration in CILSS countries. **Amadou Diarra**, Institut du Sahel, Bamako & **Abdoulaye Niassy**, Direction de la Protection des Végétaux, Dakar.

Microbial registration systems in countries other than CILSS and EU. **Larry Vaughan**, Virginia Polytechnic and State University, Blacksburg.

Updating of FAO Guidelines on registration of biological pest control agents. **Ron Parker**, EPA & FAO, Rome.

FAO Pesticide specifications. **Gero Vaagt**. FAO Pesticides Management Group, Rome.

The International Plant Protection Convention and biological control agents. **David Nowell**, FAO IPPC Secretariat, Rome.

Background information on the taxonomy and distribution of *Metarhizium*, in particular *Metarhizium anisopliae* var. *acridum.* **Graeme Hamilton**, Australian Plague Locust Commission, Canberra.

Annex 5 Risk assessment of two commercial formulations of *Metarhizium anisopliae* var. *acridum* - Summary

Summary of study results (endpoints) used in the risk assessment of Green Muscle and Green Guard following the EU registration system. The data and interpretations below are based on the dossiers provided to FAO in November 2001. It should therefore be underlined that the table does not necessarily contain a complete overview of the characteristics of the products. The comments in brackets [ ] are likely applicable if the EU registration system would be used.

Data	Green Muscle			Green Guard		
	Sufficient data	**Insufficient data**	**Findings**	**Sufficient data**	**Insufficient data**	**Findings**
Identity						
Data provided by:	X		CABI Bioscience, Ascot, United Kingdom	X		Australian Plague Locust Commission (APLC), Canberra, Australia
Scientific name	X		*Metarhizium anisopliae* var. *acridum*	X		*Metarhizium anisopliae* var. *acridum*
Isolate	X		IMI 330189	X		FI 985
Technical material; spore density	X		Dry powder; 5 x 10^{10} conidia/g dry powder	X		Dry powder; 4 x 10^{10} conidia/g dry powder
Microbial purity		X	Quality control specifications suggest that no harmful micro-organisms are likely to be present in the product. However, it is recommended that a confirmation for certain human pathogens is provided.		X	Quality control specifications suggest that no harmful micro-organisms are likely to be present in the product. However, it is recommended that a confirmation for certain human pathogens is provided.
Commercial product						
Trade name	X		Green Muscle™	X		Green Guard™
Formulation type; concentration	X		Oil Flowable (OF); 400 g conidia/L	X		Oil suspension; 321 g conidia/L
Presence of metabolites (destruxins)		X	Unlikely to be produced, based on efficacy & mammalian toxicity data. However, it is recommended that absence of destruxins is confirmed by a specific study during the production process.		X	Isolate is producing destruxin A. Analytical data should be provided to show that the amount produced is not (eco-)toxicologically significant, especially since no mammalian toxicity studies were provided.
Viability	X		>90% at packing; >80% acceptable after storage	X		>85% (based on batch analysis series) [*no minimum viability standard provided*]
Moisture content	X		<5% at packing		X	No data provided

Data		Green Muscle			Green Guard		
		Sufficient data	Insufficient data	Findings	Sufficient data	Insufficient data	Findings
	Expected shelf life (as OF formulation)	X		4 °C: 3 years 10-20 °C: 2 years 30 °C: 1 year 40 °C: 1 month 50 °C: 1 week		X	No data provided
	Contaminants		X	<0.002%; CFU determined by number; but see remark on microbial purity above		X	Between 0.000025% and 0.0025%; CFU determined by number; but see remark on microbial purity above
	Particle size	X		By volume: <10 _m: 80% <60 _m: 99.9% <100 _m: 100%			
Biological properties of the organism							
	Origin	X		Niger, isolated from the grasshopper *Ornithacris cavroisi* (Acrididae)	X		Australia, isolated from the locust *Austracris guttulosa* (Acrididae)
	Target organisms	X		Locusts and grasshoppers (Acridoidea)	X		Locusts and grasshoppers (Acridoidea)
	Mode of action	X		Systemic pathogen; mechanic & enzymatic penetration of the cuticle	X		Systemic pathogen; mechanic & enzymatic penetration of the cuticle; production of destruxins could possibly contribute to mortality process.
	Virulence	X		*Schistocerca gregaria*: LD_{50} (5 days) = 5 x 10^4 conidia/ insect ; LD_{90} (6 days) = 5 x 10^4 conidia/insect (conidia suspended in oil)	X		*Chortoicetes terminifera*: LD_{50} (time?) 420 conidia/insect *Phaulacridium vittatum*: LD_{50} (time?) 1200 conidia/insect *Locusta migratoria*: LD_{50} (time?) 4400 conidia/insect
	Host range	X		All available data suggest that the isolate does not adversely affect arthropods other than locusts and grasshoppers, under natural conditions	X		All available data suggest that the isolate does not adversely affect arthropods other than locusts and grasshoppers, under natural conditions
	Optimal temperature for spore germination	X		30°C; almost no germination occurred at >40°C	X		Fastest colony growth at 32°C; strong decrease at 35°C, and no measurable growth at >40°C
	Optimal temperature for hyphal extension	X		27°C; strong decrease at 35°C, and no measurable growth at >40°C			

Data	Green Muscle			Green Guard		
	Sufficient data	Insufficient data	Findings	Sufficient data	Insufficient data	Findings
Effect of relative humidity	X		Conidia formulated in oil can infect insects regardless of ambient humidity	X		Conidia formulated in oil can infect insects regardless of ambient humidity
Effect of light		X	No data provided. UV light considered to be detrimental to spore survival. However, the infectivity of the product still has a half-life of 7-8 days under hot/arid field conditions	X		Estimated half-life when exposed to direct sunlight is 7-11 hours. However, the infectivity of the product still has a half-life of 4-5 days under hot/arid field conditions
Sensitivity to fungicides	X		Sensitive		X	No data provided
Genetic stability during production process	X		Quality assurance methodology appears to prevent loss of virulence or change of morphological characteristics	X		Quality assurance methodology appears to prevent loss of virulence or change of morphological characteristics
Genetic stability under natural conditions		[X]	No data provided, but this aspect remains unclear for most microbial pest control agents		[X]	No data provided, but this aspect remains unclear for most microbial pest control agents
Mammalian toxicity, pathogenicity & infectivity of the isolate ("technical concentrate")						
Acute oral toxicity	X		LD_{50} (rat) >2000 mg/kg (189M SU formulation)		X	No data provided for the isolate [*it would be recommended that study is submitted*].
Acute dermal toxicity	X		LD_{50} (rat) >2000 mg/kg (dry spores)		X	No data provided for the isolate [*it would be recommended that study is submitted*].
Acute dermal toxicity & irritation	[X]		LD_{50} (rabbit) >2000 mg/kg; slight skin irritant (dry spores) [*definitive report would need to be provided*]			
Acute inhalation toxicity	[X]		LC_{50} (rat) >4.85 mg/L (or >2.5×10^8 conidia/L) (dry spores)		X	No data provided for the isolate. Noted is that the spore size of this isolate is about twice that of IMI 330189, and inhalation of spores will therefore be less deep [*it would be recommended that study is submitted*].
Acute inhalation toxicity	[X]		Rat. No mortality or pathogenicity at 1.1×10^8 conidia/animal (both for viable and non-viable dry spores); complete clearance of spores extrapolated to occur in 21-36 days. [*definitive report would need to be provided; ideally to be repeated with prolonged test period to assess clearance time from lungs*]			

Data	Green Muscle			Green Guard		
	Sufficient data	**Insufficient data**	**Findings**	**Sufficient data**	**Insufficient data**	**Findings**
Acute intra-peritoneal toxicity		X	Rat. No mortality or pathogenicity at 9.1 x 10^8 conidia/animal (spore suspension); conidia persisted in spleen and liver during observation period (14 days), but not in intraperatoneal cavity; spores remained viable but did not grow [*no agreement reached on need for prolonged test period to determine clearance times from organs*]		X	No data provided for the isolate [*it would be recommended that study is submitted*].
Eye irritation	[X]		Rabbit. Non-irritating at 5 x 10^9 conidia/animal (dry spores) [*second study exists but was not provided; data would need to be submitted*]		X	No data provided for the isolate [*it would be recommended that study is submitted*].
Dermal irritation	X		Rabbit. Non-irritating at 2.5 x 10^{10} conidia/animal (dry spores)		X	No data provided for the isolate [*it would be recommended that study is submitted*].
Infective dose and transmissibility	X		Very exceptional cases of mammalian pathogenicity have been observed with some isolates of *Metarhizium*. However, species of *Metarhizium* are not normally considered to be invasively pathogenic in mammals	X		Very exceptional cases of mammalian pathogenicity have been observed with some isolates of *Metarhizium*. However, species of *Metarhizium* are not normally considered to be invasively pathogenic in mammals
Skin sensitization		X	Guinea Pig. Study results inconclusive [*new study would need to be submitted*]		X	Dry spores considered to be sensitizing and appropriate protective clothing during production process recommended. Oil formulated spores not considered sensitizing [*statement to be confirmed*].
Genotoxicity (in vitro)		X	Not provided. [*Ames test would be recommended*]		X	No data provided for the isolate [*Ames test would be recommended*].
Genotoxicity (in vivo)		[X]	Need for such data depends on results in vitro study		[X]	Need for such data depends on results in vitro study.

Data		Green Muscle			Green Guard		
		Sufficient data	Insufficient data	Findings	Sufficient data	Insufficient data	Findings
	Short-term toxicity, pathogenicity & infectivity	[X]		In absence of symptoms of pathogenicity or toxicity in acute studies, and absence of proliferation in organs and tissues infected at human body temperature, short-term studies do not appear to be necessary. [*However, absence of toxin production needs to be confirmed (see "presence of metabolites")*]		[X]	Need for such data depends on results acute toxicity studies..
Mammalian toxicity, pathogenicity & infectivity of the commercial formulation							
	Acute oral, dermal & inhalation toxicity; skin & eye irritation, skin sensitization		[X]	Formulants of Green Muscle OF have low toxicity; one formulant is a moderate skin irritant; Green Muscle OF is expected to have comparable (or lower) toxicity than the technical concentrate. [*However, acute toxicity studies with the formulation are recommended to confirm this assessment*]	X		Formulant (corn oil) essentially non-toxic; Green Guard is expected to have comparable (or lower) toxicity than the technical concentrate. No direct need for studies with formulated product.
Residues							
	Acceptable Daily Intake (ADI)	[X]		No ADI needs to be proposed since: micro-organism does not grow at human body temperature; no adverse effects observed in toxicity studies; no toxins reported in the formulation [*to be confirmed*].		[X]	Data are not available to set, or waive, an ADI.
	Maximum Residue Limits (MRL)	X		Since no ADI has to be determined, no MRLs are needed to be set either. No residue trials on crops required.		[X]	See ADI
Fate and behaviour in the environment							
	Persistence and multiplication in soil	X		Naturally, the isolate can routinely be found in the environment; half-life after ULV application is 6-8 days under Sahelian conditions; no specific concerns with respect to persistence	X		Study provided on presence of viable spores in soil after experimental treatment against locusts; this did not result in colonies of the isolate being formed, suggesting the survival of spores in the soil is low.

Data		Green Muscle			Green Guard		
		Sufficient data	Insufficient data	Findings	Sufficient data	Insufficient data	Findings
	Persistence and multiplication in (ground-)water	X		Contamination of ground-water is very unlikely	X		Contamination of ground-water is very unlikely. Studies provided on concentrations of spores found in surface water after treatment showed that they were well below the LD_{50} of the most sensitive of aquatic organisms tested (ranged from 2 - 130 conidia/ml).
Ecotoxicology							
	Effects on birds	[X]		No effects observed in ring-necked pheasants after consumption of spore-coated feed or infected grasshoppers [*full report would need to be submitted*]		[X]	No data provided for the isolate, but reference was made to a study carried out with IMI 330189. No detrimental effects on birds are expected.
	Acute toxicity, fish	[X]		Zebra fish. LC_{50} (96 hours, static) >100 mg/L [*full report would need to be submitted*]	[X]		Eastern rainbow fish (fry). 8 day, semi-static test at dose equivalent to 3 x 10^{13} conidia/ha: no effects on degree of imbalance of fry [*full report would need to be submitted*]
	Acute toxicity, fish	[X]		Rainbow trout. LC_{50} (96 hours, static) >100 mg/L [*full report would need to be submitted*]			
	Acute toxicity, crustaceans	[X]		Water flea (*Daphnia magna*). EC_{50} (48 hours, static) >100 mg/L [*full report would need to be submitted*]	[X]		Mayfly larvae (*Ulmerophlebia* sp.). LC_{50} > 2 x 10^6 conidia/ml [*full report would need to be submitted*].
	Acute toxicity, crustaceans	[X]		Fairy shrimp (*Streptocephalus sudanicus*). Mortality observed without fungal growth [*full report would need to be submitted*]	[X]		Water flea (Ceriodaphnia dubia) LC_{50} > 5000 conidia/ml [*full report would need to be submitted*].
	Effects on non-target arthropods	X		See "host range,,	X		See "host range,,.
	Toxicity, earthworms	[X]		(*Eisenia fetida*) LC_{50} (14 days) >1000 mg/kg substrate [*full report would need to be submitted*]	X		Isolate was not found in soil after treatments, so exposure of earthworms unlikely and tests not carried out.
	Toxicity, reptiles [normally not required]	X		No mortality of *Acanthodactylus dumerili* after exposure to 5 x 10^8 conidia/L air. No conidia were recovered from lung and liver tissues.	X		Not required.
	Plants, phytotoxicity	X		No phytoxicity observed on millet, sorghum or cassava	X		No data provided, but no phytoxicity expected.
Recommended precautions							

Data		Green Muscle			Green Guard		
		Sufficient data	Insufficient data	Findings	Sufficient data	Insufficient data	Findings
	During handling of the dry powder	X		"Do not eat, drink of smoke; avoid formation of respirable particles; do not wear contact lenses (the spores swell on contact with water)"	X		"Use adequate ventilation to keep the airborne concentrations of this material below (Worksafe Australia) exposure standards for vegetable oil mists. If a risk of exposure exists, wear approved respirator. Local exhaust ventilation and/or enclosure of the process is preferred in these case".
	During handling of formulated product	X		"Avoid exposure when measuring or pouring; wash hands immediately after use".	X		"Avoid inhalation of spray mists. Workers should wash exposed skin several times daily with soap and water. Use barrier cream and PVC gloves".
	During storage of formulated product	X		"Store in a cool, dark, dry place, away from children or animals".	X		"Protect from light and store away from heat. Store in the original container in a dry area".
	During transport	X		"Not classified as dangerous in the meaning of transport regulations".	X		"Not classified as dangerous good by the Australian Code on the Transport of Dangerous Goods by Road and Rail".
	In case of fire	X		"Extinguish using water, foam, dry powder or carbon dioxide".	X		"Not applicable".
	Re-entry period for humans or livestock	X		Not required (see Residues)		[X]	Cannot be (yet) determined
	Procedures for destruction & decontamination	X		Excess formulation may be disposed of by pouring over straw or other combustible material, and subsequent burning; do no flush into surface water or sanitary sewer systems.	X		Triple wash containers and place contaminated materials in labelled containers and dispose of in an approved local landfill.
	Material Safety Data Sheet		X	To be established	X		Available.

Annex 6 Status of biopesticide registration in Africa - Summary[21]

Introduction

To ensure that pesticides are effective, of suitable quality and of low hazard to humans and the environment, there have been various attempts to strengthen pesticide registration in Africa. In 1992 the member states of the Permanent Inter-State Committee for Drought Control in the Sahel (CILSS) in West Africa signed a Common Regulation for the Registration of Pesticides. The CILSS member states are Burkina Faso, Cape Verde, Chad, The Gambia, Guinea Bissau, Mali, Mauritania, Niger and Senegal. Countries of the humid zone of West Africa, comprising Benin, Ivory Coast, Ghana, Guinea, and Togo, have harmonized requirements for submitting data to national regulatory authorities. In Eastern and Southern Africa, harmonized requirements are still in their infancy.

Regulatory procedures are more advanced for synthetic pesticides than for biopesticides. The availability and the flow of biopesticides into the African market have been constrained by various factors including the small and specialized market, the lack of harmonized national registration procedures and the absence of registration schemes in some countries. Further to these constraints, Africa lacks adequate institutional capacity necessary to support the development and promotion of biopesticides. The slow mode of action and narrow host range of biopesticides when compared to synthetic pesticides make them less attractive to growers who are currently accustomed to quick knock-down and the broad spectrum action of synthetic pesticides. All these factors have resulted in making biopesticides less competitive as compared to conventional pesticides that have well established markets.

In view of this background, guidelines for a regional harmonized registration and regulation system for biopesticides have to be developed to enhance the use of biopesticides in the region.

Biopesticides registration in CILSS member states.

The objective of the Common Regulation agreed upon by CILSS member states is to combine the experience and expertise of member states with respect to the evaluation and registration of pesticides in order to ensure their rational and judicious use, as well as the protection of human health and the environment. It concerns the authorization, distribution, use, and control of active ingredients and formulated products of pesticides in the member states. It is applicable to both synthetic chemical pesticides and biopesticides. The Common Regulation defines the responsibilities of the member states, the duties of the regional structure and the registration conditions.

During the years that followed the signature of the Common Regulation, CILSS member states have modified their national phytosanitary legislation, in order to take into account pesticide registration by the Sahelian Pesticide Committee (CSP) as well as the implementation of pre- and post-registration activities such as pesticide efficacy evaluation, control of pesticide import and use, and the monitoring of ecological and health effects.

The common pesticide registration body of CILSS is the CSP. It assesses registration dossiers submitted by the agro-chemical industry and grants sales permits valid for all its member states. It became operational in 1994 after the development of dossier specifications for synthetic pesticide registration.

After a series of workshops on biopesticide registration in Bamako (Mali) and Cotonou (Benin), the composition of a dossier for biopesticide registration was developed by the CSP in 2000, six years after that for synthetic pesticides.

[21] Summary prepared by Amadou Diarra, CILSS – Comité Sahélien des Pesticides

During the first meeting in 1999 in Bamako, the workshop reviewed the availability of existing documents and the rationale for registration of biological pesticides. It agreed upon definitions and a framework of a registration document. During the second meeting in Bamako in 2000, the workshop discussed the first draft of the Directives on biopesticide registration. The pan-African workshop on biopesticide registration in Cotonou (Benin) was crucial in the sense that members of the CSP present in that meeting worked out a decision scheme for biopesticide registration. Based upon that scheme, the CSP granted, in 2001, a provisional registration for Green Muscle (*Metarhizium anisopliae*) for the control of locusts and grasshoppers in CILSS member states. The final composition of the dossier for biopesticide registration was finalized later in the year.

The CILSS biopesticide registration dossier is composed of the following sections:
- an application form for the formulated product dully signed by the applicant;
- a comprehensive summary of all the dossiers presented;
- a dossier on the identity of the formulated product;
- a dossier on the identification of the biological agent;
- a dossier on the biological efficacy of the formulated product;
- a toxicological dossier;
- an environmental dossier;
- a dossier on the label and packaging;
- a sample of the formulated product.

To ease biopesticide registration, a tiered system has been introduced in the evaluation of dossiers. This translates into initially reduced data requirements, for example:

Toxicological studies (non target, mammals *etc*).

Tier 1 : an evaluation of the potential risk due to pathogenicity, infectivity and toxicity;
Tier 2 : more information is needed where infectivity or toxicity is expected without any evidence of pathogenicity

Lessons learned

The development of registration procedures is a long process. It requires capacity building, willingness to accept data from other areas and the assumption that ecological differences and similarities are more important than political boundaries. The CILSS area is a rather environmentally homogeneous area with similar pests and agronomic problems. Reducing problems related to drought has been, since the 1970s, a leitmotiv to bring these countries together. They have tried to attain food security and manage natural resources together.

Experiences with biopesticides in CILSS member states

Large-scale use of biopesticides in CILSS member states is not well documented. *Metarhizium anisopliae* var. *acridum* has been widely tested against grasshoppers and locusts in the Sahel, but larger scale use only started in Niger in 2001. However, several experiments have been successful with the utilisation of *Bacillus thuringiensis* to control lepidopterous and coleopterous insects as well as mosquitoes. *Beauveria bassiana* has also been successfully tested against grasshoppers and locusts in many countries. Gypsy moth and beet army worm are also successfully controlled with formulated NPV.

Biopesticide registration in some other countries in West Africa

Countries belonging to the humid zone of West Africa have tried to harmonize pesticide registration. Benin, Ivory Coast, Ghana, Guinea and Togo have harmonized the administrative forms to register pesticides. However, registration is done at the national level.

Metarhizium spp. have been developed by the IITA Branch in Benin. The use of *Metarhizium* to control grasshoppers in rice fields has been promoted. These countries, like the CILSS member states, do not have much experience with large scale use of biopesticides.

Biopesticide registration in Eastern Africa

The Eastern African community includes Ethiopia, Kenya, Tanzania and Uganda. Guidelines for a regional harmonized registration and regulation system for biopesticides do not exist in East Africa. One of the major constraints is the lack of adequate institutional capacity necessary to support the development and promotion of biopesticides in the region.

During the pan-African workshop in Benin, the overall objective of the Eastern African work-group was to achieve consensus on harmonization of biopesticide registration procedures in the East African region. The specific objectives were to examine areas of commonalities and differences for developing harmonized guidelines for biopesticide registration procedures for the region and to promote their safe use. The work-group agreed upon general registration procedures. However there was no consensus concerning the harmonization of ecotoxicologial data. By contrast, in West Africa the CSP is supported with supplemental data produced in the Sahel by the CERES/LOCUSTOX Foundation based in Dakar, Senegal. Data generated in one of the CILSS countries are valid for the registration of products in all nine CILSS countries. In Eastern Africa, no specialized laboratory exists that produces such data on behalf of the sub-region. Ecotoxicological data are accepted by Eastern African countries on a case-by-case basis following judgements on the comparability of the relevant ecological zones.

CILSS countries accept the results of efficacy tests obtained from field trials in any of the nine member countries. Eastern Africa, however, is ecologically much more heterogeneous compared with West Africa and, as for ecotoxicological data, the appropriateness of efficacy data from different regions has to be assessed on a case-by-case basis. Non-target data should be obtained from species closely related or similar with those species identified as important for the ecological zone where the product is intended to be used. In the case of efficacy data, Eastern African authorities consider only such data which were generated locally, in their own respective countries.

During the pan-African workshop in Benin, representatives from Eastern Africa expressed hope that a regional structure providing ecotoxicological data for the sub region could be established. The structure could be similar to CERES/LOCUSTOX. It was further proposed to establish a regional network of national institutions for Eastern Africa in collaboration with DLCO as well as an international research institute (for instance ICIPE) in the region active in this field. Collaboration with CILSS and the pesticide industry would also be advantageous. The national institutions would need to be strengthened in terms of physical and personnel capacities. The East African countries hope to be supported by FAO in these efforts.

Experiences with biopesticides in Eastern Africa

Experiences with *Metarhizium, Bacillus thuringiensis,* and *Beauveria bassiana* in Sudan, Ethiopia, Eritrea, Egypt and Yemen were presented during the pan-African workshop in Benin. The target organisms were *Spodoptera littoralis*, *Schistocerca gregaria* and *Anacridium melanorhodon* in Sudan, and grasshoppers in Yemen. Trials were conducted in Egypt and Sudan with positive results. The EMPRES-CRC research initiative played an important role in these findings. In Yemen, no side-effects were observed on honey bees. Research on native strains are conducted in Eritrea and Ethiopia. Sudan has discontinued this type of research.

All countries will now support the registration process of biopesticides and specific proposals are under review. Biopesticide registration is part of pesticide legislation in Egypt and Sudan. No

biopesticide registration system has been yet established for Eritrea, Ethiopia and Yemen. Ethiopia has draft legislation for biological control agents, including biopesticides.

Summary

Many countries do not have specific guidelines for microbial pesticides. Among those that do, these guidelines include detailed technical procedures regarding data requirements and testing protocols. Recent efforts in Africa have resulted in microbial registration guidelines in the nine West African countries of CILSS, Madagascar and South Africa. Guidelines in different stages of draft or adoption have been written in Ethiopia and Kenya. The publications used most often as the conceptual foundation of these efforts are the FAO Guidelines on the Registration of Biocontrol Agents (FAO, 1988), and the mammalian toxicology recommendations for microbial pesticides published by WHO (1981).

In order to operationalize a favoured status for microbial pesticides, authorities in Africa have adopted some of the following tactics to reduce the cost of registering biopesticides:

- Tiered testing
- Reduced registration fees
- Waivers of some tests
- Recognizing common properties within certain pathogen groups for common regulatory treatment.
- Provisional registration

Because most personnel in registration authorities have little experience with biological control agents, they may be hesitant to make decisions. Access to information resources and pooling of experience through workshops on biopesticides, will increase the knowledge and confidence of decision makers.

In general, biopesticides are safer to use than most currently available synthetic pesticides. Efficacy can be equal or even superior to chemicals, but the application requirements may be different from the experience of users and may require education for proper use and with respect to performance characteristics. Safety for users, bystanders, animals and the environment are the characteristics that justify a general preference for biopesticides over standard chemical pesticides. Accidental exposure is likely to have less severe consequences compared to synthetic chemicals. Use of biopesticides, where appropriate, provides a means to reduce future accumulation of pesticides and their associated disposal problems. Furthermore, unlike synthetic chemical pesticides, entrepreneurs in developing countries have the potential to develop and manufacture new products for local and regional markets. Such future benefits should be considered by registration authorities in determining incentives for registering biopesticides and the lowering of barriers to registration. Some of these barriers are:

- Quarantine
- Heavy regulatory burden for the development of biopesticide registration guidelines
- Small markets for biopesticides
- Requirements for locally generated efficacy data
- Difficulty for registrants in obtaining affordable, high quality toxicology data in Africa
- Lack of microbial experience by regulatory decision makers