

REBECA: Report of the second workshop of Work Package 4, 'Macrobia' (Invertebrate) Biological Control Agents, held in Frankfurt, July 5-6, 2007

The main purpose of this workshop was to reach agreement on the recommendations to be made at the forthcoming Brussels Conference and in the Final Report on the project, in line with the primary objective of REBECA and specifically of Work Package 4: to develop a harmonized regulatory system for invertebrate biological control agents in Europe.

The workshop represented a continuity of activity toward this objective starting from (i) the first workshop in Wageningen in April 2006, which outlined the principles that should characterize a balanced regulatory system, (ii) the REBECA Conference in Salzau in September 2006 which endorsed these principles, and (iii) the small group meetings which produced the 'Discussion Documents' to be considered at the workshop.

The recommendations arising from the workshop can be summarized in relation to the four discussion documents:

1. Guidance Document (Appendix I)

This document is intended to be a summary statement of the information that should be included in dossiers submitted to an EU member state for a release permit (licence) for a native or non-native species, and be designed to assist industry and regulators in this process. The document should follow the same format as the paper published by Bigler *et al.*, (2005), enabling further detail to be acquired when necessary for applications on native species, research-only non-native species, and first and second country commercial releases.

The meeting approved the submitted Guidance Document for use across the EU. In further discussion it was recommended that the Guidance Document should be adapted to become a standardised 'Permit Application form' (dossier), by including text boxes under each section in which applicants would insert required information as appropriate to the specific organism/product. By reference to standard numbered sections, regulators from different member states would be able to communicate on information contained in the dossier. The standardized Application Form was subsequently produced, based on the recommendations of the meeting (Appendix II)

It was concluded that much of the information contained on the application form would be available from the literature (name, taxonomic affiliation, origin, distribution etc), and that the most crucial area would be the Environmental Risk

Assessment (ERA). The meeting also endorsed the Discussion Document on ERA Methods (see below), and as a result, recommended that in the ERA section of the application form it should be indicated that the risk assessment should be 'tiered' (hierarchical), such that not all assessments/tests were necessary for all species (i.e. waivers/exemptions could be applied), and that the order of the assessments/tests could be varied, depending on the species and purpose of the release.

Overall, the most important recommendation on the Guidance Document/Application form was that it should be adopted by all member states, enabling a company to produce a single data file that could be submitted to all EU countries.

2. ERA Methods Document (Appendix III)

This document was discussed in detail and each of the 27 numbered points and 11 'key points' were considered in turn. The meeting endorsed the ERA Methods Document as part of the 'Permit Application form', with some minor changes, as indicated below (see Appendix III for detail):

- (i) A comparison of risks and benefits with other methods of control should not be a mandatory requirement in a dossier, but included on optional basis.
- (ii) It was important to stress that whilst the ERA was set out in the order of establishment, host range and dispersal, this sequence of assessments was flexible, and that not all tests were required for every species.
- (iii) Naturalised species were different to native species, and it should not be assumed that naturalized species posed no risk.
- (iv) Assessment of diapausing ability would not be high priority for a classical biological control agent (where establishment was the aim); however, inability to diapause would be a desirable attribute in a non-native inundative release (in both glasshouses and open-fields).
- (v) The laboratory 5°C survival assay should be adopted as a predictor of field survival (without the need for field experiments), but companies should indicate in the Permit Application form to which countries/climatic area the data applied.
- (vi) Where host range testing was desirable, the meeting saw merit in adopting a two-stage process, in which the first stage would be carried out with 3-4 species to provide an indication of specificity or polyphagy, and thus enable companies to decide whether to invest in wider testing on a greater number of species.

- (vii) It was agreed that where establishment was not possible, it was not necessary to carry out assessments on host range and dispersal, but a summary of direct and indirect effects should be made, as would be the case for a native species.

It was agreed that with these amendments and some re-ordering of other points, the ERA Methods Document could be placed alongside the Guidance Document for use by regulators and industry.

3. ERA Methods for Nematodes (Appendix IV)

The meeting recognized that much of the discussion in REBECA (and elsewhere) on ERA methods for invertebrate biocontrol agents had been focused on insects and mites, and it was not clear to what extent the same approach could be applied to nematodes.

A Discussion Document on nematodes provided a review of this subject (Appendix IV). The key points to emerge were:

- (i) Entomopathogenic nematodes are closely associated with specific symbiotic bacteria, but with the exception of *Heterorhabditis indica* and the bacterium *Photorhabdus asymbiotica*, there were no risks to human health.
- (ii) In comparison with insects and mites, nematodes had much lower dispersal and establishment potential (and any effects were transient and short-lived), and were also highly host specific. In general therefore, environmental risks can be assessed without performing specific tests, but where this seemed desirable, there were reliable methods available.

Overall, the meeting concluded that nematodes should be included in the same ERA system as insects and mites, acknowledging that the order and necessity for any tests was flexible and subject to agreement with regulators.

4. Positive List (Appendix V)

The Positive List was first produced by EPPO in 2002 according to the criteria set out in Appendix V. The list was divided into two sections: (i) species that have been successfully used in classical biological control, and (ii) commercially produced agents for inundative release that have been used for at least 5 years in at least 5 EPPO countries without any reported negative effects. Following a detailed presentation on the Positive List Discussion Document, the meeting endorsed the recommendations that (a) the existing list should be reviewed

according to the revised criteria set out in the document, and that any species removed from the list should be made known to the biological control community (member state regulators, companies) with reasons for exclusion; and (b) applications be invited to include new species on the list, again, according to the revised criteria (Appendix V). One comment of interest to emerge was that companies might not apply to place species on the Positive List, as 'approval' would make it easier for competitor companies to market the same species without the normal ERA requirements.

The Positive List Discussion Document also contained recommendations on (i) how the Expert Group might function and under whose authority, and (ii) the extension of its activities to provide advice to member states (especially those without regulation or regulators) on applications for the first release of a non-native invertebrate biological control agent (see flow diagram in Appendix V).

As further information in this discussion, it was reported that the Director General of EPPO had recently contacted the REBECA coordinator to confirm that EPPO intended to reactivate its interest in biological control and the Positive List and would collaborate with IOBC (WPRS) to create a new Expert Group for this purpose.

A study carried out as part of the REBECA project reviewing regulation of invertebrate biological control agents in Australia, New Zealand, Canada and the USA (Hunt et al., 2007) also suggests that an Expert Panel be established but recommended that it be placed under the jurisdiction of the EU. It proposes that a harmonized regulatory system may be achieved if it is implemented via legislation and administered by an EU governmental body. The Expert Panel would review release applications received by the EU administrative body and would provide a recommendation on release approval. The final decision would then be made by the European representatives on the EU administrative.

The topic of EU-level regulation was discussed in detail at this meeting and some support was shown for the proposal. Advantageous features of this approach are that all countries would be aware of which species had been authorised for release and where, and there could be 'mutual recognition' between countries of safe releases. It would also ensure a harmonized process of invertebrate biological control agent regulation across all European member states. A number of concerns were also expressed about this system: (i) The EU through SANCO had previously indicated that it had no desire to regulate invertebrate biocontrol agents, and (ii) The establishment of an Agency might require legislation, and therefore would take 5-10 years to achieve.

Another concern was that there is no guarantee that the Agency or Expert Group would accept the REBECA recommendations contained in the Guidance, ERA and Positive List Documents as the basis for its assessments. It was also

acknowledged that irrespective of the locality of a release, non-native species were likely to be transported 'across Europe' through international trade, and no system of licensing or legislation (member state or pan-European) could prevent this. However, with an EU-level system of regulation, representatives from neighbouring countries would be able to participate in final decisions for release approvals and issues of border-crossing by invertebrate biological control agents could be raised and incorporated into the decision-making process at this stage.

The Positive List Discussion Document acknowledged the difficulties that might be encountered in achieving this objective of an EU Expert Group, and consequently made a 'pragmatic' recommendation that the EPPO/IOBC collaboration should be supported because it could be developed in the near future, and whilst its advice was non-binding, if the Guidance Document (Appendix I) became an 'EPPO Technical Report', it would be distributed to all EU member states within the EPPO region. At present, the EPPO/IOBC Expert Group was being set up to review and update the Positive List, and it would have to consider whether it could take on the related task of providing advice to member states on first release permit applications.

5. Related Issues: IPR and ownership of research

Throughout the REBECA project, there has been an ongoing debate on the related issues of the inability of companies to patent natural products, the inter-company relationships between those that invest in R&D and those that do not (or do so at a lower level), and the ownership of data derived from publicly funded research and its use in permit applications by individual companies. At one level, the discussion considered whether this was an issue on which REBECA should offer a view, or if the matter was more appropriately discussed within the IBMA. This topic is addressed in the EPPO List Discussion Document in relation to a point already raised above, whereby companies might not apply to place species on the Positive List due to the competitive nature of their business. The criteria for placing a species on the previous list of commercially produced agents for inundative release was that the agent must have been used for at least 5 years in at least 5 EPPO countries without any reported negative effects. The proposal in the EPPO List Discussion Document again states that a period of 5 years may be advantageous since it will allow companies to off set the financial output for conducting tests necessary for a release application. However, some companies at this meeting viewed this as being too long and suggested that 2 years may be more realistic if this time-delay is implemented once again. In general, the company view expressed at the meeting was that there was an expectation that companies should produce their own ERA documentation and that the granting of a permit to one company was not the basis for issuing permits to other companies without independently produced

ERA documentation. However, an exception to this view would apply if the initial data had been produced from publicly funded research.

6. Views of industry

A report was received on a recent meeting of IBMA which considered the current regulatory procedures for invertebrate biocontrol agents in Europe, and made a series of recommendations for the future. It was evident that there was close agreement between the views of IBMA and those that have been developed within Work Package 4 of REBECA.

7. Conclusions

Looking ahead to the REBECA Conference in September, the meeting was satisfied that:

- (i) Work Package 4 had produced an informative Guidance Document for industry and regulators that should form the basis for a standardized 'Permit Application' template.
- (ii) The ERA advisory document had been produced in a logical and flexible format, in which the hierarchical structure enabled waivers and exemptions to be readily identified.
- (iii) Nematodes could be easily accommodated within the same ERA system.
- (iv) It was desirable for the EPPO Positive List to be reviewed and updated.
- (v) An Expert Group set up through EPPO and IOBC provided the best way forward in the short term to review the Positive List, and should evolve to provide advice on 'first release' applications as and when required.
- (vi) In the longer term, an 'EU Agency' for invertebrate biocontrol agents was desirable, provided that it operated in line with the recommendations of REBECA as set out in the appendices attached to this report.