ADVISORY COMMITTEE ON RELEASES TO THE ENVIRONMENT
REPORT ON THE ACRE INFORMATION GATHERING WORKSHOP ON GM INSECTS

Introduction

1. The ACRE information gathering workshop on genetically modified insects was held as an open meeting on 14th October 2010. The meeting was organised on the initiative of ACRE's Public Engagement Sub-group. The topic of GM insects was chosen as products are currently under development, which in some cases would be suitable for release in Europe. ACRE considered it important to scope, at an early stage, the implications of GM insects for environmental risk assessment and the regulatory system.

2. Three experts[1] involved in the development and risk assessment of GM insects gave presentations at the workshop and took questions from ACRE and the audience. A summary follows of the information gathered by ACRE during this workshop and the implications for effective regulation.

The technology

3. Most work on GM arthropods is fundamental research, taking place under contained conditions in the laboratory. In some cases, however, applied research seeks to develop GM insects for specific purposes, such as pest management. These applications would require release of the GM insect to the environment.

4. The furthest advanced applied research has one of two aims: either to control insect vectors of human disease or to control populations of crop pests. Two main approaches for meeting these aims are currently being developed, the self-limiting and the self-sustaining approach. Key features of these approaches are briefly described below.

5. *The self-limiting approach*
   The aim of the self-limiting (or population suppression) approach is to eliminate the target insect population by releasing sterile male GM insects. Large numbers of the GM insects are released to breed with the wild population, producing non-viable offspring. This approach is self-limiting as the modified insect and the modified genes would naturally become extinct in the environment unless re-released at regular intervals. There are examples of GM insects developed using this approach that have reached the field trial stage outside of Europe.

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[1] Dr. Luke Alphey, Oxitec Ltd., UK; Dr. Michael Eckerstorfer, Federal Environment Agency, Austria; Prof. Paul Eggleston, Keele University, UK. Full minutes of the meeting and speakers' presentations are available on the ACRE website at: http://www.defra.gov.uk/acre/index.htm.

6. The self-limiting approach is essentially similar to the non-GM Sterile Insect Technique (SIT) in which sterile males are produced by irradiation. SIT has been successfully used to eradicate insect pests (for example the New World screw worm, *Cochliomyia hominivorax*). It is also currently used in Europe to control the Mediterranean fruit fly (*Ceratitis capitata*). GM-induced sterility may have certain advantages over SIT. For example, the SIT irradiation treatment can reduce the fitness of the released organisms and therefore its efficacy.

7. *The self-sustaining approach*
   The aim of the self-sustaining (or population replacement) approach is to drive population change. For example, mosquitoes with genetically engineered resistance to the malaria parasite are being developed, which would be released to breed with the wild population. Self-sustaining strategies require appropriate technologies to drive the spread of the beneficial transgene in the wild target insect population. Modified genes are transferred between generations and thus persist within a population. GM insects are currently being developed using this approach and tested under laboratory conditions. For this technology, field trials are still some way off.

GM insects under development

8. Outside of Europe, field trials have already been undertaken with GM insects developed using the self-limiting approach. These trials have involved genetically modified pink bollworm (*Pectinophora gossypiella*), a pest of cotton, and the mosquito *Aedes aegypti*, which transmits dengue fever.

9. The self-limiting approach is also being used to develop GM insects which could be used for pest management in Europe. This includes the olive fly (*Bactrocera oleae*), the Mediterranean fruit fly (*Ceratitis capitata*) and diamondback moth (*Plutella xylostella*). Research using this approach is also underway on the mosquito *Aedes albopictus*, a vector of dengue fever. This mosquito is present in southern Europe and is predicted to become more widespread with climate change.

10. In research, using the self-sustaining approach, UK researchers are seeking to develop *Anopheles gambiae* mosquitoes which are genetically modified to carry resistance to the malaria parasite. A number of technical challenges remain before field trials could be attempted using this approach.

11. The approaches for developing GM insects described above are furthest advanced. In the future, however, other arthropods may be genetically modified with the intention of release to the environment. This could include beneficial species (for example pollinators and bio-control agents) or potentially those produced for food (various crustaceans).

Regulation and risk analysis

12. In Europe, applications to release GM insects to the environment would be assessed under Directive 2001/18/EC. This Directive was developed primarily for GM crops, although it is also currently applied to non-crop products, such as GM medicines. In considering potential releases of GM insects to the environment, it is important to give consideration as to whether the current regulatory framework is fit for purpose.

13. A recent report produced for the European Food Safety Authority (EFSA)[2], reviewed the parameters and issues that should be raised in an environmental risk assessment of a GM insect. The authors followed the framework set out under Directive 2001/18/EC.

14. The report identified 25 issues to be addressed in the risk assessment of a GM insect. The authors concluded that the issues raised by GM insects for environmental risk assessment were broadly the same as for GM crops, although the emphasis and detail required to address these issues would be different. Further consideration of some of these issues follows below.

15. *Gene flow*. An example of an issue that is likely to differ in detail from the situation with GM crops is that of gene flow. Some GM crops may hybridize with a number of wild relatives, and so the consequences of gene flow are considered in detail during the risk assessment. ACRE noted, however, that due to the greater mating specificity of insects, the risk of interbreeding of a GM insect with related species is likely to be negligible.

16. *Dispersal*. Another issue that may differ from GM crops is the extent of dispersal of GM insects in the environment. The natural mobility of many insects may suggest that dispersal distances would be greater. ACRE noted, however, that for some insects, dispersal is typically localized occurring over only short distances. Relatively rare but long distance dispersers can, however, be very important in the dispersal and ecology of some insect species. Factors such as the short survival time of insects may also be relevant to consider (and contrast with the potential for long survival times of the seeds of some crop species).

17. *Appropriate comparators*. Directive 2001/18/EC requires that the genetically modified organism is compared with an unmodified equivalent. Interesting questions arise with regard to the selection of an appropriate comparator (or comparators) for GM insects. For some comparisons the non-GM counterpart of the same insect species may be relevant, or in the case of SIT, sterile

[2] Benedict et al. 2010. Defining Environmental Risk Assessment Criteria for Genetically Modified Insects to be placed on the EU Market. EFSA report CT/EFSA/GMO/2009/03
http://www.efsa.europa.eu/en/scdocs/doc/71e.pdf

insects produced by irradiation may illustrate how the similar phenotype may behave in the field. For other comparisons concerning environmental impact, the technology used to control the non-GM counterpart (e.g. an insecticide) may be most appropriate.

18. *Receiving environments*. The receiving environments for GM insects are likely to be more diverse than hitherto considered for GM plants, including urban environments and semi-natural habitats as well as agro-ecosystems. This in itself may pose more regulatory challenges, in particular assessing any potential impact on biodiversity. If the release of a GM mosquito resulted in local or global extinction of the insect and its loss from both aquatic (larval) and terrestrial (adult) food webs, consideration would need to be given as to the impact on wider biodiversity. In many cases this information is not comprehensively understood. One aspect of this is that the degree of redundancy in many food webs is not well characterised.

19. *Post-market monitoring*. Directive 2001/18/EC requires that monitoring is undertaken, following the release of a genetically modified organism to the environment. This monitoring is to test assumptions made in the environmental risk assessment and to identify any unanticipated adverse effects. In the case of GM insects, the uncertainty around the potential impacts on wider biodiversity raises questions about what kind of strategy would be suitable for post-market monitoring.

20. An important question is whether GM insects raise any fundamentally new regulatory issues. Following consideration of the available information, ACRE concluded that the issues raised during the course of a risk assessment are likely to have many parallels with the framework currently applied to GM plants and GM medicines. Certain limitations were, however, also identified, which are considered in the following section.

Limitations of the existing framework.

21. ACRE consider that, whilst the current regulatory framework is broadly appropriate for risk assessment of GM insects, there are some areas of uncertainty, some limitations that need to be addressed, and some challenges.

22. There is a degree of uncertainty in the potential impacts on wider biodiversity if the release of a GM insect led to its elimination from the food web. In this respect, the uncertainties may be more significant for the self-limiting approach as this may be used to drive a species to local extinction. The extent to which a release may be reversible is likely to be less for the self-sustaining systems.

23. The data required to assess impacts on wider biodiversity include detailed quantitative knowledge of the relevant food webs across the range of receiving environments, and the question arises as to whether this is proportionate to the risks involved.

24. Another issue is that the risks should be appropriately considered against the risks of an alternative approach or the risks of inaction. From this point of view the issue of ensuring appropriate comparators are chosen becomes particularly relevant.

25. This issue is drawn into particularly sharp focus when considering GM insects developed to combat human diseases. An example is provided by mosquito transmitted dengue, for which there are currently no vaccines or drugs to treat the disease. The insects have also developed resistance to some insecticides, so an additional control is required. This needs to be focused on the vector; spraying with an insecticide and removal of breeding sites may help to reduce mosquito populations, but these measures alone are not sufficient to control the disease. In this case there are clear risks associated with the alternative approach to controlling the mosquito. There are also clear human health risks in not taking action to control the mosquito.

26. This provides an example of a case where a holistic approach is needed, which considers the risks of the disease to human health and the risks of alternative control methods against any risks specific to the GM technology. To enable an effective comparison, the relative predicted efficacies of different approaches may also need to be considered. This poses a challenge for the regulatory system, which as currently interpreted focuses on identifying the environmental risks of the GM approach.

27. Consideration will need to be given to the way in which the regulatory system operates. Effective decision-making in relation to such GM applications will need to be made in light of a suitably holistic consideration of risks of the GM approach against the full range of risks associated with existing alternative approaches and the risks of inaction. This might include the development of comparative scenarios. The challenge will be in developing new tools to promote comparative risk assessment and decision making tools which are proportionate, transparent, rigorous and consistent.