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HSE Headquarters
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Dear [redacted]

5th December 2011

Feedback from Scientific Advisory Committee on Genetic Modification (SACGM)

1 I am writing to provide you with feedback from SACGM on your paper 'Potential trial of 'genetically sterile' diamondback moth'. This feedback covers three main areas: the non-indigenous nature of the parental strain, the extent of biological containment afforded by the tTA lethality gene and quality control. In addition, further issues are identified where some clarification may be needed to support any future proposals.

Non-indigenous nature of parental strain.

2 The first key point in this feedback does not relate to the genetic modifications you have introduced into your strain. Rather the issue is that the parent from which it was derived is of North American origin. This complicates the regulatory position in a way that would not apply if the parent was an indigenous strain. As things stand, there is uncertainty as to whether your non-indigenous strain may contain insecticide resistance genes that are not present in UK moths. This kind of environmental risk is specifically covered by Plant Health legislation that is enforced by the Food and Environment Research Agency (FERA). I therefore recommend that you contact FERA for more detailed advice.

3 I am highlighting this issue because it would seem important to address it as matter of priority. My understanding is that you wish to proceed in the direction of an 'open' release at a site within the UK. It would seem unlikely that you will receive authorisation for such work (including work in a polytunnel) until the issue of the non-indigenous nature of the parental strain is resolved. This issue would become even more problematic if you proposed to undertake trials with a test system consisting of a polytunnel of plants artificially infected with an unmodified version of the North American strain.

The extent of biological containment afforded by the tTA lethality gene.

4 The second key area where I am providing feedback is on the extent of the biological containment afforded by the tTA lethality gene. SACGM considered that, on a theoretical basis, there was a reasonable case to suggest your proposed trial would limit contact of the GMO with humans and the environment. However, it was their view that, before it would be justifiable to

completely withdraw physical containment, on the basis of the biological containment, more experimental evidence was needed to show that these theoretical expectations would be realised in practice.

5 The main evidence that the Committee wanted to see was actual experimental data to substantiate the predicted decline of the frequency of the RIDL allele over the generations. The aim should be to obtain robust evidence that after a few generations numbers decline to negligible levels. Therefore, it would be important that the testing undertaken at the end of these experiments should have sufficient resolution to detect low numbers. Initially such work could be undertaken in an insectary.

6 In addition, the Committee considered there were two matters that required clarification in terms of the penetrance of female lethality. First, more precision was required on the exact level of penetrance. The current statement that it is of the order of 95% to 100% was not considered sufficient. Second it was important to show that the small minority of females who do survive despite inheriting the tTA construct do not do so because of intrinsic, heritable resistance, which they could transmit to their offspring along with tTA. Testing this would require examining the outcome of breeding using the survivor females. The key issue would be to show that these survivor females are either sterile or produce progeny exhibiting the expected level of female lethality (~95% or whatever).

7 There are also three further issues relating to biological containment. The first follows on from the point immediately above. It is the need for confirmation that the female lethality of the tTA gene is not dependent on the strain used, i.e. that UK strains are not more resistant to the tTA system than your North American strain. A second issue is that more information is required on the extent to which diamondback moths can interbreed with other closely-related moths. Third, there is a need to address the question of whether it is conceivable that heritable resistance to tTA could develop over time by a process of mutation and selection.

Quality control

8 Another key area is that SACGM place a great deal of importance on project management and quality control procedures. The Committee are aware that other researchers have undertaken projects involving mass rearing of insects that have not gone as planned. There have been failures in quality control and operational planning resulting in low release numbers and incomplete monitoring. Thus, as part of a future justification for an open release, more information would be required to show that the planned procedures were sufficiently robust to deliver the agreed protocol.

Additional issues

9 Based on the evidence presented to date the Committee were unsure as to the distances over which released moths would spread. Therefore, they recommended that further evidence should be gathered on this point. In

particular, during any early trials of an 'open' release it would be important to gather robust evidence to support further work.

10 Further evidence should be gathered to demonstrate whether or not crops which had been used for a trial of RIDL would be 'contaminated' with some residual material (e.g. eggs and larvae) that might be of concern if it were to enter the food chain. It is only based on such evidence that a decision could be made as to whether the crop should be destroyed or could be harvested as normal.

11 If a trial were undertaken under the Contained Use Regulations on a commercial farm, questions would arise as to whether this premises should be notified and whether there should be a local genetic modification safety committee (GMSC). In addressing these issues the key point would be whether the farm was a separate legal entity to the sponsor of the trial i.e. whether work was being undertaken for the first time by a new dutyholder under the Regulations. If so, the premises would require notification as a new centre undertaking work with GMOs. However, it would be acceptable for this new centre to rely on a risk assessment drawn up by the trial sponsor, rather than having to establish a new GMSC.

The next steps.

12 From the above feedback it should be clear that the advice SACGM has provided to the Competent Authority does not, at this stage, support an 'open' trial. The Competent Authority will be writing to you shortly to explain your options under both the Contained Use and Deliberate Release Regulations.

13 One final point is that SACGM would not want this feedback to be too discouraging. Within the requirements of the legislation and the need to allay public concerns, they wanted to be as supportive as possible of this technology. They hoped that you would see their comments as raising genuine questions over hazard and risk rather than being unduly cautious.

Yours sincerely

[redacted]
(Secretary to SACGM)

[redacted]

From: [redacted]
Sent: 15 December 2011 10:45
To: [redacted]
Cc: [redacted]
Subject: Press on Diamond Back Moth

Dear both

In case you haven't seen these yet.

FYI – in case you haven't seen them.

Frankenmoth: Health fears over plans to release millions of GM ...
Daily Mail
The company involved, Oxitec, is keen to begin trials next year, ... Oxitec's chief executive said there was a demand from British farmers for genetically ...

Daily Mail

Millions of GM moths could be released to combat crop pests
Telegraph.co.uk
Oxitec, the company behind the idea, hopes to begin trials next year but faces opposition from groups who say the untested technology could threaten ...

Telegraph.co.uk

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From: [redacted]@oxitec.com]
Sent: 13 January 2012 12:33
To: [redacted]
Cc: [redacted]
Subject: RE: SACGM

Dear [redacted]

Thank you for this. Going for option B – using a UK-caught strain of DBM – would be reasonably practical if that could be done by introgression of 'native' genetic material into our candidate strain(s). With other insect strains, we have done this by outcrossing to a given native strain for ~5 generations, which would replace something like 95% of the founder strain's genetic material with native genetic material. As wild diamondback moth are likely to be a 'genetic patchwork' of different regional strains due to their capacity to periodically migrate between continents, we think that this level of introgression would provide a suitably 'native' genetic background. Introgressing new genetic material into our candidate strains may reduce their capacity for good laboratory rearing, so this may present other problems for us. For us, making a strain again from scratch (i.e. not by introgression), using a UK-derived background strain, would be technically highly demanding and unfeasible.

We would marginally prefer to follow option A: to conduct releases with our candidate strains in their current genetic background (a non-native strain that has been maintained in laboratory culture for a number of years). We were given this strain by a collaborating company who use it as a chemical-susceptible experimental comparator. They have provided some data on its susceptibility traits, which I'd be happy to share, but we recognise that assessment guidelines recommended by yourself and colleagues will likely ask for more. We anticipate that such tests would be best conducted by a second party, and we would also welcome any guidance on this – for example, Fera itself could act as a suitable independent assessor of the background strain's resistance traits.

I'd be happy to discuss any of these points further, if that would be helpful. Would you mind outlining the proposed process to be followed, and which other agencies will be involved? We'll continue to work on experiments in the lab related to other points made in the SACGM feedback document.

[redacted] who do you suggest as the Fera point of contact in your absence, should I have questions?

Best wishes,

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From: [redacted]@fera.gsi.gov.uk]
Sent: 12 January 2012 12:10
To: [redacted]
Cc: [redacted]
Subject: RE: SACGM

Dear [redacted]

Apologies for the slight delay in getting back to you,

Regarding the issue of the origin/strain of the DBM, my advice would be, that unless there is some insurmountable technical reason why not, then option b) is preferable (i.e. modifying a UK-derived strain). It not only saves you from having to prove the negative (that there are no risks of any kind) but it also would – in my opinion – be a definitive advantage in terms of allaying some potential concerns about the work. At least it is one less thing to worry about?

If however, you do go down the route of seeking permission to release a non-native strain, then we will need to provide you with a list of requirements in terms of characterising the chosen strain and demonstrating that it presents no greater risk. I think we need a document for this, so that it is clear to everyone concerned that a risk assessment has been carried out and no risks were identified. I (or one of my colleagues) will follow up with this, assuming you wish to take this route. We will probably need to consult a few other Government agencies, just to make sure that there are no concerns from their perspective (i.e. conservation for example).

We are breaking new ground here, so it is essential to get everything right and make sure we have covered all the potential concerns and demonstrated that we have considered all potential risks.

We will start working up a document, and doing the necessary consultation, but perhaps you could let us know your intentions once you have firmed them up.

Please copy in all of the cc'ed above as I will be away for a few weeks after 19th Jan (annual leave).

Best regards,

[redacted]

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Please consider the environment before printing this e-mail

From: [redacted]@oxitec.com]
Sent: 10 January 2012 10:17
To: [redacted]
Subject: FW: SACGM

Dear [redacted]
Happy new year. I'm writing to follow up on the outcomes described in the attached document from the SACGM meeting last year (attached). One of the key items was that our diamondback moth strain is of North

American origin, and that their release may introduce new resistance alleles into the UK population. I'm keen to get some advice on this, if you don't mind? It seems that we have two options: (a) to characterise the resistance profile of our lab strain; or (b) to introgress our strain into a UK-caught strain. In terms of what I think would be the best option, my preference would be the former, but I wanted to seek your advice as to what would satisfy yourself and other members of the committee.
It would be great to discuss this over the phone, at a convenient time for you.
Best wishes

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From: [redacted]@oxitec.com]
Sent: 19 January 2012 10:46
To: [redacted]
Cc: [redacted]
Subject: RE: Request under FOI / Environmental Information Regulations

Simon

We have reviewed the documents and find no information that we would wish to claim as commercial in confidence in the background documents 'Potential UK trial of genetically sterile diamondback moth' and the additional paper 'RIDL: a self-limiting genotype in the field'

Many thanks

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From: [redacted]hse.gsi.gov.uk [mailto:[redacted]hse.gsi.gov.uk]
Sent: 18 January 2012 15:35
To: [redacted]
Cc: [redacted]hse.gsi.gov.uk
Subject: Request under FOI / Environmental Information Regulations

[redacted]

We have received a formal request for further information relating to the diamondback moth project that was discussed at SACGM. In particular we have been asked to disclose both the original background document 'Potential UK trial of genetically sterile diamondback moth' and the additional paper 'RIDL: a self-limiting genotype in the field'.

I am therefore writing to check whether there is any information in these documents that you would regard as commercial information. If you believe this to be the case there may be an exemption under regulation 12(5)(e) of the Environmental Information Regulations. This exemption allows us to withhold from disclosure any information that is commercially valuable and private to the owner.

Before you consider this in any detail, I should warn you that the law does not allow you to make any kind

of general assertion that disclosure would be harmful to your commercial interests. Any claim for exemption has to be supported by reasoned arguments about the exact information where disclosure would cause commercial harm. In particular, this means that it is not acceptable for a company to mark a whole document as commercial in confidence. You should also recognise that the option to exempt information from disclosure can only be applied once a public interest test has been applied. This public interest test requires the government body holding the information to balance the public interest in withholding information against the public interest in making it available.

I have looked through the documents again. As far as I can see the names of individuals are not mentioned anywhere, as these would certainly be subject to exemption. One area where I can see a possibility that commercial confidentiality may apply is the mechanism used to make the expression of the lethality gene specific to females. For example I could envisage that this could be subject to a patent application. However, I do note that there is a publication by Thomas et al in 2000.

Overall my preliminary view is that we should be releasing both documents in their entirety unless you can make a case for exemption of any specific information.

I would be happy to discuss further. We have to make our formal response to the information request within 20 working days. Therefore I would appreciate if you would get back to me by next Wednesday 25th January.

Thanks

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Biotechnology Portfolio Holder + Specialist Inspector

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