GeneWatch UK

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Complaint 346/2013/ANA

Dear Mr Höfstotter

Thank you for your letter for 3rd July 2013, enclosing EFSA's response to our complaint 346/2013/ANA. GeneWatch UK's observations on EFSA's opinion are below.

1. **On the failure to address conflict of interest concerning the members of EFSA's Working Group on "GM insects"**

We note that the relevant Declarations of Interest (DoIs) have now been removed from EFSA's website. We consider this bad practice, particularly when a complaint is ongoing. We enclose the relevant declarations with this correspondence.

Michael Bonsall

GeneWatch UK maintains its view that Michael Bonsall's conflicts of interest should have barred him from membership of the GM insects Working Group.

EFSA states that Michael Bonsall did correctly declare his employment with the University of Oxford. However, he did not declare that his employer (Oxford University) in an investor in Oxitec. Isis Innovation (Oxford University's technology transfer arm) was responsible for helping to set up the company and assisting to obtain venture capital investment.[1] Michael Bonsall is a Reader in Zoology[2] in the same department as Luke Alphey[3], Oxitec's founder and Chief Scientific Officer. In August 2008, Oxford Spin-out Equity Management (OSEM) was set up to manage the University's shareholdings in its spin-out companies and seek ways of maximising the value of its equity stakes: Oxitec is now part of its portfolio.[4,5] In his DoI, Michael Bonsall explicitly stated that Oxitec does not provide any financial benefit to Oxford University. However, this is disingenuous. Oxford University expects the value of its investment to rise if Oxitec's products are commercialised: in such

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circumstances the University will receive a direct financial benefit. Prospects for commercialisation will be enhanced by weak regulatory oversight: thus proposals in the draft Guidance consultation document for weaker requirements for so-called "sterile" insects (as detailed in GeneWatch UK's submission to the consultation: http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/EFSA_GWresponse.pdf) and a number of other matters (such as the proposed treatment of GM insects in the food chain, discussed further below) would directly benefit Oxitec and, by extension, Bonsall's employer.

Under EFSA's conflict of interest rules (Annex VII to EFSA's response) Article I4.IV (page 5) employment in any body with an interest in the subject matter should be declared. Contrary to what EFSA claims in its response, the financial interests of a university employer are not excluded. However, nor does this imply that no university expert can ever be appointed! As a first step, the existence of any investments by the expert's employer in any relevant company should be declared, including when the employer is a university or not-for-profit institute. The need to do so is enhanced, rather than reduced, by EFSA's observation that public-private joint initiatives and programmes are the rule, rather than the exception.

In this particular case, not only did Bonsall's employer have a direct interest in Oxitec, via its investment in its spin-out company Oxitec, but Bonsall was also undertaking joint research with the company. Further, this extended to a project being undertaken jointly with Oxitec in Bonsall's capacity as an employee of the University (one of its main investors), with the express intention of influencing regulatory processes. In such circumstances, there is a clear conflict-of-interest, which should have barred Dr Bonsall from taking part in the GM insects Working Group.

The most relevant grant (which was declared in Bonsall's DoI) covered the period from 28th June 2010 to 27th June 2013, whilst Bonsall was a member of EFSA's GM Insects Working Group. The grant description is here: http://www.bbsrc.ac.uk/PA/grants/AwardDetails.aspx?FundingReference=BB%2fH01814X%2f1 . The project summary states, *inter alia: "We will use mathematical models developed at the University of Oxford, alongside laboratory experiments and trials conducted by our project partner Oxitec Ltd, a small British biotech company that is at the leading edge of producing transgenic insects. We are both working with various regulatory and policy-making bodies around the world, and aim to produce a policy document that we hope will form a key part of the information that such stakeholders need to assess the risks and benefits of this new technology. It is important that decisions and regulations are underpinned by a good understanding of insect biology and ecology, and of relevant interactions between different elements of the complex ecological systems in which we, our livestock and crops, and those insects currently coexist*." [Emphasis added].
Bonsall's co-investigator on this project was Dr Nina Alphey, who we understand to be Luke Alphey's wife.

EFSA states that employment by a university should not be a conflict-of-interest and that there was no financial flow between Oxitec and Oxford University in the context of the BBSRC grant. This misses the point. The BBSRC grant was intended to facilitate the representation of Oxitec and Oxford University's views to regulatory bodies in relation to the oversight of GM insects. Both the university (Bonsall's employer and Oxitec's investor) and Oxitec would stand to benefit if regulatory standards were weak. This process was part of a much broader global attempt by Oxitec to influence regulatory processes, as documented in our joint NGO briefing: http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Regnbrief_fin2.pdf

In such circumstances, Article 10.1(iv) (conflict of interest in employment) should have been applied, which should have made it impossible for Dr Bonsall to be considered for membership of the Working Group. Failure to exclude him would mean that any university or institute with an

investment in a spin-out company could secure access to EFSA Committees, Panels or Working Groups in order to influence Guidance or decisions in relation to the company's products. To prevent this, joint research with a company with relevant commercial interests invested in by one's employer should be a bar to membership of EFSA's Scientific Committees, Panels and Working Groups, regardless of whether the employer/investor is a commercial company or not.

EFSA states that it does not understand where the conflict of interest lies, yet Bonsall's conflict-of-interest meant he was required to leave the room during a discussion of Oxitec's GM insects by the UK Advisory Committee on Releases to the Environment (ACRE): see Minutes of the 134th Meeting of ACRE at Nobel House, London, Thursday, 1st December 2011 (paragraph 10.4). http://www.defra.gov.uk/acre/files/ACREMINUTES20111201.pdf which states "*Dr Bonsall declared a conflict of interest as he had been working with the company, Oxitec Ltd, on this insect. He left the room while this item was discussed*". EFSA has failed to comment on why ACRE regards Dr Bonsall as having a conflict-of-interest, whilst EFSA apparently does not.

Further, Bonsall admitted he was under industry pressure as stated in the Sunday Times article referred to in our original complaint (a copy is enclosed). This pressure can only have come from Oxitec, since it is the only commercial company with an interest in this area.

Comments by ACRE on the draft EFSA Guidance

EFSA states that Michael Bonsall and Jeff Bale's membership of the UK Advisory Committee on Releases to the Environment (ACRE) does not act as a bar to their membership of EFSA's GM insects working group, because ACRE is regarded as a Food Safety Organisation (FSO). Again, this misses the point. We stated (and maintain) that Bonsall and Bale should not have been allowed to be involved in preparing ACRE's comments on the EFSA draft Guidance as this amounts to reviewing their own work. This is barred under EFSA's policy, as contained in their Annex VI Article 9.1(d). Failure to implement this bar leads to the nonsensical situation where a small number of experts are consulted about the merits of their own proposals!

Other Working Group members

Michael Bonsall declared his joint BBSRC grant with Oxitec (as noted above) but other Working Group members did not correctly declare joint grants. EFSA's policy (their Annex VI, Article 1.4.VI) requires the declaration of any research funding "on the subject matter". Although it is not specified whether or not the declaration should state any involvement of relevant commercial interests in this research, it is self-evident that such involvement may present a conflict-of-interest and should be transparent. EFSA's claim that the increased role of public-private joint initiatives would lead to a ban on the vast majority of experts again misses the point: conflicts-of-interest that may arise via public-private research partnerships must be declared.

EFSA claims that GeneWatch said that joint grants with a company with relevant interests in the topic should "disqualify the expert for life". We recognise that EFSA's policy requires declarations to cover only the period of the appointment and 5 years prior to it, we have not suggested extending this for life. Nor did we state that experts making such declarations should necessarily be disqualified. We said (and continue to maintain) that:

- John Mumford, who declared his WHO Mosqguide grant, should have stated that this was a joint project with Oxitec. Mumford (and his wife Mary Quinlan) are co-authors on three journal papers with Oxitec resulting from this project, all of which comment on regulatory aspects (the lead author for these papers is Oxitec's head of Regulatory Affairs, Camilla Beech)[6,7,8];

- George Christophides, who declared his involvement in the INFRAVEC project, should have stated that this is a joint project with Oxitec: http://www.infravec.eu/index.pl?pos=02.00
- Romeo Bellini should have declared his involvement in the INFRAVEC Project (listed on the above link under CENTRO AGRICOLTURA E AMBIENTE GIORGIO NICOLI SRL) and should have stated that this is a joint project with Oxitec (as above).

Whilst we recognise that, under EFSA's existing rules, involvement of experts working on joint projects with a company does not necessarily bar them from taking part in Working Groups, we respectfully suggest that the presence of four experts (including Bonsall) working with the same company is a matter of concern (see comments below on the overall composition of the working group).

GeneWatch accepts that it made a mistake regarding mixing up Jozsef Kiss and Iztvan Kiss and we apologise for this.

Luke Alphey

We accept EFSA's apology regarding the failure to correctly declare Luke Alphey's conflict of interest as the founder and Chief Scientific Officer of Oxitec, the only company with a current interest in commercialising GM insects. We suggest that a note to this effect should be published with the minutes of the Working Group. We recognise that EFSA's conflict-of-interest rules do not prevent Dr Alphey from appearing as a hearing expert.

Overall composition of the working group

We maintain our view that, had all interests been correctly declared, it would have become obvious that the overall composition of the Working Group, together with its decision to call Luke Alphey as one of only two hearing experts, was biased in favour of the commercial interests of a single company, Oxitec.

We note that EFSA claims in its Annex XI (response to the European Court of Auditors, page 82) that it is important that "*no one expert can unduly influence the decisions of the Panel*". However, the presence of multiple members on the same Working Group with ties to the same company must surely undermine this, especially when the same company provides a hearing expert. Finally we note that the Court of Auditors' report does not describe EFSA's policies as "advanced and sophisticated" (as EFSA claims) but rather notes that "*There are shortcomings in the assessment of these declarations and management of conflict of interest situations across all of the selected Agencies*" (para 93).

We maintain that EFSA should amend its conflicts-of-interest rules to limit the number of experts on any given Scientific Committee, Panel or Working Groups undertaking joint research activities with companies whose business activities will be affected by the work being undertaken. This is necessary for EFSA to meet its legal obligations to provide independent opinions and advice. We note that Regulation 178/2002/EC stresses the importance of EFSA's independence, for example in Preamble (35),(36) and (37).

2. About the complaint that EFSA's consultation failed to cover the ingestion route and implications of GM insects in the food chain

In its response, EFSA claims that the ingestion route, including the implications of GM insects in the food chain is now covered by the more elaborated paragraph in the Guidance which reads:

"*This Guidance Document considers primarily effects of GM animals on human health through routes of exposure other than ingestion or intake; these include ocular and nasal exposure as well as exposure through dermal contact and inhalation (see sections 4.1.7, 4.2.7 and 4.3.9). However, applicants should also assess the likelihood of oral exposure of humans to GM animals or their products which are not intended for food or feed uses. If such exposure is likely and ingestion or intake will occur at levels which could potentially place humans at risk, then applicants should apply the assessment procedures described in the EFSA Guidance Document on the risk assessment of food and feed from GM animals and on animal health and welfare aspects (EFSA, 2012a)*."

However, EFSA again misses the point. EFSA did not properly consult on the ingestion route, or how to deal with the issue of GM insects in the food chain. The importance of public consultations is set out in EFSA's Founding Regulation and EFSA has a consultation policy: http://www.efsa.europa.eu/en/keydocs/docs/consultationpolicy.pdf . The policy states that the consultation must clarify the consultation target audiences and the nature of relevant information. In fact, EFSA provided no information regarding the potential contamination of fruit or vegetable supplies with GM insects such as Medfly, Olive fly, Diamond back moth or tomato leaf hopper and did not include these issues in either of its consultations (on food and feed, or on ERA). Nor did it provide any information about the potential for people to swallow GM insects, which are expected to be released in large numbers.

In its mandate to EFSA (EFSA ENV.B3 D(2007) 2004, dated 19th February 2007), the Commission stated "*we would like to request EFSA to develop, building on the work done in the context of Codex Alimentarius, a guideline on the safety evaluation of GM animals that would address both food/feed safety and environmental safety of this technology*". This letter distinguishes two types of GM animal: the first group involves the whole animal being available for the food market; the second group is not intended for food production, but may be genetically modified to produce specific substances in milk, eggs or blood or serve as medical research models. GM insects do not fall into either of these categories.

Although the Commission's mandate letter refers to only two types of GM animal, EFSA mentions GM insects in its response of 24th July 2008, stating: "*EFSA intends to launch several open calls for tenders, starting with GM fishes and including GM mammals and insects at a later stage*" [emphasis added]. GM insects being developed for commercial application include insects for use in agricultural production, such as GM pests (e.g. fruit flies, olive flies) and GM pollinators (e.g. bees), which fall within the broad definition of food law in Preamble (11) of Regulation (EC) No 178/2002 (i.e. laws "*including provisions on materials and articles in contact with food, animal feed and other agricultural inputs at the level of primary production*"), but they also include GM mosquitoes, being developed in attempts to reduce the incidence of tropical diseases such as malaria and dengue fever, which fall outside this definition of food law. GM insects do not fall within the scope of the *Codex Alimentarius* guidance on GM animals as they are not animals intended to be eaten or with a history of safe use as food/feed, however, GM agricultural pests may appear as contaminants in food/feed and this may fall under the definition of GM food/feed under Regulation (EC) No.1829/2003 on genetically modified food and feed, where the determining criterion is whether or not material from the genetically modified source material is present in the food and feed (paragraph (16)).

The only commercial company with GM insects close to commercialisation is Oxitec: http://www.oxitec.com/agriculture/our-products/ . Its GM agricultural pests are genetically engineered so that most of the females die at the larval (caterpillar) stage, whilst males survive to adulthood. Adult males are intended to be released in large numbers to mate with wild insects, outnumbering the wild population by a factor of ten or more. Their female offspring then die as caterpillars, perhaps inside olives or tomatoes, or on the leaves of cabbages. There is therefore

potential for large numbers of dead GM caterpillars (and some live ones) to end up in the food chain. An application to make open experimental releases of GM olive flies in netted olive groves in Spain was made by Oxitec earlier this year: http://gmoinfo.jrc.ec.europa.eu/bsnifs-gmo/B-ES-13-07-EN.pdf . An application for open releases of GM Mediterranean Fruit Fly (Medfly, *Ceratitis capitata*) in fruit orchards in Brazil is also currently awaiting a decision by the Brazilian regulators CTNBio (http://www.ctnbio.gov.br/index.php/content/view/17825.html in Portuguese). It is currently unclear whether any of this fruit will be imported to the EU. Oxitec has also attempted (so far, unsuccessfully) to release GM diamond back moths under "contained use" regulations in the UK, arguing that its insects have "biological containment". Possible scenarios that EFSA therefore should have considered in order to fulfil its mandate to consider food/feed safety are:

(i) Swallowing of GM insects (pests or mosquitoes) released in the EU (which requires an ERA);
(ii) The entry of GM insects into the food/feed supply as contaminants on or inside fruit and vegetables from an approved EU open release (which requires an ERA, but also consideration under Regulation (EC) No.1829/2003 on genetically modified food and feed);
(iii) The entry of GM insects into the food/feed supply as contaminants on or inside fruit and vegetables from an approved open release in another country (which may not require an ERA in the EU, but should require consideration under Regulation (EC) No.1829/2003 on genetically modified food and feed).

The process EFSA adopted to fulfil its mandate was firstly to adopt its Guidance on the risk assessment of food and feed from genetically modified animals: http://www.efsa.europa.eu/en/consultationsclosed/call/110810.htm . This document and the consultation on it explicitly stated that that "*Insects and other invertebrates were not taken into account, with the exception of honey bees that are used in agricultural practice*". In fact, the presence of GM honey bees in the food chain itself was not considered, but the production of honey from GM bees (which as a food product falls within the scope of *Codex Alimentarius*) was included. In its response to the consultation at the time, GeneWatch UK noted that GM insects in the food chain would require further consideration. EFSA's claim in its response that this (food and feed) Guidance reflects the outcome of consultation is seriously misleading: it reflects the outcome of a consultation from which the issue of GM insects in the food chain was explicitly excluded.

Subsequently, EFSA consulted on and adopted its Guidance on Environmental Risk Assessment (ERA) of GM animals (EFSA's response Annex IX). The draft Guidance said:
"*This document provides guidance to applicants on how to conduct the ERA of GM animals to be released into the environment and placed on the EU market according to Regulation (EC) No 240 1829/2003 (EC, 2003) or Directive 2001/18/EC (EC, 2001)*".
And:
"*Furthermore, although this Guidance Document does not give detailed guidance on the risk assessment of the accidental intake of GM animals not intended for food and feed uses by humans (e.g. GM insects), applicants should assess this likelihood and assess any risk by implementing principles in the Guidance Document on the risk assessment of food and feed from GM animals and on animal health and welfare aspects (EFSA, 2012a). Potential impacts of such GM animals on human health, through other routes of exposure (than ingestion), are addressed in sections 4.1.7, 4.2.6 and 4.3.9.*"

The scope of this has been amended and now states:
"*This document provides guidance to applicants and risk assessors on how to conduct the ERA of* ***living*** *GM animals to be placed on the EU market in accordance with Regulation (EC) No 1829/2003 (EC, 2003) or Directive 2001/18/EC (EC, 2001). It provides detailed guidance to assist applicants in the preparation and presentation of the ERA part of their applications*."

Thus:

1. There has still been no consultation regarding risk assessment of the ingestion route or of GM insects in the food chain. Applicants have simply been instructed to use a process which was adopted following a previous consultation that explicitly excluded GM insects.
2. Restriction of the scope of the Guidance to the ERA for living GM animals, makes it even clearer that the process applicants should follow in order to import foods such as fruit and vegetables produced using GM insects (but not released in the EU) has not been defined or been the subject of any consultation (i.e. the issue of dead GM insect larvae in food is missing completely, and the issue of how remaining living larvae or adults in food supplies will be dealt with is also unclear). This means that EFSA has not fulfilled the mandate given to it to assess food/feed safety.

Regulation EC) No 1367/2006 implements the provisions of the Aarhus Convention in the EU. *Inter alia*, this provides for public participation concerning plans and programmes relating to the environment, including GMOs. Article 9 requires that Community institutions and bodies shall provide, through appropriate practical and/or other provisions, early and effective opportunities for the public to participate during the preparation, modification or review of plans or programmes relating to the environment when all options are still open. In particular, where the Commission prepares a proposal for such a plan or programme which is submitted to other Community institutions or bodies for decision, it shall provide for public participation at that preparatory stage. GeneWatch UK maintains that an effective opportunity to participate in decisions about allowing GM insects into the food chain was not provided by the EFSA consultations, since the first (food and feed) consultation excluded GM insects and the second (ERA) consultation did not include the issue on the (incorrect) grounds that it was covered by the first.

GeneWatch UK maintains its view that:

- It was unclear to consultees that the single sentence in lines 267-271 of the consultation amounted to a consultation on applying the principles contained in an earlier consultation (which specifically excluded GM insects) to GM insects in the food chain, as EFSA and DG SANCO appear to be claiming. There has been no proper consultation on these matters.
- The principles outlined in the earlier consultation on GM animals in food and feed were not developed for GM insects and there is no international standard under *Codex Alimentarius* or elsewhere for such an approach. Determining the best process to deal with this issue therefore requires in-depth consideration and a proper public consultation.
- In contrast to other exposure routes, no information about possible health and environmental risks of ingesting GM insects or introducing GM insects into the food chain was provided in the consultation. This breaches EFSA's consultation policy, which requires clarity on the issues covered and the nature of relevant information.

Since the remit of the ERA consultation has been clarified to state that it covers only the release of living GMOs within the EU, a separate consultation is needed to the entry of GM insects into the food chain in the EU, including the entry of dead, as well as living, insects on fruit or vegetables imported from non-EU countries.

3. What EFSA should do to put things right

In our original complaint, we stated that EFSA's working group on GM insects must be re-constituted to remove all conflicts-of-interest and bias and a new process begun to develop the draft Guidance for consultation. We note that EFSA highlights in its response that the working group has been disbanded on completion of its work, and its final Guidance has been adopted. We find this action regrettable, since in our view EFSA should have awaited the outcome of this complaint before proceeding with adoption of the Guidance. Whilst we accept that there have been a number of substantive improvements to the Guidance, not all of our concerns have been resolved. We maintain our view, as described above, that the issue of GM insects in the food chain has not been properly addressed, and that conflicts of interest on the working group were not properly declared, and should have resulted in the removal of at least one member of the group.

Rather than begin the entire process again, we propose that:

(1) EFSA publicly acknowledges that it has not dealt correctly with the requirement to consult on issues relating to the potential presence of GM insects in the food chain (whether imported or released in the EU), and prepares a new consultation covering this issue.
(2) EFSA publicly acknowledges that his conflicts-of-interest mean that Dr Michael Bonsall should not have been appointed to the GM Insects Working Group.
(3) EFSA publicly acknowledges that Mumford, Christophides and Bellini should have declared that they were involved in joint research projects with Oxitec.
(4) EFSA takes the action stipulated in Article 15(4) of Annex VI to its response, which requires a review by its Internal Audit Capability (IAC) of the Guidance when an expert is in breach of the rules. This review should be open and transparent and the findings should be published.
(5) EFSA publicly acknowledges that neither Michael Bonsall nor Jeff Bale were entitled to comment on the draft Guidance on behalf of ACRE, since this breached the requirement not to comment on their own work (EFSA's response Annex VI, Article 9, 1(d)).
(6) EFSA amends its conflicts-of-interest policy to:

(i) Explicitly require the declaration of any involvement in joint research projects (during the relevant 5 year period) with companies that have relevant commercial interests;
(ii) Explicitly require the declaration of any investments by the expert's employer in any companies with a relevant commercial interest, including when the employer is a university or not-for-profit institute;
(iii) Explicitly make joint research with a company with relevant commercial interests invested in by one's employer (e.g. a spin-out company) a bar to membership of EFSA's Scientific Committees, Panels and Working Groups;
(iv) Limit the number of experts on any given Scientific Committee, Panel or Working Groups undertaking joint research activities with companies whose business activities will be affected by the work being undertaken;
(v) Include clear, transparent and consistent breach of trust policies and procedures, as recommended by the European Court of Auditors (Annex XI to EFSA's response) Recommendation 6, noting that, for Working Group experts, dismissal of someone no longer in post does not amount to a credible sanction.

With thanks for your assistance,

Yours sincerely

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[1] http://www.isis-innovation.com/
[2] http://www.zoo.ox.ac.uk/people/view/bonsall_mb.htm
[3] http://www.oxitec.com/luke-alphey-appointed-visiting-professor-at-oxford-university/
[4] www.osem.ox.ac.uk
[5] http://www.osem.ox.ac.uk/portfolio/index.html#healthCare
[6] Beech, C.J. et al., 2009. Deployment of innovative genetic vector control strategies: Progress on regulatory and biosafety aspects, capacity building and development of best-practice guidance. As. *Pac. J. Mol. Biol. & Biotech*., **17**(3), pp.75–85.
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[8] Beech, C.J. et al., 2009. Deployment of innovative genetic vector control strategies: Progress on regulatory and biosafety aspects, capacity building and development of best-practice guidance. As. *Pac. J. Mol. Biol. & Biotech*., **17**(3), pp.75–85.