

**ADVISORY COMMITTEE ON RELEASES TO THE ENVIRONMENT  
MINUTES OF THE 134<sup>TH</sup> MEETING OF ACRE AT NOBEL HOUSE, LONDON,  
THURSDAY, 1<sup>ST</sup> DECEMBER 2011**

**Present:**

Prof Chris Pollock (chairman)  
Prof Jim Dunwell  
Mr Jim Orson  
Prof Keith Lindsey  
Prof Jeff Bale  
Prof David Hopkins  
Dr Ieuan Joyce  
Prof Les Firbank  
Dr Mike Bonsall  
Prof Kathy Bamford

**Invited expert:**

Dr Mike Skinner

**Assessors:**

Dr Jonathan Davey	SASA
Dr Simon Warne	HSE
Mr Dave Jefferies	FSA

**Defra:**

Dr L Ball (secretary)  
Ms S Brown  
Dr S Popple  
Mr M Rowe  
Mr D Sherlock

Apologies were received from Prof Hails, Prof Peters and Prof Bullock. The chairman welcomed Dr Mike Skinner who was assisting ACRE in its assessment of a GM vaccine application. Dr Skinner is a senior lecturer in the Department of Medicine at Imperial College London and member of SACGM(CU).

The Committee was notified that Dr Kath Bainbridge has been on a career break since October but would be back in time for the next meeting.

**1. Minutes of the 133<sup>rd</sup> meeting, 4<sup>th</sup> August 2011**

**ACRE/11/M3**

The minutes were agreed with one amendment.

**2. Policy update**

### **2.1 Update on the national decision making proposals**

Members were informed there had been two working groups under the Polish presidency but there had been little progress, with the debate remaining very polarised. This will go as a progress report to the December Environment Council and then pass to the incoming Danish presidency.

### **2.2 ECJ ruling on honey**

This ruling had concluded that pollen was an ingredient of honey, so that there would be a requirement for GM labelling if GM content was greater than 0.9%. The Food Standards Agency leads on this but Defra is working closely with them because of the broader implications, including for field trials. There was also an impact on third country imports where there could be non-authorised GM content. The solution may be a change in legislation to rectify the situation, but the UK will continue to push for pragmatic and proportionate policies. This will be discussed in Standing Committee on 12<sup>th</sup> December.

## **3. Matters arising**

Since the last ACRE meeting Member States have voted on 2 applications, for A5547-127 soyabean (ref. EFSA-GMO-NL-2008-52) and a renewal of 40-3-2 soyabean (EFSA-GMO-RX-40-3-2) to import and use GMOs as food and feed. As there was no qualified majority the applications have been referred to the Appeals Committee which is expected to consider them in January. This is the first time the new comitology rules have been applied to a GM food and feed dossier.

## **4. Matters agreed by circulation**

Since the last ACRE meeting and prior to the vote at standing committee, ACRE's advice has been published on the application for A5547-127 soyabean. Advice has been agreed by circulation and published since the last meeting on 356043 (ref. EFSA-GMO-UK-2007-43) and MON87701 soyabeans (ref. EFSA-GMO-BE-2010-79). These applications are for food and feed uses, import and processing, excluding cultivation. ACRE agreed with EFSA's opinion, which was that these GMOs do not pose a greater risk to human health or the environment than their conventional counterparts, in the context of their proposed uses.

## **5. Update on notifications for authorisation under the GM Food and Feed Regulation (EC) No. 1829/2003** **ACRE/11/P16**

The secretariat informed ACRE that four new applications had been submitted under the GM Food and Feed Regulation since ACRE's meeting in August 2011. All four applications are for import and processing, food and feed use (excluding cultivation). These are FG72 soybean (ref. EFSA/GMO/BE/2011/98), Bt11 x 59122 x MIR604 x 1507 x GA21 maize (ref. EFSA/GMO/DE/2011/99), MON87705 x MON89788 soybean (EFSA/GMO/NL/2011/100) and MON88302 oilseed rape (ref. EFSA/GMO/BE/2011/101).

This is the first time that a GM soybean containing event FG72 has been notified under the GM Food and Feed Regulation. As such, ACRE was provided with a summary of the application. Given the extremely limited potential for environmental exposure of this GMO in the UK, ACRE advised that it would discuss the application after EFSA had published its opinion.

ACRE was informed that an application to cultivate Bt11 x MIR604 x GA21 maize (ref. EFSA/GMO/UK/2010/84) had been validated. The Committee will be asked to consider Bt11 x MIR604 x GA21 maize when the risk assessment for all single events has been finalised.

ACRE was also informed that there have been two new EFSA opinions on applications to cultivate GMOs: MON88017 maize and 1507 maize. EFSA's opinion on 1507 maize updates elements of its existing opinion. ACRE will be consulted on this by circulation. ACRE will be asked to produce final advice on MON88017 maize at its February meeting.

**6. Application from BN ImmunoTherapeutics, Inc. under Part B of Directive 2001/18/EC to carry out a trial involving a therapeutic vaccine consisting of attenuated GM viruses – ref. 11/R44/01** **ACRE/11/P17**

ACRE invited Dr Mike Skinner from the Science Advisory Committee on Genetically Modification (for Contained Use) to join it in assessing this application from BNIT to release a GM vaccine (PROSTVAC V/F) at study sites in England and Wales. Dr Skinner is a virologist with particular expertise in poxviruses.

PROSTVAC V/F is designed to eradicate prostate serum antigen-expressing tumour cells in men with prostate cancer.

The vaccine comprises two live attenuated GM viral vectors. PROSTVAC- V is a modified, attenuated vaccinia virus whereas PROSTVAC- F is a modified, attenuated fowl pox virus. Both GMOs contain the same transgenes - a PSA gene and genes encoding three immunological co-stimulatory molecules (referred to as TRICOM).

ACRE was asked to advise on the risks posed to the environment and to humans that are not patients involved in the trial. Patient safety will be assessed by the MHRA who are responsible for clinical trial authorisations.

ACRE noted that the parental, non-recombinant strain of the vaccinia virus was derived from the same seed stock virus as the Dryfax vaccine, which was used to vaccinate humans against smallpox for over 200 yrs. The applicants have demonstrated through a neurovirulence test in mice that it is more attenuated than the mix of vaccinia viruses comprising the Dryfax vaccine. The parental strain of the fowlpox virus is a USDA licensed poultry vaccine widely used for vaccinating chickens against fowlpox. Therefore, ACRE considered that there was a history of safe use.

ACRE first considers the molecular characterisation of the GMOs, taking into account the stability of the genotypes and methods for their identification. It discussed hazards associated with the insertion of the transgenes into a gene (that has homology to the ankyrin repeat gene family) in PROSTVAC-F. The committee discussed evidence on the role of genes in the ankyrin repeat family in pox viruses. It concluded that the parental strain of PROSTVAC-F is highly attenuated and that knocking out this single gene will not restore it to the full virulence of the wild type virus. ACRE concluded that the molecular characterisation of these GMOs had been carried out to a high standard.

ACRE also considered evidence on the characteristics of these viruses that demonstrates that they are very unlikely to recombine with each other or with other viruses or to insert into the genome of the host cell.

ACRE then assessed the environmental risks associated with the release of these two GMOs by considering routes of potential environmental exposure and by considering the consequences for the environment and humans (who are not patients in this trial).

ACRE noted that PROSTVAC-F is replication defective in humans and that fowlpox is a virus that infects chickens and turkeys – it would not be expected to infect pet species or pigeons etc.

ACRE considered potential routes of shedding and likely duration. For both GMOs, it concluded that this will be restricted to the site of vaccination and that shedding will be minimised through intramuscular injection and, in the case of PROSTVAC-V, through bandaging the wound. It concluded that shedding from other sites is unlikely. The applicant noted that this could be associated with complications. However, ACRE noted the exclusion criteria proposed for patients by the applicant, which will significantly reduce the likelihood of complications.

In the case of PROSTVAC-V injection, ACRE noted that patients would have been vaccinated against smallpox previously. Consequently, patients are unlikely to develop sequel and replication is unlikely because the patients' immune systems will react against the vaccine.

The applicant describes how patients will dispose of contaminated material and dressings associated with the wound-site. ACRE was sceptical about patient compliance in returning this material to the clinic. Whilst the committee considered that the risk to the environment and to human health would be negligible if this material were disposed of in the sewer system or via municipal waste, it considered that procedures likely to result in higher compliance should be adopted. For example, requiring patients to sterilise/ disinfect material prior to disposal.

ACRE discussed the potential for transmission to healthcare staff involved in the trial and in particular, through needle stick injury. ACRE considered that the risk of harm was negligible; it noted safety data from previous clinical trials. However, the committee considered that the applicant should consider local best practice rather than referring to WHO protocol. It advised that procedures should be proportionate but clearly defined. For example, with respect to disposing of material from the trial.

In conclusion, ACRE considered that the applicant had provided a comprehensive and clear environmental risk assessment. However, it advised that if the release of these GMOs is approved that conditions for handling material involved in the trial should be described clearly.

ACRE will not finalise its advice until the public consultations on these applications (submitted to the English and Welsh authorities) have concluded on December 19th. ACRE will consider any representations that have a scientific content and reflect this in its written advice.

*Action: ACRE to agree written advice to Defra and Welsh Ministers after the public consultations on the applications have concluded.*

## **7. Research report: Environmental risks from research trials and marketing of genetically modified (GM) veterinary and human medicines      ACRE/11/P20**

ACRE was asked to comment on the draft report for the research project CB0303: Environmental risks from research trials and marketing of genetically modified (GM) veterinary and human medicines and particular to advise the secretariat of quality and robustness of the study.

ACRE highlighted some short-comings in the research and noted that the scientific language used in places should be improved. The committee provided advice on how to take the work forward.

*Action: Secretariat to provide feedback from ACRE to project officer.*

## **8. Authorisation of glufosinate ammonium-tolerant genetically modified MS8, RF3 and MS8 x RF3 oilseed rape – ref. EFSA-GMO-BE-2010-81      ACRE/11/P18**

MS8/RF3 oilseed rape has received a number of authorisations for placing on the EU market. These cover import, processing and industrial food/feed uses but not cultivation. ACRE was asked to reconsider the advice it published in 2004 on this GMO in the light of new information produced by the applicant, EFSA opinions and information on oilseed rape imported into the UK. Committee members were asked to consider and comment on the likelihood and consequences of MS8/RF3 plants growing from spilled grain during import; and what if any, management/ monitoring measures would be appropriate.

ACRE considered that the risk to the environment posed by spilled grain was no greater than for non-GM oilseed rape. This was on the basis of three layers of evidence that in combination indicate a negligible risk:

- limited environmental exposure. This is because of the proximity of the crushing and processing plants to the receiving ports (i.e. only non-living material will be transported inland).

- if MS8/RF3 grain was spilled it would not persist or invade new habitats to a greater extent than non-GM OSR. In addition, ACRE noted that the use of glufosinate ammonium herbicides is not significant in semi-natural environments.
- feral oilseed rape populations in the UK are not self-perpetuating and therefore will decrease over time in semi-natural environments unless the grain is replenished through further spillage<sup>1</sup>

ACRE noted that the management guidelines for dealing with spillage supplied by the applicant were thorough.

In considering its previous advice, ACRE noted that coexistence measures were not within its remit because these concern choice rather than risk to the environment and to human health. It requested that the secretariat update its advice on MS8/Rf3 oilseed rape to better reflect its responsibilities.

*Action: ACRE secretariat to amend existing ACRE advice in the light of ACRE's discussion and to circulate to the committee for comment and agreement.*

## **9. Framework document governing the working relationship between Defra and ACRE and updated Code of Practice for Scientific Advisory Committees**

### **ACRE/11/P19**

In line with Cabinet Office and Treasury guidance, sponsoring departments are required to draw up a written agreement with their arms length bodies that sets out the relationship between them. Members considered a draft framework document which incorporated the existing terms of reference for ACRE and gathered together in one place existing advice on good practice. ACRE was broadly content with the draft framework document and asked for the Devolved Administrations to be consulted to ensure the relationship with them was accurately reflected.

ACRE members were given copies of the updated Code of Practice for Scientific Advisory Committees, published at the end of November. ACRE had contributed to the consultation on the draft of this document. The update has expanded and clarified advice from the previous Code but will not impact on ACRE significantly. The Code outlines good practice for committees, which ACRE is already following, but there are some new responsibilities imposed on the secretariat and additional advice on its role.

*ACTION- Secretariat to circulate framework document to members for any comments and check with Devolved Administrations*

## **10. Items for information**

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<sup>1</sup> Devos et al 2011 Feral genetically modified herbicide tolerant oilseed rape from seed import spills: are concerns scientifically justified? Transgenic Res 10.1007/s11248-011-9515-9

### **10.1 Oral update on post-market environmental monitoring**

The draft report would be circulated shortly and discussed at the next meeting, in February. The methodology and preliminary findings have been presented at an EU working group. The focus of the report is on the use of existing surveillance networks.

### **10.2 EFSA scientific opinion – statistical significance and biological relevance** **ACRE/11/INF14**

ACRE noted this document and commented that it was of a high quality.

### **10.3 Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA** **ACRE/11/INF15**

This paper, published in Cell Research, had been identified by ACRE members as presenting interesting but as yet, uncorroborated results and conclusions. The committee noted that its relevance would be primarily for diet and health. The paper reports the first evidence that small regulatory RNAs, called microRNAs, produced by plants can regulate gene expression in mammals. The researchers detected plant-derived microRNAs produced in the blood and tissues of humans and other plant-eating mammals. One particular microRNA, MIR168a, which is present naturally in high concentrations in rice and cruciferous vegetables was found to inhibit a protein that helps to remove low-density lipoprotein ('bad cholesterol'). The researchers acknowledge in their paper that these findings are surprising.

ACRE considered that animal and plant material containing these molecules has been part of the human diet for hundreds of thousands of years and that humans have therefore evolved in the presence of such molecules. The committee noted that the current regulatory pipeline does not include any GMOs that have been modified to produce microRNAs. There are GM plants that have been modified so that they produce small silencing RNAs. ACRE considered that current risk assessment procedures were appropriate for addressing possible risks to the environment on a case by case basis.

A member of the secretariat for the Advisory Committee on Novel Foods (ACNFP) attended the meeting and informed ACRE of the discussion that had taken place during the ACNFP meeting on November 24<sup>th</sup>. Both committees agreed that further work would be needed to validate the findings and that they would track the issue with interest

*Action: ACRE to keep apprised of research in this area and to coordinate with the ACNFP as necessary.*

### **10.4 Potential trial of a 'genetically sterile' insect under the Contained Use Regulations** **ACRE/11/INF16**

ACRE was informed of a request sent to HSE by a small biotechnology company, Oxitec who develop GM insects for use as agents of biological control. The company had queried whether trials involving insects modified to express a repressible dominant lethal trait could be carried out under the contained use regulations and if so, what physical barriers would be required. HSE consulted its Advisory Committee

on Genetic Modification (Contained Use). The Secretary of SACGM(CU) attended the ACRE meeting and summarised the SACGM's discussion. Defra is part of the competent authority for the contained use of GMOs and as such it had asked ACRE members as well as an external expert to comment ahead of SACGM's meeting, which was held on November 7th. ACRE agreed with SACGM in concluding that, in theory, the technology would confer a high degree of genetic containment. However, it considered that more empirical evidence was needed to confirm that this would be the case in practice; in particular, with regard to the level of penetration of the lethal trait into wild type populations and the rate of loss of the associated transgenic construct. The secretariat asked ACRE to consider what information it would expect to see if an application to release this GMO was submitted in the future. It was asked to consider whether there would be a conundrum in proving the requisite information i.e. whether data from open field trials would be needed to support applications to carry out such trials. ACRE did not consider this would be the case.

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.

**10.5 Statement complementing the EFSA GMO Panel scientific opinion on maize MON89034 x 1507 x MON88017 X 59122, to cover all sub-combinations - ref. EFSA-GMO-CZ-2008-62** **ACRE/11/INF17**

ACRE noted this paper to update EFSA's risk assessment on a stacked event, which now takes into account the sub-combinations of this event. The overall conclusion on the risk posed by this GMO has not altered.

**10.6 Executive summary of an evaluation of the EU legislative framework in the field of cultivation of GMOs under Directive 2001/18/EC and Regulation (EC)No 1829/2003, and the placing on the market of GMOs as or in products under Directive 2001/18/EC** **ACRE/11/INF18**

ACRE welcomed this as a useful contribution to the debate on the legislative framework.

**10.7 Field-evolved resistance to Bt maize by western corn rootworm** **ACRE/11/INF19**

ACRE noted this document, describing the first example of field evolved resistance in western corn rootworm.

**11. Any other business**

None

**12. Date and time of the next meeting**

Thursday 9<sup>th</sup> February at 10.30am in Nobel House.

**ACRE Secretariat  
December 2011.**