ADVISORY COMMITTEE ON RELEASES TO THE ENVIRONMENT

Advice on an application for deliberate release of a GMO for research and development purposes

Applicant: University of Leeds

Application: To release potato lines genetically modified for resistance to potato cyst nematodes

Ref: 09/R31/01

Date: 22 March 2010

Advice of the Advisory Committee on Releases to the Environment to the Secretary of State under section 124 of the Environmental Protection Act 1990

ACRE is satisfied that all appropriate measures have been taken to avoid adverse effects to human health and the environment from the proposed release. ACRE sees no reason for the release not to proceed according to the following advice.

To avoid possible adverse effects to human health and the environment, the applicant should:

1. Ensure that the GM potatoes produced as a result of this release will not be put into the human food chain or fed to livestock.

2. Ensure that any GM or non GM potato plant material remaining in the area of release at the end of the trial is inactivated.

3. Ensure that in the two years following harvest of the GM potato tubers, the area of release is left fallow and not ploughed; but at least annual shallow tillage in the spring is used to stimulate germination of any true potato seed.

4. Treat any groundkeepers and volunteers growing from true seed in the fallow years with an application of glyphosate herbicide or hand pull potato plants prior to flowering.

5. Ensure that during any post-trial monitoring period remaining after the fallow period that a crop is cultivated on the release site which would permit easy identification and control of groundkeepers and volunteers.

6. Control all groundkeepers and volunteers continuously until a period of two years has elapsed during which no groundkeepers or volunteers have been observed. The appropriate herbicides should be used to control potato plants growing from true seed and from groundkeepers prior to flowering. Alternatively, plants growing from groundkeepers may be hand pulled.

7. Ensure a separation distance of 20 metres to non-GM potato plants growing around the trial site to minimise the probability of cross-pollination occurring.

1 Application reference 09/R31/1 dated 4 January 2010.
Comment
ACRE considered the risks to human health and the environment posed by the proposed release of potatoes genetically modified for resistance to potato cyst nematodes. The Committee has addressed a number of points in its safety assessment including scientific issues raised in public representations.

Key characteristics of this release for risk assessment are that:-

i) The trial will be on a very small scale. This application is to release a maximum of 12,000 GM potatoes over a 3 year period. The applicant has proposed that the release will take place at one site. The site that GM potato plants will occupy is an experimental plot of no more than 0.1 hectare in each year of the trial.

ii) The GM potatoes produced as a result of this release will not be put into the human food chain or fed to livestock.

A gene conferring resistance to the antibiotics neomycin and kanamycin (nptII) is present in the GM lines to be released. ACRE has previously considered the issue of the presence of antibiotic resistance marker genes, including the statement from the European Medicines Agency (EMA) on the importance of preserving the therapeutic relevance of the antibiotics kanamycin and neomycin. ACRE is of the opinion that the therapeutic effect of antibiotics that are substrates for NPTII will not be compromised by the presence of the nptII gene in GM plants. ACRE’s advice on this issue is that (a) the likelihood of transfer of a functional gene from plant material to bacteria is extremely low; (b) bacteria with resistance to these antibiotics are widespread in the environment; and (c) the acquisition of an intact gene is only one of the possible mechanisms by which bacteria may develop resistance. All these points apply to this case of the proposed trial of GM potato cyst nematode (PCN) repellent potatoes.

With regard to the issue of horizontal gene transfer (HGT) from plants to soil prokaryotes, ACRE is of the opinion that HGT between plants and soil prokaryotes under field conditions is a rare phenomenon. Furthermore the absence of prokaryotic features (i.e. plasmid vector backbone sequences), will reduce the probability of HGT. Even if it is assumed that this rare recombination event does occur, the consequences are predicted to be negligible since genes are highly unlikely to recombine as fully functional transcription units.

ACRE is of the opinion that that none of the inserted DNA (inverted repeats - GPCP and MICP to inhibit nematode digestion through RNAi; inverted repeats - MIOX to inhibit feeding site establishment through RNAi; Maize ribosomal inactivating protein b32RIP to inhibit feeding site and anther development; selectable marker - nptII; constitutive promoter – nos; constitutive promoter - CaMV 35S; root specific promoter – ARSK-1; root and anther specific promoter – MIOX; transcription terminators – nos and ocs) or gene products are likely to result in a risk to human health or the environment in the context of the proposed release.

With respect to potatoes transformed with the RNAi constructs, ACRE is satisfied that these will silence only genes which have significant sequence similarity. The applicants state that no genes within the human genome have high homology to the dsRNA produced by plants to be used in this trial. Evidence is also provided of rapid degradation of the dsRNA by simulated gastric fluid. dsRNAs are naturally produced in plants, but are rapidly degraded and do not accumulate to high levels inside plant cells or persist outside the cell. Specifically GPCP dsRNA is predicted to specifically inhibit digestion in potato cyst nematodes following ingestion of the transgenic potato, whilst the MICP dsRNA is specific to a nematode not present at the trial site and included as an experimental control. The MIOX inverted repeat construct uses
sequence from potato, and is expressed specifically in potato root tissue to prevent formation of the nematode feeding cell.

With respect to potatoes transformed with b32RIP, ACRE is satisfied that expression of this protein is unlikely to pose a risk to human health or the environment within this research trial. The protein is expressed naturally in maize seed and likely to be expressed in these transgenic potatoes at low levels owing to the root and anther specific promoter. The specific inhibition of feeding cell and anther development is likely to result in a specific interaction with potato cyst nematode.

The transgenic plants will be destroyed on completion of the trial and will not enter the food or animal feed chains. Potatoes are not generally eaten by wild animals due to the natural presence of toxic chemicals in plant foliage. In addition, the trial will be fenced. ACRE is therefore satisfied that release of these transgenic potatoes expressing dsRNA and b32RIP do not pose a risk to human or animal health. In addition ACRE considers that the specificity of the interaction between the host and the potato cyst nematode means that adverse effects on the environment, including non-target organisms are not likely to occur.

Cultivated potatoes are a low-risk crop for pollen-mediated gene flow because they are highly self-compatible and cannot cross with other UK wild species to produce viable offspring. A complete chain of events would have to occur in order for a potato containing a GM event to enter the human food chain. First, pollen containing a GM event would have to be produced and this occurs to a variable degree in potato plants since some cultivars produce few flowers. In the University of Leeds trial, the transformed potato cultivar is Desiree which is capable of flowering and setting seed and therefore this can be regarded as possible. The second stage would be the successful transfer of the pollen to a non-GM potato growing in a commercial crop. This relies on pollen being transported by the wind or by insects; pollen dispersal typically tails off with distance from the pollen source. ACRE recognises that rare long-distance cross-pollination events are possible, especially where pollen beetles are common in the release area. However, cross-pollination frequencies reduce dramatically over distance and pollen competition from within a non-GM potato crop reduces the likelihood of successful hybridisation further. Third, even if GM pollen successfully hybridised and resulted in GM seed, the chance of such seed successfully germinating and surviving until harvest as a tuber in a non-GM potato crop is low because potatoes are usually grown in rotations and the volunteers resulting from true seed are very vulnerable to herbicide applications and crop competition.

The applicant has proposed a separation distance of 20 metres to non-GM potato plants growing around the trial site and ACRE therefore considers that the probability of cross-pollination occurring is minimal.

ACRE notes the information provided on the layout of the release site, which proposes to surround GM potatoes (cv Desiree) with guard non-GM potatoes (cv Sante). The aim here is to protect the trial potatoes from the typical field edge effects of wind and rain. Due to the close proximity to the GM potatoes, the University of Leeds propose to treat these guard potatoes as part of the GM trial and dispose of them in the same way as the GM material. ACRE considers that this measure is appropriate to ensure that all GM potato material is inactivated at the end of the trial. The Committee recognises that other details on the layout of the release site are required primarily for enforcement and do not affect the risk assessment of this release. The Committee also notes that the release will be overseen by the GM Inspectorate and that it is appropriate given the experimental nature of the programme of work for details of the plot design to be provided just prior to the time of the release.
ACRE considered the post harvest monitoring plans proposed by the applicant. Monitoring of previous releases of potatoes has revealed that groundkeepers may persist for many years after the initial release. ACRE advises that the trial should be harvested as soon as practical after results have been obtained in order to minimise shedding of true seed. In addition ACRE advises that the ground on which potatoes have been released should remain fallow for two years following the release and not ploughed. This would allow true potato seed and tubers to remain near the soil surface and produce volunteers. Light tillage should be carried out annually in the spring to stimulate germination of true potato seed but no other form of cultivation should be used on the release area. Furthermore the Committee considers that the University of Leeds should monitor the trial area until it has been clear of potato groundkeepers and volunteers for a continuous period of two years and that crops which facilitate the removal of potato groundkeepers and volunteers should only be grown throughout the remaining post-trial monitoring period.

**Items arising from public representations**

ACRE considered nineteen representations received from members of the public on this application with respect to the scientific issues. The Committee considered the comments relating to:

- The presence of the *nptII* antibiotic resistance marker gene. ACRE has considered the issue of the presence of an antibiotic resistance marker gene in potatoes, this is detailed above.

- The potential allergenicity of gene products. ACRE notes that in three cases the mode of action is through RNAi and as such no novel protein is produced which could confer allergenicity. In the remaining transgenic line, the b32RIP gene, which is derived from naturally occurring maize, is expressed specifically in root cells and anther cells. The Committee considered this case, and concluded that the issue is not relevant owing to the small scale of the trial and because the potatoes will not enter the human or animal food chain.

- The potential of harm to non-target organisms, in particular bees. ACRE notes that the mode of action for resistance to potato cyst nematodes is designed to be highly specific between the host and the nematode. Therefore negative effects on non-target organisms are unlikely to occur. In addition, as described above, bees rarely forage in potato crops and exposure would be limited owing to the small scale of the trial.

- Risk management issues of separation distances, survival of potato tubers and cross pollination. As explained earlier in this advice, cross pollination is just one event in a chain of unlikely events that would be needed to contaminate potato crops outside the trial area. Potato cannot cross pollinate with UK wild species to produce viable offspring. Potato does not persist outside the farmed environment and the genetic modifications will not improve its fitness in this respect. The Committee considers that the other risk management issues raised in these representations did not affect the risk assessment given the scale of the release and the control measures in place.

- Risks of releasing nematodes. No nematodes will be released as part of this trial. The trial site was chosen owing to a naturally occurring infestation of potato cyst nematode, which is a common pest in the UK.
Risks of increased pesticide use
This trial will be conducted in accordance with conventional agricultural practice, with the exception that no pre-plant pesticide treatment to control nematodes will be applied. This represents a decrease in pesticide use.

ACRE is content that all issues raised had been considered thoroughly during the Committee’s assessment of the dossier. ACRE is satisfied that all scientific issues raised by the public with respect to this application have been addressed in this advice.