Advisory Committee on Releases to the Environment

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

Applicant: The Sainsbury Laboratory

Application: To release potato lines genetically modified for resistance to potato late blight

Ref: 16/R29/01

Date: April 21 2016

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, 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. Appropriate herbicides should be used to control potato plants growing from true seed and from groundkeepers prior to flowering

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

Comment

ACRE considered the risks to human health and the environment posed by the proposed release of potatoes genetically modified for resistance to potato late blight. ACRE 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:

i) The trial will be on a very small scale. 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 1 000 square metres over the three years 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.

The Sainsbury Laboratory (TSL) is applying to field trial GM potato plants (*Solanum tuberosum*) containing one of six resistance (*R*) genes. These confer resistance to different isolates of potato late blight (*Phytophthora infestans*). The *R* genes are derived from wild potato relatives *S. venturii* and *S. americanum* and from the *S. tuberosum* variety Sarpo Mira. Sarpo Mira's increased resistance to potato late blight is also derived from introducing *R* genes from wild potato relatives into a commercial line. However, this was achieved through conventional crossing rather than by using a bacterium to transfer the genes.

The GM line containing the R gene from *S. venturii* was authorised for use in a previous trial (which took place in 2010- 2012).

This application is unusual in that TSL has made GM lines containing only two of the six *R* genes described. The molecular characterisation of the lines that have been made is of a high quality but includes information that is not required for the risk assessment in this particular case. This includes information on copy number and levels of *R* gene expression. Molecular characterisation data on GM potato lines containing the four other *R* genes must be provided before they can be planted. This information is required to ensure that the risk assessment and management measures described in the application and agreed by ACRE apply. These data should provide evidence that backbone T-DNA is not present in the GMOs as the TSL has not assessed the potential risks of genetic elements from the vector backbone being inserted in the GM potato.

These *R* genes are members of the nucleotide binding site-leucine rich repeat (NB-LRR) family. This type of gene is already abundant in potato and other plant genomes. Many non-GM potato varieties cultivated in Europe already contain genes of this class, derived from another potato wild relative, *Solanum demissum*. Introduction of these additional *R* genes to the GM potatoes is intended to increase the range of late blight pathotypes to which potato is resistant. There is no evidence of *R* genes of the NB-LRR family conferring toxic or allergenic properties. The corresponding promoter and terminator regions from the potato wild relatives have been transferred along with the *R* genes.

Insertion of the *nptII* gene that confers resistance to the antibiotics neomycin and kanamycin was raised in most of the public representations on this application. ACRE has considered this issue on a number of occasions previously, including after a statement by the European Medicines Agency (EMA) on the importance of preserving the therapeutic

relevance of the antibiotics kanamycin and neomycin. ACRE remains 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 late blight resistant potatoes.

Some of the GM potatoes lines will contain the *bar* gene, rather than the *nptII* gene, as a marker gene to distinguish the GM potatoes from untransformed potatoes. This gene derives from the soil bacterium *Streptomyces hygroscopicus* and confers resistance to glufosinate ammonium-containing herbicides (which will not be used on the trial site). The potential for horizontal gene transfer (HGT) from plants to soil bacteria has been discussed above with respect to the *nptII* gene. HGT between plants and soil prokaryotes under field conditions is a rare phenomenon. Even if it did occur, the gene is highly unlikely to recombine as a fully functional transcription unit, and so would not be expressed.

Cultivated potatoes are a low-risk crop for pollen-mediated gene flow because they are highly self-compatible and cannot cross with other wild or ornamental species in the UK 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 depending on the variety. Both of the varieties used in this trial (Desiree and Maris Piper) can produce flowers and set seed. 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 area of the trial site. 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. ACRE considers that this will minimise the likelihood of cross-pollination occurring.

ACRE notes the information provided on the layout of the release site, which proposes to surround GM potatoes with guard non-GM potatoes. The aim 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 TSL should 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 the measures proposed

by TSL to inactivate material from the trial site are appropriate. Other details on the layout of the trial site are required primarily for enforcement and do not affect the risk assessment. ACRE also notes that the trial 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 several years after the initial release. ACRE considers that these derive from tubers or fragments of tubers left in the soil after harvesting. ACRE advises that hand-pulling, as opposed to mechanical lifting, is more likely to leave this material at the trial site. ACRE considers establishment of potato plants arising from true seed as an unlikely event in agriculturally managed situations, However, as a precautionary measure, ACRE advises that the trial site be managed so that any potential for true seed to persist and germinate into GM plants in future years is also minimised. ACRE advises that the trial site should be harvested, and potato tops removed from the field, as soon as soon as practical after results have been obtained in order to minimise maturation and any potential 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 ACRE considers that TSL 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 fifteen representations[1] received from members of the public on this application. One of these was submitted on behalf of twenty two organisations. ACRE considered the comments relating to the potential for this particular trial to cause harm to human health and the environment. This does not include a food safety assessment as any consent that is issued for this trial will not permit material from the trial to enter the food or animal feed chains. Concerns about whether the trial should have been funded, whether it would be successful and whether there are existing non-GM varieties with resistance to potato blight are not safety issues and as such, are not within ACRE's remit. ACRE took into account all comments that had any bearing on the safety of this trial. These were on:

- Cross-pollination and persistence of seed. A number of the comments raised concern about the potential impact on 'natural relatives'. Studies show that cross-hybridisation does not occur between potato and wild and ornamental species in the UK. The varieties used in the trial do produce pollen and there is limited potential for

[1] A few of these representations were directed at another GM trial application being considered by Defra.

them to cross with varieties of non-GM potatoes. A representation highlighted that other insects as well as bees can transport pollen. ACRE noted the potential for pollen beetles to carry pollen from the site. ACRE discussed in detail the steps required for cross-pollination to result in the presence of GM potato plants outside of the trial site that could then enter the food or feed chain. This is described in the advice above. ACRE's conclusion is that the risk is minimal.

ACRE discussed the potential for true seed to persist at the trial site and generate volunteer plants in future years. Agronomic experts on the committee were of the view that fragments of tubers resulting from hand-pulling of plants at harvest was the main source of GM potatoes persisting at trial sites. However, ACRE advised on precautionary measures to ensure that any viable true seed is encouraged to germinate and that any resulting plants are destroyed by herbicide treatment.

A representation also raised concern that animals might transport GM tubers away from the trial site. ACRE discussed this but considered that the fencing around the site would minimise this risk. In addition, potato does not persist outside the farmed environment and the genetic modifications to these GM potatoes will not improve their fitness in this respect.

- The majority of representations were concerned about the use of an antibiotic resistance "marker" gene (*nptII*) that could transfer to disease-causing bacteria. ACRE's consideration of this issue is detailed in the advice above.

- A number of representations referred to the potential for unexpected effects associated with the process of producing these potatoes that could lead to environmental harm. ACRE discussed the biology of potatoes and the sort of changes that could lead to harm in the context of this trial. ACRE noted that if these GM potatoes were for food/ feed use, data on glycoalkaloid levels would be required to ensure that they do not exceed acceptable levels of these natural toxins. However, these data are not necessary for the GM potatoes used in this trial because measures will be imposed to prevent material from the trial entering the food/ feed chain.

ACRE also considered the potential for unexpected effects associated with the introduction of additional *R* genes into the genome of the potato lines. ACRE noted that the mode of action for resistance to potato late blight is designed to be highly specific between the host and the pathogen. Therefore negative effects on non-target organisms, such as bees, are unlikely to occur.