



DECISION

Date	19 April 2013
Application Code	APP201381
Application Type	Determination of whether or not any organism is a new organism under section 26 of the Hazardous Substances and New Organisms (HSNO) Act 1996
Applicant	New Zealand Forest Research Institute Limited (Scion)
Date Application Received	19 October 2012
Consideration Date	18 March 2013
Considered by	A decision-making committee of the Environmental Protection Authority (the Committee) ¹ Louise Malone (Chair) Helen Atkins Kerry Laing
Purpose of the Application	To determine whether the use of custom Zinc Finger Nucleases (ZFNs) and custom Transcription Activator-Like Effectors (TALEs) results in organisms classed as genetically modified organisms, and therefore new organisms for the purposes of the HSNO Act

1. Decision

1.1 The Environmental Protection Authority (EPA) determined under section 26 of the Hazardous Substances and New Organisms (HSNO) Act 1996 (the Act) that organisms resulting from the use of Zinc Finger Nuclease type 1 (ZFN-1) and Transcription Activator-Like Effector nucleases (TALEs) are not considered genetically modified, and therefore, are not new organisms for the purposes of the Act.

2. Purpose of the Application

2.1 An application was lodged to determine whether organisms resulting from the use of ZFN-1 and TALEs are genetically modified organisms (GMOs) for the purposes of the Act.

¹ The Committee referred to in this decision is the subcommittee that has made the decision on this application under delegated authority in accordance with section 18A of the Act.

3. Application and consideration process

- 3.1 The application was formally received on 19 October 2012.
- 3.2 The information that the EPA took into consideration included:
 - The application;
 - Internal EPA advice;
 - Comments submitted by the applicant in response to EPA staff advice; and
 - Comments submitted by the Sustainability Council of New Zealand.
- 3.3 The determination was made in accordance with section 26 of the Act. It is noted that the HSNO Methodology Order 1998 relating to the identification, assessment and evaluation of risks, costs and benefits is largely not applicable to section 26 determinations. Applications under section 26 of the Act do not require public notification.
- 3.4 In relation to the comments from the Sustainability Council, these were made informally. The Council had expressed an interest in this technology in the past and had previously contacted the EPA to enquire into its position on ZFN-1. The applicant was given the opportunity to comment on the Council's comments and these were all taken into consideration by the Committee.
- 3.5 In accordance with section 26(2)(b) of the Act, the Department of Conservation and Ministry for Primary Industries were informed of the application and given the opportunity to comment.
- 3.6 The Department of Conservation declined to comment, noting that they do not have the in-house capability to comment on a determination of this nature.
- 3.7 The Ministry for Primary Industries noted that they did not have any knowledge or experience dealing with ZFNs or TALEs with respect to whether their use results in a genetically modified organism.

4. Reasons for the Decision

- 4.1 For an organism to be determined to be a new organism, the organism must be shown to meet the criteria in section 2A(1) of the Act.
- 4.2 The relevant consideration for this determination was whether organisms arising from the use of ZFN-1 and TALEs met the description of 2A(1)(d) a genetically modified organism.

4.3 Section 2 of the Act defines a genetically modified organism as:

Genetically modified organism means, unless expressly provided otherwise by regulations, any organism in which any of the genes or other genetic material-

- a) have been modified by in vitro techniques; or*
- b) are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by in vitro techniques.*

4.4 The Committee determined that the use of ZFN-1 and TALEs results in organisms in which the genes or genetic material have been modified by *in vitro* techniques. The relevant consideration then was whether these techniques have been excluded by the Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998 (the Regulations).

4.5 Clause 3(1)(b) of the Regulations provides that:

(1) For the purposes of the Act, the following organisms are not to be regarded as genetically modified:

(b) organisms that are regenerated from organs, tissues, or cell culture, including those produced through selection and propagation of somaclonal variants, embryo rescue, and cell fusion (including protoplast fusion or chemical or radiation treatments that cause changes in chromosome number or cause chromosome rearrangements):

4.6 EPA staff provided advice on whether the ZFN-1 and TALEs techniques were more scientifically similar to genetic modification or chemical mutagenesis. Staff compared and contrasted the techniques, noting that in terms of the scale of the genetic modification, and the lack of foreign material being inserted into the genome in ZFN-1/TALEs techniques, they were more similar to chemical mutagenesis, while the extensive use of *in vitro* techniques, and the fact that they are used to target a specific genetic sequence and bind to a specific DNA site make them more similar to genetic modification techniques.

4.7 EPA staff considered that ZFN-1/TALEs could be regarded as analogous to either chemical mutagenesis or genetic modification. However, given the high degree of *in vitro* manipulation required by ZFN-1/TALEs, EPA staff recommended that these techniques should be considered as more similar to genetic modification techniques, and thus not exempted by the Regulations.

4.8 The Committee reviewed the EPA staff advice, and considered feedback from the applicant on the staff advice. The Committee considered the experimental process and the products of the ZFN-1 and TALEs techniques and compared them to the processes and products of conventional chemical mutagenesis and genetic modification. The Committee noted that ZFN-1 and TALEs techniques show close similarities to both chemical mutagenesis and genetic modification. However, they considered

that because these techniques involve the exposure of the cell to a chemical agent (in this case, a protein) that induces changes to the genetic sequence without the introduction of foreign DNA and without the use of homologous recombination, the use of ZFN-1 and TALEs proteins to induce changes in the genetic code is more similar to chemical mutagenesis. The Committee noted that the Regulations exclude products of chemical mutagenesis from consideration under the Act.

- 4.9 The Committee considered that the Regulations should not be considered as an exhaustive list. Techniques that are comparable and sufficiently similar to those listed in the Regulations should also be excluded, and organisms arising from them should not be considered GMOs.
- 4.10 The Committee determined that organisms arising from the use of mutagenic techniques using ZFN-1 and comparable TALEs technology are exempt by the Regulations. This determination does not address the use of ZFN-2, ZFN-3, or the use of TALEs or other hybrid proteins to induce genetic changes where a repair template is used, or where homologous recombination is utilised to repair DNA damage induced by the introduced protein.
- 4.11 The Committee noted that this determination highlights the need for a review of the Regulations, as they are not keeping pace with a rapidly evolving field of science. They recommended that the Regulations be reviewed by staff at Ministry for the Environment, to improve their clarity.

Conclusion

- 4.12 In accordance with section 26 of the Act, and having regard to the relevant information, the EPA has determined that organisms resulting from the use of Zinc Finger Nuclease type 1 (ZFN-1) and Transcription Activator-Like Effectors (TALEs) are not considered genetically modified, and therefore, are not new organisms for the purposes of the Act.

Louise Malone
Chair, Decision Making Committee
Environmental Protection Authority

Date