

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

STATEMENT ON STUDIES OF POTATOES GENETICALLY MODIFIED TO PRODUCE *Galanthus nivalis* LECTIN



Introduction

1. The Committee was asked to provide advice to the Advisory Committee on Novel Foods and Processes (ACNFP) on the toxicological aspects of certain studies which had been carried out at the Rowett Research Institute. These unpublished studies involved the administration to rats of various potato-containing diets. The diets contained potatoes either with or without the addition of non-potato lectins (the snowdrop, *Galanthus nivalis*, lectin or the jack bean lectin, Concanavalin A) or potatoes which had been genetically modified to produce the snowdrop lectin.

2. These studies had received considerable publicity following statements about adverse effects on the rats made on a television programme. Accordingly, the Secretariat of the ACNFP had sought to obtain copies of detailed scientific reports relating to these studies. However, it had only been able to obtain certain documents that were already in the public domain and a manuscript submitted for publication by Dr Stanley Ewen and Dr Arpad Pusztai. The documents that were considered by the Committee on Toxicity are listed below.

3. The Committee was particularly asked to consider the significance of:

- the effects reported on the body and organ weights of the rats,
- the results of the lymphocyte proliferation assay, and
- the histological changes reported in the gastrointestinal tract.

4. Dr Pusztai and Dr Ewen were invited to attend the meeting of the Committee. Only Dr Ewen was able to be present. He made a presentation to the Committee on the histopathology of the gastrointestinal tract of rats from one of the studies on the genetically modified potatoes. He also answered questions from Committee members during the subsequent discussions.

The Committee's Discussions

5. In the course of their consideration the Committee indicated that certain important information about the studies was not provided in the documentation available. Although Dr Ewen was able to provide additional details on the histopathology he was not able to provide answers to questions

relating to the design of the studies or matters relating to the body and organ weight changes and the lymphocyte proliferation assay.

6. In response to a specific question, the Committee was informed by the ACNFP Secretariat that it was understood that the genetically modified lines of potatoes were not intended for release on the market and that an application for such a release had not been made to the ACNFP.

Body and organ weight changes

7. The Committee recognised that an exact knowledge of the composition of the diet and the use of appropriate statistical methods were crucial to the interpretation of the changes in body and organ weights that had been recorded in the studies. The known adverse effects on the health of laboratory rats of raw potato starch in the diet were pointed out. In addition, the importance of minor changes in composition and palatability of diets in determining the body weight in the rat was stressed. Although it was clear that attempts had been made to ensure that the animals had received an adequate diet, there was a lack of critical information that would allow the Committee to satisfy themselves that this had been achieved. In relation to this, concern was expressed about the marked differences in composition of the genetically modified potatoes used in some experiments in comparison with control potatoes, which could have had physiological and metabolic effects on the rats irrespective of the genetic modification.

Lymphocyte proliferation assay

8. The variability of the results from this assay has been described in the report of the Audit committee of the Rowett Research Institute (Bourne et al., 1998). The Committee noted that this variability meant that large numerical differences would not necessarily indicate a statistically significant effect and that it was necessary to relate any changes in the immune system to those occurring in other organs of the animals.

Histopathology

9. Dr Ewen made a presentation of the histopathology of the gastrointestinal tract. In this he showed slides recording changes to the thickness of the mucosa in the stomach and sections of the small intestine occurring after feeding of diets containing genetically modified potato. A common feature was elongation of the crypt and villi of the jejunum and ileum. The Committee enquired as to whether measures that would discriminate between hypertrophy and hyperplasia had been made. They were informed that this had not yet been done. The histopathology related only to the gastrointestinal tract of the rats from one of the studies (Anon., 1999), it was pointed out that it would be usual for a toxicology study to have incorporated a full examination of all the major organs. The Committee was of the view that this would have provided an opportunity for seeking an explanation of any changes to the immune system or of organ weights.

Conclusions

10. On the basis of the information made available, the Committee expressed concern about the design of the studies, e.g. the limited numbers of animals used and the adequacy of the diets. It appeared that a limited set of studies had been used to address many questions relating to nutritional, toxicological and immunological matters. The design of the studies may not have been adequate for this purpose.

11. It was agreed that the studies could be used to provide an indication of the investigations and procedures that would be needed in any future work in this area. However, these studies could not be used, by themselves, for defining the effects on the rat of potatoes containing the transgene for the *Galanthus nivalis* lectin.

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Documents considered by the Committee

Anon. (1999). The effects of raw and cooked transgenic (GNA-expressing) potatoes on metabolism of rats were evaluated in a 10 day feeding trial [D227], pp 6.

Bourne FJ, Chesson A, Davies H and Flint H (1998). SOAEFD flexible fund project RO 818: Audit of data produced at the Rowett Research Institute (Date of audit: 21st August 1998).

Bourne FJ, Chesson A, Davies H and Flint H (1999). The Audit Committee's Response to Dr Arpad Pusztai's Alternative Report of 22 October 1998. 16 February 1999.

Ewen SWB and Pusztai A (1999). Diets containing genetically modified (GM) potatoes expressing *Galanthus nivalis* (GNA) lectin are associated with proliferation of the mucosal cells of the rat gut, unpublished manuscript.

Horgan GW and Glasbey CA (1999). Statistical analysis of experiments on genetically modified potatoes conducted at the Rowett Research Institute. Preliminary Report. 1 March 1999. Biomathematics and Statistics Scotland.

[Pusztai A] (1998). SOAEFD Flexible Fund Project RO 818: Report of Project Coordinator on data produced at the Rowett Research Institute (RRI). [22 October 1998].

Pusztai A (1999). Letter of 23 April 1999 to Dr JB Greig, COT Secretariat.