Dr. Elizabeth Lewis
2233 Argentia Road
Suite 308, Mississauga
ON L5N 2X7, Canada

RE: Substantial Equivalence Opinion for RESVERATROL

January 11th, 2012

Dear Elizabeth,

I am contacting you in regard to the application by your client, Fluxome Sciences A/S for an opinion under *Article 3.4.* of the novel food Regulation EC No. 258/97 on the substantial equivalence of resveratrol made with a genetically modified microorganism (GMM) to resveratrol derived from Japanese knotweed (*Polygonum cuspidatum*) and which has a history of consumption in food supplements within the EU before May 15, 1997. Based on the information provided, the Food Safety Authority of Ireland (FSAI) is satisfied that resveratrol produced by Fluxome Sciences A/S is substantially equivalent to resveratrol produced from Japanese knotweed with respect to its composition, nutritional value, metabolism, intended use and level of undesirable substances.

A summary of the information considered and the FSAI opinion is included. If you are satisfied with this opinion you should notify the European Commission, in accordance with *Article 5* of Regulation EC No. 258/97 prior to placing this product on the market.

Commission contact details:

Mr Andreas Klepsch
European Commission
DG SANCO, E6
Rue de la Loi 200
B-1049 Brussels, Belgium

Regards,

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Dr. Pat O'Mahony
Chief Specialist, Food Technology

SUBSTANTIAL EQUIVALENCE OPINION

RESVERATROL

The Food Safety Authority of Ireland (FSAI) received an application on December 8th 2011 from Fluxome Sciences A/S for an opinion on the substantial equivalence of resveratrol produced with a genetically modified microorganism (GMM) to resveratrol derived from the plant *Polygonum cuspidatum* (Japanese knotweed) which has a history of consumption within the EU prior to 1997. The ingredient is classed as a novel food under *Article 1.2(d)* of the novel food Regulation (EC No. 258/97) "Foods and food ingredients consisting of or isolated from micro-organisms, fungi or algae. This designation is consistent with that adopted for another novel ingredient (Ice Structuring Protein) produced with a GMM which was authorised in 2009 (Commission Decision 2009/344/EC). In such cases the GMM is classed as a processing aid since the ingredient is produced "with" rather than "from" a GMM and no residual GMM material present in the final ingredient. For these reasons the regulatory status of resveratrol from the GMM (*Saccharomyces cerevisiae*) is clear in that it falls within the novel food Regulation rather than the GM Food and Feed Regulation (EC No. 1829/2003).

Composition

The novel ingredient is isolated from the growth media without disruption of the genetically modified *Saccharomyces cerevisiae* which is demonstrably absent from the final ingredient. The applicant demonstrates that the novel ingredient is almost identical to the same ingredient derived from a plant source, Japanese knotweed (*P. cuspidatum*) in that it is made up of more than 98% *trans*-resveratrol and with equivalent ash and moisture levels. Any residual impurities present in the novel ingredient are also present in the plant derivative, or else present at such low levels to be of no safety concern. The biosynthetic pathways for resveratrol from the two sources differ in that the plant pathway consists of five stages compared to two in the GMM, with most metabolic intermediates and impurities being removed during the purification stages.

Nutritional Value and Metabolism

The high purity level of resveratrol from the GMM (>98%) is similar to that from the plant source and therefore it is unlikely there will be any significant variation with respect to nutritional value or metabolism.

Intended Uses

The applicant indicates that the novel ingredient will compete with or replace plant derived resveratrol already on the EU market in supplement form. Food supplements currently on the EU market contain plant-derived resveratrol either as the sole ingredient or as one of a number of ingredients, with maximum recommended daily resveratrol intakes of up to 500mg.

Level of Undesirable Substances

The novel ingredient is produced to >98% purity, with any residual impurities being unquantifiable or present at very low levels, and generally found in the plant derived resveratrol at similar levels. Due to the production and subsequent purification processes there is little likelihood of allergenic protein being present in the novel ingredient, as confirmed by protein analysis results. Heavy metal and microbiological analyses of the novel ingredient are equivalent to those for the plant derived resveratrol.

Conclusions

The FSAI is satisfied that in view of the information provided by Fluxome Sciences A/S, resveratrol produced with genetically modified *S. cerevisiae* is substantially equivalent to resveratrol derived from Japanese knotweed (*P. cuspidatum*) with respect to its composition, nutritional value, metabolism, intended use and level of undesirable substances.