

ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES.

JUICES AND NECTARS WITH ADDED PHYTOSTEROLS

ISSUE

At the November meeting, Members requested further information on an application for authorisation of fruit juices (including tomato juice) and fruit nectars with added phytosterols under the novel foods regulation (EC) 258/97 (ACNFP/69/1). The Committee is asked to consider the applicant's responses and whether it recommends authorisation of this application.

Background

1. An application has been submitted by Coca-Cola Services s.a. for the authorisation of fruit juices (including tomato juice) and fruit nectars with added phytosterols as novel foods (NF). This application was accepted by the UK Competent Authority, on the 28th October 2004. In accordance with Article 6(3) of the novel foods regulation (EC) 258/97, the UK has 3 months to prepare an initial assessment report. The European Commission will then circulate this initial assessment to the Competent Authorities in the other Member States for comment.
2. At the November meeting Members highlighted three issues to be addressed by the applicant:
 - (a) how the products with added sterols would be distinguished from their conventional non-fortified counterparts
 - (b) the potential attractiveness of single serving packs to children; and
 - (c) the implications of the small particle size of the ingredient.
3. The Secretariat wrote to the applicant on 13 December, seeking clarification of each of these issues and the applicant responded on 7 January 2005 (Letters attached at Appendices 1 and 2 respectively).

Committee Action required

3. The Committee is asked whether the additional information supplied by the applicant adequately addresses the concerns raised at the previous meeting and whether it can now complete its assessment of this product.
4. If so, the Committee is asked whether it is content with the text of the draft opinion attached as Appendix 2. Once the text has been agreed, the draft opinion will be published via the website for a short period of public comment. The Committee's final opinion will be forwarded to the Commission as the basis for the UK's formal assessment report on this application.
5. If not, the Committee is asked to indicate what additional data would be required.

**Secretariat
January 2005**

Appendixes attached:

- Appendix 1: Letter detailing ACNFP comments
- Appendix 2: Applicant's response to ACNFP
- Appendix 3: Draft Opinion (restricted)

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

**APPLICATION FOR THE APPROVAL OF JUICES AND NECTARS WITH ADDED
PHYTOSTEROLS**

LETTER DETAILING ACNFP COMMENTS

13th December 2004

Reference: NFU 539

RE: JUICES AND NECTARS WITH ADDED PHYTOSTEROLS

Dear Sir

Concerning your application for the approval in respect of (EC) 258/97 of the above products. Your dossier was discussed by the ACNFP on the 25th November 2004.

The Committee was generally content with your application but requested clarification on a number of issues.

1. Members expressed concern that the products might not be easily distinguished from counterparts that did not contain added phytosterols. They would welcome further information on the presentation of the proposed phytosterol-containing products, in order to assess the risk of inadvertent consumption by individuals who do not want to lower their blood cholesterol. In practical terms members were of the view that such packaging must be clearly distinguishable as differing from all unfortified products, notwithstanding the requirements of Regulation (EC)608/2004.
2. Members also observed that the sale of your products in 250ml cartons would be attractive to children and questioned whether they should be marketed in this form.
3. Members also requested additional information to clarify the precise nature and size of the micro-particles and to assess whether these presented any additional concerns compared with existing phytosterol formulations.

The next ACNFP meeting is scheduled for the 26th January 2005. It is our intention that we draft an opinion for discussion by members at this meeting, assuming that you are able to provide substantive answers to these three points. I would be grateful therefore if you could respond to all the points raised in this letter as soon as possible, and in good time before the finalisation of papers for this meeting.

Could you also confirm that you have sent a copy of your application dossier to the Commission as is required by regulation (EC)258/97

Yours sincerely

Dr Chris Jones
Novel Foods Additives and Supplements Division

ACNFP 70/3 APPENDIX 2

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

**APPLICATION FOR THE APPROVAL OF JUICES AND NECTARS WITH ADDED
PHYTOSTEROLS**

APPLICANT'S RESPONSE TO ACNFP

Your ref.: NFU 539

Re: Juices and Nectars with Added Phytosterols

Dear Dr Jones,

Your letter of 13 December refers. I hope the following answers address the ACNFP's questions:

1. The phytosterol-containing juices / nectars will be in distinctive packaging. We would like to continue in Europe with the Minute Maid Heartwise' brand name, described in our application (Sect. X-1, p. 16) which we do not believe can be construed as a claim. We would however replace the heart-shaped orange with a normal cut orange and 'Europeanise' the rest of the label. An alternative would be to have a panel on the front label, with 'Healthy Heart' as the generic product name for phytosterol-containing juices. Given the size of the package and the label graphics – plus the extra cost of the product – we believe this will significantly reduce the likelihood of children consuming the product.
2. We will not produce single serving sizes of 250 ml.
3. Cargill fine particle plant sterols used in juice formulation have an average particle size of about 10 micrometers. They are produced by mechanical, cryogenic grinding. The particles are suspended in juices by agitation and without use of emulsifiers.

Free plant sterols, like purified cholesterol, are a waxy, semi-crystalline solid and are insoluble in water. Plant sterol/stanol esters were developed because they are more soluble in food fats and therefore easier to deliver effectively in food. They are a non-crystalline, semi-solid at room temperature. Plant sterol esters are, therefore, expected to be more bioavailable than the (free) plant sterols which are present in food as multi-molecular particles and not in true solution.

Cargill fine particle plant sterol technology was developed to allow plant sterols to effectively be incorporated into low fat foods. The technology was needed to both make the cholesterol reducing benefit equivalent to phytosterol esters and to maintain acceptable palatability in the foods. The results of Devaraj, et al., (2004) (copy of paper submitted with application) with 2 grams per day of fine particle plant sterols are equivalent to, but do not exceed, those seen with an overlapping range of plant sterol ester studies using 0.8 to 3.0 grams of phytosterol equivalent per day. This suggests comparable bioavailability of free plant sterols and plant sterol esters.

Delaney et al (2004) compared the absorption of several different free and esterified plant sterol preparations in Sprague Dawley rats. The preparations included plant sterols and sterol esters dissolved in soybean oil and plant sterols dispersed in emulsifiers. The animals were fed via gavage 42 mg/kg of formulated phytosterols, approximately the optimal human daily intake for cholesterol reduction. Phytosterols were poorly absorbed in all formulations, with maximal plasma concentrations reaching only 1.5 to 2.5 times baseline levels and less than 3 mg/dL. Plasma concentrations of beta-sitosterol and campesterol were lower in rats treated with emulsified phytosterols than in rats fed free phytosterols dissolved in soybean oil. However because the pharmacokinetic profile of water-soluble phytosterols is similar to that of phytosterols in a lipid vehicle, the researchers concluded that the safety profile of water-soluble phytosterols is likely similar to free phytosterols and phytosterol esters delivered in a lipid vehicle.

Another study compared the effect of a low-fat milk supplemented with 2.2 g of plant sterol equivalents in either free or esterified forms in normocholesterolemic humans who consumed the products for 1 week (Richelle et al, 2004). Cholesterol absorption was reduced by 60% by both treatments. Both plant sterol forms reduced beta-carotene and alpha-tocopherol bioavailability, but the reduction in beta-carotene and alpha-tocopherol was less with free plant sterols than with plant sterol esters. In another publication from the same research center (Pouteau et al, 2003) it was reported that the diameter of the plant sterols in the low-fat milk was less than 5 micrometers. These findings are consistent with free plant sterols, even when present as small particles, not being more bioavailable than plant sterol esters.

Christiansen et al (2001) observed in their 6-month study of free microcrystalline plant sterols in hypercholesterolemic subjects that a dose of 1.5 g/day had a similar cholesterol lowering effect as 3 g/day. There was no difference in serum concentrations of sitosterol between groups receiving plant sterol doses of either the 1.5 or 3 g/day. Small increases over control values were observed, although all

levels were very low. The effect of increasing doses of microcrystalline suspension of plant sterols (consisting primarily of sitosterol) in rape seed oil was similar to that observed with increasing doses of plant sterol esters, such that doses above 1.6 to 2 g/day had no additional effect on cholesterol reduction. While the particle size of the microcrystals was not described, there was no evidence that the preparation dramatically increased plant sterol bioavailability.

We are not aware of any data that suggests that Cargill plant sterols would be more bioavailable or have increased safety concerns as compared to plant sterol esters.

Finally I confirm that I have submitted a copy of the application to the Commission, as required under Directive 258/97/EC.

References

Christiansen LI, Lahteenmaki PLA, Mannelin MR et al, 2001. Cholesterol-lowering effect of spreads enriched with microcrystalline plant sterols in hypercholesterolemic subjects. *Eur J Nutr* 40:66-73.

Delaney B, Stevens LA, Schmelzer W et al, 2004. Oral absorption of phytosterols and emulsified phytosterols by Sprague-Dawley rats. *J Nutr Biochem*. 15:289-95.

Devaraj S, Jialal I, Vega S, 2004. Plant sterol-fortified orange juice effectively lowers cholesterol levels in mildly hypercholesterolemic healthy individuals. *Arterioscler Thromb Vasc Biol* 24:24-48.

Pouteau E, Monnard I, Piguet-Welsch C et al, 2003. Non-esterified plant sterols solubilized in low fat milks inhibit cholesterol absorption. *Eur J Nutr* 42:154-64.

Richelle M, Enslin M, Hager C et al, 2004. Both free and esterified plant sterols reduce cholesterol absorption and the bioavailability of beta-carotene and alpha-tocopherol in normocholesterolemic humans. *Am J Clin Nutr* 80:171-7.