

25 January 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
rm 1061
Rockville MD 20852

Dear Sir/Madam

DOCKET NO 98P-0683 Food Labelling: Health Claims; Soy Protein and Coronary Heart Disease

The Food Commission wishes to submit comments on the above proposal. The Food Commission is an independent consumer organisation and publishers of the *Food Magazine*. In the UK we are one of many NGO's working under the umbrella of the National Food Alliance to establish acceptable criteria, for the use of health claims on foods in the absence of any specific regulations. Certainly any new approvals for health claims in the US influence companies and regulatory bodies in other countries. We are therefore concerned to ensure that only legitimate, scientifically substantiated claims, which are genuinely beneficial to public health, are permitted.

With regard to Protein Technologies International Inc (PTI) petition to have the above health claim authorized, we have a number of concerns detailed below.

1. Scientific Validity of Evidence

The PTI application to the FDA focuses on the role of isoflavones as being the component of soy protein responsible for observed effects of lowering cholesterol and LDL cholesterol. However closer examination of the research literature, as the FDA concludes, shows that 'the evidence is not sufficient to establish that the presence of isoflavones accounts for or is related to the effect on blood lipids (p62988). Furthermore the FDA's concludes 'Given the limited number of studies and the contradictory outcomes, FDA is not persuaded that the isoflavone component of soy protein is a relevant factor to the diet-disease relationship' (p62988).

The Food Commission supports these conclusions. A recent government-funded UK review by the Medical Research Council's Institute for Environment and Health¹ of the possible beneficial effects of phytoestrogens came to similar conclusions. 'Though some epidemiological studies suggest that consumption of foods containing phytoestrogens may have beneficial effects, almost no evidence exists to link these effects directly to phytoestrogens; many other components of soya and linseed are biologically active in various experimental systems and may be responsible for the observed effects in humans.'

As the petitioner's case was based on its assumptions about the role of phytoestrogens (isoflavones), the Food Commission is surprised, in the light of the FDA conclusions above, that it is taking PTI's application further. This is all the more surprising as neither PTI nor the FDA seeks to determine what are the factors in soy, if not isoflavones, which may account for observed effects on serum lipids.

Scientific evidence now points towards a number of factors in the diet which may play a role in cholesterol reduction. As the IEH concludes: 'it may be important to consider other components of the diet when attempting to identify potentially protective dietary factors. ...components of soya and linseed other than phytoestrogens may contribute to or be responsible for the apparent hypcholesterolemic properties of these products' Factors which have been identified include flavonoids, dietary fibre, phytosterols, amino acid composition of the protein and α -linolenic acid. Some of these factors, but not all, can be found in soya. But what is clear at this stage is that knowledge of these factors and their potential mechanisms are poorly understood. As the IEH report states: 'it is clear that further investigations will be necessary to understand the mechanism for cholesterol reduction by soya proteins.'

Therefore the Food Commission believes it is inappropriate for the FDA to be considering permitting a health claims for soy protein while the scientific understanding of the factors involved and the mechanisms of action are so poorly identified and understood. Neither the FDA nor Protein Technologies have attempted to identify, quantify or explain the mode of action of factors other than phytoestrogens which may be responsible for, or contribute to, observed serum cholesterol reductions.

The Food Commission believes it is irresponsible to advocate that the general population increase its consumption of a food stuff without understanding the biological or physiological effects such a dietary change may have? Any risk assessment of such a dietary change would need to balance beneficial effects against potential adverse effects. And as the active components have not been identified, let alone quantified, no acceptable assessment of risks can be carried out.

Therefore the FDA should not consider permitting the proposed health claim until active component(s) have been identified and quantified and a risk assessment scientifically carried out.

¹ MRC Institute for Environment and Health, IEH assessment on Phytoestrogens in the Human Diet, Final Report to the Ministry of Agriculture, Fisheries and Food, November 1997.

2. Ability to achieve recommended dietary change

As we state above, we do not consider there is sufficient knowledge on the active components in soy and the amounts that would need to be considered appropriate to achieve reduced cholesterol levels. However the PTI and FDA are proposing that 25g of soy protein is appropriate. It is recommended that this can be consumed over four daily eating occasions and hence justifies the minimum level of 6.25g soy per serving for a claim to be permitted. The Food Commission questions whether it is realistic that most members of the general population will be able or willing to change their diets to include soy protein foods at four eating occasions daily, each day. The submission presents no evidence that free-living individuals who are not taking part in a scientific study find this level of dietary change practicable. If it is likely that a significant percentage of the general population would find such a dietary change difficult to make then the health claim will have little value in achieving public health objectives and should therefore not be permitted.

The requirements for minimum levels of soy protein should be reconsidered in the light of the ability of the general public to make the dietary changes necessary to meet recommended daily consumption levels.

3. Misleading impressions

If the FDA permits this health claim, we believe there is a risk that there will be undue focus on one particular foodstuff for the prevention of heart disease. From PTI's point of view this may have economic advantages, which is no doubt part of their motivation for their application. However such focus on soy may well distract attention away from other foods in the diet for which there is much clear scientific evidence of their health benefits, eg fresh fruit and vegetables, not only for the role in the prevention of heart disease but also for the prevention of other diet-related diseases.

Furthermore other dietary factors may be more effective than soy in promoting cholesterol reduction. For example, a summary of recent studies investigating effects of soya or linseed on blood lipid levels in men and women (attached) indicates that linseed appears to have been more effective than soya in reducing cholesterol (IEH report). Therefore we believe it is inappropriate, while scientific knowledge is limited, to approve this health claim for soy.

Also we believe that in highlighting one particular health benefit of soy protein, that it is likely that the claim would also be seen by the general public to be an endorsement of other health benefits which are sometimes claimed for soya (cancer prevention, osteoporosis prevention, relief of menopausal symptoms etc). Although scientific evidence, at this time, is far from adequate to support such claims, this hasn't stopped articles in magazines and newspaper, writers of books and others from advocating health benefits for soy often in an exaggerated way.

Therefore it is likely that this health claim could create a misleading impression of the health benefits of the food as a whole.

4. Safety issues

There are a number of safety issues regarding the promotion of increased consumption of soy. We consider that neither PTI nor the FDA has begun to address some of the safety questions raised by a health claim that would advocate increased consumption of soy protein by the general population. There may for example be certain groups within the general population for whom the effects of increased soy consumption could confer health risks.

The effects of isoflavones on adult women known to date include changes to the sex steroid hormone status². PTI and the FDA equate these changes to those seen in women treated with tamoxifen. However tamoxifen is known to increase the risk of some types of cancer and to promote the growth of breast cancer cells in women with some types of breast cancer. Furthermore studies in the USA and UK examining tamoxifen's use as a cancer prevention agent have been stopped due to the increased risk of some cancers. It would appear that no consideration has been given either by PTI nor the FDA to the advisability of women taking tamoxifen who might respond to such a health claim by increasing their intake of soy. Is this advisable and would products carry warning labels advising such women?

The evidence that soy can stimulate breast cell proliferation also raises health concerns³. As Walter Willett, chair of the nutrition department at the Harvard School of Public Health has said 'We're playing with a complicated biology that we don't understand.'⁴

Soy isoflavones may also cause thyroid dysfunction in humans. Malignant goitre has occurred in experimental animals fed soy⁵ and there is potential for soy isoflavones to cause thyroid cancer in humans.

And for children, is there a safe age that soya is considered beneficial to children? PTI advocates that health claims will be directed towards children over the age of 4. But there is no scientific evidence provided as to why this is considered to be a suitable age. Because soy formula contains high levels of isoflavones many regulatory agencies around the world are advising that soy infant formula is not advisable unless directed by a doctor or health professionals for a specific medical condition. With limited data and hence uncertainty about potential risks to children is there adequate evidence that children over four should be encouraged to consume greater amounts of soy?

An increasing percentage of soy is now genetically engineered. Such genetic modification may affect levels of naturally occurring components such as isoflavones and other potentially biologically active components. The Food Commission considers that more research is required to assess these effects and to establish whether such genetic modification raises any additional safety concerns.

² Cassidy A et al. Biological effects of a diet of soy protein rich in isoflavones on the menstrual cycle of premenopausal women. *Am J Clin Nutr* 60: 333-340, 1994.

³ see for example Petrakis NL et al. Stimulatory influence of soy protein isolate on breast secretion in pre- and postmenopausal women. *Cancer Epid Bio Prev* 5: 785-794, 1996 and Second International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, p35, 1996.

⁴ Bonny Leibman, *The Soy Story*, Nutrition Action Healthletter, 25: 7 September 1998

⁵ Kimura S et al. Development of malignant goitre by defatted soybean with iodine-free diet in rats. *Gann* 67: 763-765, 1976.

These examples above clearly show that there are many outstanding safety concerns and therefore it would be highly inappropriate to advocate that the general population increase its consumption of soy while such concerns remain outstanding.

The Food Commission trusts that the FDA will fully investigate the issues raised by our response before making a decision about the wisdom of permitting this health claim.

I would like to be kept informed of any further consultation on this application and the results of any further deliberations.

Yours sincerely

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Co-director