

Maisons-Alfort, 2 July 2008

## **OPINION**

**Of the French Food Safety Agency**

**regarding the evaluation of evidence for the health claim that "the daily consumption of 25 g of soy protein, combined with a diet low in fat and saturated fat, may help lower blood cholesterol."**

THE DIRECTOR-GENERAL

On 14 March 2005, the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) requested, by letter dated 9 March 2005, that the French Food Safety Agency (AFSSA) assess the evidence for the health claim that "the daily consumption of 25 g of soy protein, combined with a diet low in fat and saturated fat, may help lower blood cholesterol".

Having consulted the "Human Nutrition" Scientific Panel on 26 May 2005, AFSSA is issuing the following opinion:

Considering that the request is to assess the evidence for the health claim that "the daily consumption of 25 g of soy protein, combined with a diet low in fat and saturated fat, may help lower blood cholesterol"; that however, in the petitioner's application, the claim was worded as follows: "Soy protein, combined with a diet low in fat and saturated fat, may help lower blood cholesterol";

Considering that, according to the applicant, the products likely to support the claim in this request are soy proteins present in soy-based foods (soy drinks, tofu, soybeans), soy products (soy protein isolates, soy protein concentrates, soy flour) and foods in which soy protein is used as an ingredient; that therefore these are products in which, strictly speaking, the proteins play a variable role; and that these products are presented as intended for general consumption;

Considering that, in the United States in 1999, the Food and Drug Administration (FDA) approved a claim associating the daily consumption of at least 25 g of soy protein with reduced coronary disease risk when combined with a diet low in saturated fat and cholesterol; that in addition, on 2 April 2001, AFSSA delivered an opinion on the assessment of a health claim concerning the reduction of cholesterolaemia through soy protein (Request No. 2000-SA-0148); that this claim was "The consumption of 25 g of soy protein, combined with a diet low in fat and saturated fat, may help lower blood cholesterol"; that in the opinion's conclusions, AFSSA held that "given the uncertainties on the nature of the compounds present in 'soy protein' fractions, the respective roles of these compounds in reducing cholesterolaemia and their mechanisms of action, the use of the claim is premature"; that consequently, it must be determined whether complementary data has been published since the 2 April 2001 opinion was issued that might resolve uncertainties—under the conditions detailed in the claim—on the reality of the effect, on the compounds responsible and on the mechanisms involved;

Considering that, regarding their nutritional value and safety, soy proteins provide a well-balanced source of essential amino acids; that in AFSSA's opinion of 2 April 2001, the potential risks linked to soy consumption are "the allergenic nature of a number of soy proteins and the presence of anti-proteases that potentially induce pancreatic disease, that isoflavones that can alter hormone balance and phytates that affect the bioavailability of minerals"; that in addition, the benefits and safety of phytoestrogens, compounds that may be associated with soy proteins, were assessed in AFSSA's report on phytoestrogens<sup>1</sup>;

<sup>1</sup> AFSSA Report: "Safety and Benefits of Phytoestrogens in Food - Recommendations" - March 2005

**Regarding the reality of the effect claimed, under the conditions detailed in the claim:**

Considering that the applicant has supplied three meta-analyses; that the first is the meta-analysis used in the FDA's evaluation in 1999;

Considering that the second meta-analysis is the one that led the *Joint Health Claim Initiative* (JHCI), in the United Kingdom in 2002, to approve the claim that "the addition of 25 g of soy daily to a diet low in saturated fat may help reduce blood cholesterol"; that this meta-analysis includes five publications representing nine trials that met inclusion criteria regarding the level of daily soy protein intake (lower than or equal to 30 g), the nature of the trials (randomised controlled clinical trials) and saturated fat intake (lower than or equal to 12.5% of daily calorie intake); that, of these five publications, two present methodological biases (the control diet could not be used as a reference for comparison or dietary behaviour changes after the introduction of the soy product); that another publication shows that a daily intake of 20 g of soy protein lowers cholesterol and LDL cholesterol in subjects with normal cholesterol levels; that the last two studies show that soy protein isolates significantly reduce cholesterol in subjects with moderate hypercholesterolaemia on a lipid-lowering diet (e.g. NCEP<sup>2</sup>), based on a daily intake of 25 g for one study and regardless of the intake level for the other study;

Considering that the third meta-analysis examines data published between 1998 and 2004; that this meta-analysis includes 19 publications, of which four had already been examined by the JHCI; that all of these studies present conflicting results; that in addition, the other 15 studies analysed cannot be taken into consideration in support of the claim, for one or more of the following reasons: (i) the subjects were not following a lipid-lowering diet; (ii) the daily intake level used is greater than 30 g or, in one study, is not specified; (iii) in one study, a soy protein hydrolysate (associated with phospholipids) is used instead of soy proteins; that consequently, only the two studies used in the JHCI's meta-analysis provide data that may substantiate the claim;

Considering a study published after 2004 concludes that the lipid response to a lipid-lowering diet with or without soy is modified by the inflammation status in moderately hypercholesterolaemic adults;

Considering that, consequently, on the basis of the only two studies that could be considered, the cholesterol-lowering effect of soy protein-based preparations is significant and observed in moderately hypercholesterolaemic subjects; that however, this effect is not correlated with soy protein intake;

**Regarding the nature of the compounds responsible and mechanisms of the claimed effect:**

Considering that in the products concerned by the claim, other—often unidentified—compounds are associated with proteins to a varying degree; that according to the authors, the compounds likely to be responsible for the claimed effect are protein fractions along with isoflavones, fibres, phytates, phospholipids, saponines, phytosterols, etc.; that a synergetic effect of these compounds is also suggested by some authors; that nevertheless, AFSSA's report on phytoestrogens has shown that isoflavones alone are not responsible for the cholesterol-lowering effect, but that the consumption of soy proteins and/or associated compounds (except for isoflavones) helps reduce cholesterolaemia; that in addition, the influence of these different factors is often not taken into account in the literature supplied by the applicant; that consequently, the compounds responsible for the cholesterol-lowering effect of soy products (proteins in the strictest sense and/or other associated compounds) are not precisely identified;

Considering that, regarding the mechanisms of action, the applicant claims an effect based on a change in the enterohepatic cycle of cholesterol, induced through the stimulation of bile acid

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<sup>2</sup> NCEP: *National Cholesterol Education Programme*

secretion, reduced cholesterol absorption and changes to hepatic metabolism, with which various hormone responses are associated; that there are however other possible mechanisms of action; that these mechanisms once again have not been proven and have been, for the most part, described only in animals; that the mechanisms of action affecting the cholesterol-lowering effect have not yet been elucidated;

Considering that consequently, it is impossible to attest to the allegations of the health claim for all soy-based products, whatever they may be and however they are produced;

**Regarding the claim's wording:**

Considering that the claim's wording ("may help") expresses the scientific uncertainties outlined above; that nevertheless, such a claim, being of uncertain character, would have a limited scope and would not be useful in terms of consumer information, and could in fact lead to confusion;

To conclude, AFSSA deems that the use of the claim that "the daily consumption of 25 g of soy protein, combined with a diet low in fat and saturated fat, may help lower blood cholesterol" is premature, given the uncertainty on the active compounds and mechanisms of action, as well as the weakness of the scientific data presented to support the claim. Therefore AFSSA maintains its opinion of 2 April 2001 and reiterates the need to conduct scientific studies on well-characterised soy protein extracts to assess their effectiveness compared to animal proteins as well as other plant proteins.

**Pascale Briand**