

ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES

PSYLLIUM SEED HUSK

ISSUE

The Irish Competent Authority has prepared an initial opinion on an application for the authorisation of Psyllium seed husk (PSH) as a novel food ingredient under the novel foods regulation (EC) No 258/97. The Committee is asked whether it agrees with the initial opinion and whether it has any further comments or objections to make on this application. The Committee's advice will form the basis for the UK's formal response.

Introduction

1. On 23 April 2008, the European Commission forwarded the Irish Competent Authority's (CA) positive initial opinion on an application made by Kellogg Company under Article 4 (1) of Regulation (EC) 258/97, for the authorisation of PSH as a novel food ingredient. According to the timescales set out in the Regulation, the UK and other Member States have until 21 June 2008 to provide comments and/or reasoned objections to the opinion.
2. A confidential version of the application dossier is attached as **Annex 1**, which contains six appendices (A-F) and the Irish Initial Assessment Report is attached in **Annex 2** (restricted).

Background

3. PSH is obtained from the seeds of *Plantago ovata* (Plantaginaceae) by mechanical separation, milling and subsequent processing. It contains a high level of hemicellulose, which consists of a xylan backbone linked with units of arabinose, rhamnose and galacturonic acid. PSH is able to form a gel in water and is classified as a mucilaginous compound. The applicant states that the beneficial properties of PSH are the same as those associated with other rich sources of dietary fibre.
4. The applicant has already marketed breakfast cereals containing PSH in North America and Australia and now intends to use PSH to fortify cereal bars and breakfast cereals in the EU.
5. The present application for authorisation of PSH was prepared pursuant to Commission Recommendation (97/618/EC) of 29 July 1997 concerning the scientific aspects and presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients. PSH has been classified as complex novel foods which are not, or

are derived from sources which have no, been genetically modified- the source of the novel food has a history of use in the community (Class 2.1). The requirements for a submission for this class are as follows:

I	Specification of the NF	X	VIII	<i>Ability to survive in and colonise the human gut</i>	-
II	Effect of the production process applied to the NF	X	IX	Anticipated intake/extent of use of the NF	X
III	History of the organism used as the source of the NF	X	X	Information from previous human exposure to the NF or its source	X
IV	<i>Effect of the genetic modification on the properties of the host organism</i>	-	XI	Nutritional information on the NF	X
V	<i>Genetic stability of the GMO</i>	-	XII	Microbiological information on the NF	X
VI	<i>Specificity of expression of novel genetic material</i>	-	XIII	Toxicological information on the NF	X
VII	<i>Transfer of genetic material from GM microorganisms</i>	-			

The information presented in the dossier is structured accordingly and is considered below under these schemes.

I. Specification of the novel food

Annex 1, p 6-14

6. PSH is a free flowing powder with a pale colour, containing some dark flecks. PSH has a faint odour and a bland mucilaginous taste. It contains about 85% carbohydrate, the majority of which is classed as "fibre" (p.31 Table XI.1-1). Microbiological specifications are as follows:

standard aerobic plate counts	125,000/g (maximum)
<i>Salmonella</i> , <i>Staphylococcus aureus</i> and <i>Pseudomonas aeruginosa</i>	negative per 25g
<i>Escherichia coli</i>	<3 MPN/g
yeasts and moulds	4,000/g (maximum)

7. PSH has a purity of 95% and contains no more than 5% light extraneous matter (agricultural impurities) and no more than 1% heavy extraneous matter.
8. Batch on batch variation was assessed by chemical and physical analyses of three different lots of PSH, as shown in Annex 1, page 9. The results of these analyses showed that all batches met the required specification criteria for PSH.
9. Analyses were also performed to determine the potential presence of mycotoxins. Two batches of PSH were analysed for aflatoxins, ochratoxin A, and the tricothecenes (deoxynivalenol (DON), fusarenon-X (FUS-X), HT-2 toxin, nivalenol (NIV) and T-2 toxin (T-2)). No detectable levels of these mycotoxins were found in the tested samples. Analysis reports can be found in Annex 1, Annex B1.

10. Supplementary analyses were performed to determine the presence of aflatoxins, ochratoxin A and the tricothecenes in three further samples of PSH. The majority of results were shown to be below the reporting limit, except the tricothecenes HT-2 and T-2 which were quantified in one sample at 78.6 and 66.1 µg/kg, respectively (Annex 1, Pg 10-11). The applicant notes that the SCF in 2001 has set a combined temporary tolerable daily intake (t-TDI) for T-2 and HT-2 of 0.06 µg/kg bodyweight. The applicant has calculated that regular consumption of PSH containing these levels of tricothecenes (a worst case scenario) would not cause consumers to exceed the SCF's t-TDI.
11. The applicant has reported the results of supplementary heavy metal analyses on eight batches of PSH. The results were all below 0.5 mg/kg (lead: 0.13-0.41; arsenic 0.03-0.09; cadmium 0.016-0.029; mercury <0.009 mg/kg).
12. PSH samples from two batches were analysed for the presence of a wide variety of pesticide residues (Annex 1, Annex C1). No pesticide residues were detected (LOD 0.01 ppm).
13. The Irish CA did not report any concerns with respect to PSH-associated mycotoxins or heavy metals in their initial opinion and are satisfied with the compositional data provided.

II. Effect of the production process applied to the novel food

Annex 1, p 15-18

14. The production process for PSH is described in detail in Annex 1. Psyllium grain is harvested in March or April and PSH is separated from seeds by mechanical separation followed by milling. PSH is then bagged for shipment. These stages are performed in India. PSH is subsequently shipped to the US for further processing and blending. Consignments are inspected, fumigated or treated for insect/microbial contamination. The 95% pure PSH is dried and chilled before quality control checking and mixing into a psyllium pre-blend for addition to foods. The Irish CA's initial assessment report did not highlight any concerns regarding this production process.

III. History of the organism used as a source of the novel food

Annex 1, p 19-20

15. The source organism for PSH is *Plantago ovata* which is also commonly referred to as ispaghula or psyllium and is primarily grown in India, the US and Southern Europe and cultivated mainly for its use in laxatives in N. America and Australia and dietary food supplements in Europe and North America (Fybogel™, Regulan™ and Metamucil™). While the seed contains the bioactive mucilage polysaccharide, refined PSH is used mainly as a fibre source in laxatives, supplements and ready to eat cereals.

IX. Anticipated intake/extent of use of the novel food

Annex 1, p 21-27

16. The applicant intends to use their PSH product to fortify breakfast cereals and cereal bars only, at up to 3.5g per serving (the applicant proposes a use level of 12%).

17. Intakes were estimated for a range of population groups using information from the most recent NDNS surveys available to the public. Annex 1, Appendix E contains more detailed information.
18. On an all-user basis, the highest mean and 97.5th percentile intakes of PSH by the UK population from all proposed food uses in the EU were observed in male teenagers and estimated to be 4.9 and 14.7 g/person/day, respectively. Young people consumed the greatest amount of PSH on a per body weight basis with the highest mean and 97.5th percentile all-user intakes of 128 and 328 mg/kg body weight/day, respectively. These are worst-case estimates, based on the assumption that all possible foods contain PSH at the levels given in the above table.
19. The Irish CA's initial opinion does not highlight any concerns relating to consumption of excessive levels of PSH from the proposed food uses. The opinion highlights that the proposed target food products containing PSH will likely have limited appeal as cereals containing PSH have an estimated market penetration of 3%, 0.5% and 0.2% in Canada, Australia and USA, respectively. The Irish CA states that likely low appeal combined with a set 3.5g PSH per serving and the proposed allergy advisory label for sensitised individuals probably means consumers (including children) will not be likely to consume excessive amounts of PSH.

X. Information from previous human exposure to PSH or *Plantago ovata*

Annex 1, p 28-29

20. PSH-containing food supplements are widely available in the UK with typical daily recommendations of 10g normally taken as a drink. However, in Canada, the US and Australia, PSH is incorporated in a number of breakfast cereal products. PSH is also available as a dietary supplement in the US and Canada and a medicinal supplement in Germany to treat chronic constipation.
21. The Irish CA's initial opinion does not highlight any concerns relating to previous human exposure to PSH.

XI. Nutritional information on the novel food

Annex 1, p 30-35

22. The typical nutritional composition of PSH is illustrated in Annex 1, Pg 31. The profile shows that PSH is low in fat, with no saturated fat and very high in carbohydrates, fibre and soluble fibre and lower amounts of protein, ash and potassium.
23. The applicant has provided examples of studies demonstrating that PSH, being a rich source of dietary fibre, has been shown to have health benefits associated with dietary fibres, including stool bulking (increased size and softness of stools), cholesterol reduction, glycaemic control and appetite and weight control (Annex 1, Pg 31-34).
24. The applicant notes that there is a potential for PSH to increase bile acid turnover and thereby negatively affect the absorption of fat-soluble vitamins (vitamins A and E) either by greater excretion of bile salts or the binding of fat-soluble vitamins by PSH. The applicant states that results from animal and

human studies revealed slight alterations in vitamin or mineral levels, but the effects were rarely significant and statistical significance was not accompanied by biological significance (Annex 1, Pg 55-60, Pg 69). The applicant states that significant changes were typically observed in studies of shorter durations and vitamin and mineral parameters usually stabilised within normal values in studies of longer duration. The Irish CA's initial opinion did not highlight any concerns regarding this issue.

25. The Irish CA is satisfied with the nutritional information provided for PSH.

XII. Microbiological information on the novel food

Annex 1, p 8-9 and 37

26. The microbiological specifications for the novel ingredient are detailed in Annex 1, Pg 8. The analysis of three batches of 95% pure PSH revealed that all batches comply with the microbiological specifications (Annex 1, Pg 9). Microbiological analyses are carried out after the raw ingredient is imported from India to the US and the Irish CA was satisfied that batch test results are within acceptable limits. Further processing (mechanical) is carried out in the US and food grade water and food grade citric acid are used. The Irish CA is satisfied that none of these processes is expected to alter the microbiological specifications providing good hygiene and manufacturing practices are adhered to.

XIII. Toxicological information on the novel food

Annex 1, p 38-61

27. Absorption

The data provided by the applicant suggest that PSH is not significantly absorbed from the small intestine. However, one study revealed that approximately 1-6% of PSH was hydrolysed in the stomach of healthy male volunteers, resulting in the formation of free arabinose of which 85-93% was absorbed. The study concluded that the stomach was the sole location for PSH hydrolysis in humans and no additional decomposition occurs in the small bowel (Annex 1, Pg 39).

28. Fermentation

Intestinal bacterial fermentation of PSH to short chain fatty acids has been predicted based on *in vitro* studies and *in vivo* studies in rodents and monkeys (Pg 39-41). The applicant states however, that the majority of human studies have revealed that PSH was not fermented in the human bowel.

29. Acute toxicity

The applicant states there are no available published studies relating to acute toxicity of PSH but does refer to an unpublished study where mice were administered a range of single doses (1.5-6 g/kg body weight) via oral gavage and monitored for seven days. The study demonstrated that no deaths occurred during the seven day observation period. However, mice in the highest dose group were slightly sedated during the first few hours after dosing and also experienced diarrhoea.

30. Subchronic/chronic studies

PSH was administered orally to rats, cats and dogs at doses up to 25% dietary levels. The applicant states that no treatment related deaths occurred in any of these studies. Pigmentation of the epithelial cells of collecting tubules of animal kidneys was observed in rats and cats which the authors attributed to consumption of the black pigmented layer of psyllium seed. This pigmented layer is removed during the preparation of PSH for human consumption.

31. Mutagenicity, genotoxicity, carcinogenicity and developmental toxicity studies.

The applicant states that no specific studies to investigate mutagenicity, genotoxicity or carcinogenicity have been published. The applicant reports however, that a number of studies demonstrating anti-carcinogenic effects of PSH on certain known carcinogens have been published (Annex 1, Pg 43-44). The applicant notes that no studies to investigate reproductive or developmental toxicity of PSH have been conducted but highlights there have been no reports relating to reproductive or developmental effects in short term animal feeding studies.

32. Human studies

Thirty human studies (short and long term trials) investigating the effects of PSH (at doses up to 30 g/day) in healthy and hospital patients are reported in the dossier (Annex 1, Pg 46-55). The majority of these studies were efficacy studies with the reporting of side effects. The applicant reports that PSH was ingested by healthy subjects and patients from periods ranging from six days to seven years and was well tolerated at levels of up to 30 g/day over short time periods. While some studies showed that PSH consumption did not result in any significant adverse effects, other studies did report side effects. Observed side effects were mainly gastrointestinal in nature (flatulence, bloating and diarrhoea) which the applicant relates to high dietary fibre intakes and were resolved at the end of treatment. However, one study where 10.5 g/day PSH was consumed by 93 healthy individuals for 52 weeks reported five severe adverse side effects but the authors stated that only one of these was probably treatment related (individual experienced nausea at the start of the study which continued for three days and subsided allowing the individual to complete the study). The majority of individuals in this study reported mild or moderate side effects which included headaches, constipation, diarrhoea, influenza-like symptoms and vomiting Annex 1, Pg 52-53. The Secretariat notes that the highest daily intakes of PSH on an all-user basis were determined to be for male teenagers (14.7 g/person/day) a level greater than some of the adverse effect levels reported in the studies.

33. Oesophageal and gastrointestinal obstruction

The applicant is of the view that that the risk of oesophageal and gastrointestinal obstruction in relation to PSH appears to be limited to the consumption of PSH in granular form alone (laxative use) without proper hydration and not to PSH incorporated into foods. While, no data are available on oesophageal or gastrointestinal obstruction attributed to PSH-containing foods, the applicant states that any potential for oesophageal or gastrointestinal obstruction could be reduced with a labelling statement to suggest PSH-containing products should be consumed

with fluids. The applicant highlights there have been no reports of such incidents since PSH-containing foods have been introduced onto the US market.

34. The Irish CA did not express any concerns regarding the toxicological information presented in the dossier and is of the view that the use of PSH in breakfast cereals and cereal bars at the levels indicated should not pose a significant health risk to EU consumers.

Allergenicity

Annex 1, P 61-70

35. The applicant reports that the likely allergenic protein of PSH has not been elucidated but the location of the allergen has been determined to be in the endosperm and seed rather than the husk (Annex 1, Pg 61 and 70). The applicant reports that the potential allergenicity of PSH can be controlled by processing of PSH to achieve 95% purity and a light extraneous matter level of 5% (light extraneous matter refers to agricultural impurities and agricultural produce other than husks, which includes the psyllium seed and the proteins contained therein). The applicant states that the vast majority of published allergenic reactions (wheezing, congestion, anaphylaxis) to PSH have been a result of occupational exposure (nurses, pharmaceutical workers, pharmacists) exposed to PSH dust during the preparation of laxatives or formulations. The applicant states these individuals may have become sensitised to PSH as a result of this exposure and exhibited an allergenic response when challenged with highly purified PSH in cereal (Annex 1 61-66, Pg 70). The applicant's conclusion is that these individuals represent a small proportion of the population and the vast majority of people are not likely to exhibit reaction unless prior sensitisation has occurred.

Labelling

Annex 1, P34-35

36. In addition to indicating a willingness to provide advisory information to minimise the likelihood of choking, Annex 1, Pg 60, the applicant has proposed to label the product indicating that PSH may cause an allergic reaction in people sensitive to inhaled or ingested PSH powder. The Irish CA was satisfied that specific labelling of products containing PSH as described should be sufficient to warn the small sub-group of consumers who may have been sensitised to PSH and are at risk of an allergic reaction. The Irish initial opinion also states that, although PSH is not listed in EU legislation for the purposes of allergen labelling, the applicant should ensure the advisory label follows the same criteria and be clear and legible on the packaging.

COMMITTEE ACTION REQUIRED

37. The Committee is asked whether it agrees with the initial opinion from the Irish CA that PSH produced by The Kellogg Company should be granted authorisation as a novel food ingredient in cereals and cereal bars, and whether it wishes to make any comments on the application.

Annex attached:

Annex 1- Application for the approval of Psyllium seed husk (Confidential version).

Annex 2- Initial Opinion on Psyllium seed husk from the Irish Competent Authority (Restricted).