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SCIENTIFIC OPINION

Ocean Spray Cranberry Products® and urinary tract infection in women

Scientific substantiation of a health claim related to Ocean Spray Cranberry Products® and urinary tract infection in women pursuant to Article 14 of Regulation (EC) No 1924/2006[1]

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2008-117)

Adopted on 22 January 2009

PANEL MEMBERS

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SUMMARY

Following an application from Ocean Spray International Services Limited (UK) submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to Ocean Spray cranberry products® containing typically 80 mg cranberry proanthocyanidins (PAC) per serving and urinary tract infection in women.

The scope of the application was proposed to fall under a health claim referring to disease risk reduction.

The foods that are the subject of the health claim are Ocean Spray cranberry products® (juice drinks and sweetened dried berries Craisins®) containing typically 80 mg cranberry proanthocyanidins (PAC) per serving. Only the fruit of the North American cranberry plant, *Vaccinium macrocarpon* Aiton is used as a source for these products. The PAC fraction isolated from cranberries is a mixture of epicatechin oligomers of various molecular weights, with activity associated with A-type linkages. The Panel considers that the foods that are the subject of the health claim are sufficiently characterised.

[1] For citation purposes: Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from Ocean Spray International Services Limited (UK), related to the scientific substantiation of a health claim on Ocean Spray Cranberry Products® and reduced risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract. *The EFSA Journal* (2009) 943, 1-16.

The claimed effect is "helps reduce the risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract". The target population is healthy women from the age of 16 years. Urinary tract infection (UTI) refers to the presence of bacteria in the urinary tract. Symptomatic UTI are usually accompanied by bacteriuria at levels of $\geq 10^5$ cfu/mL urine. Uropathogenic strains of E. *coli* bacteria cause up to 95 % of UTIs. Bacterial adherence to mucosal surfaces is generally considered to be an important prerequisite for colonisation and infection with bacteriuria. The Panel notes that bacterial adherence precedes an infection and therefore inhibition of bacterial adhesion might result in a reduction for the risk of symptomatic UTI with bacteriuria $\geq 10^5$ cfu/mL. The Panel considers that the claimed effect "helps reduce the risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract" is beneficial to human health.

The applicant provided a considerable number of *ex vivo / in vitro* studies in which an *in vitro* inhibitory effect on bacterial adhesion to mucosal cells was demonstrated by urine obtained from healthy volunteers after the consumption of cranberry products, including the cranberry juice of the applicant. The Panel considers that these studies demonstrate an *in vitro* anti-adherence effect of urine on uropathogenic E. *coli* strains following consumption of cranberry products.

Six of a total of 12 human intervention studies claimed pertinent by the applicant, were carried out on patients suffering from neurogenic bladder, some of them children, or on patients with spinal cord injury. In another study the daily dose (1000 mg PAC) consumed was approximately 6 times higher than the use levels proposed by the applicant for the present claim (160 mg PAC/day). The Panel considers that these 7 studies are of limited relevance for the claim targeted to healthy women from the age of 16 at the proposed levels of use..

The Panel considered the other 5 human intervention studies to be pertinent to the claimed effect. Two of the 5 pertinent studies are claimed proprietary by the applicant and were designed to evaluate the effect of Ocean Spray Cranberry Juice in a randomised, double-blind, placebo-controlled study design. One of these two studies investigated the effects of 300 mL undiluted Ocean Spray cranberry juice (with estimated 100 mg PAC/day) daily consumed over 18 days in 376 elderly men and women. A total of 5.6 % of the participants developed a symptomatic UTI (primary outcome), 14 of the 189 in the placebo group and 7 from the 187 in the cranberry juice group. As the actual infection rate was lower than anticipated, the study had less than 50 % power to detect a significant difference between the intervention and control group. The short duration and lack of statistical power of this study considerably limit its value as a source of evidence to support the claimed effect.

The second randomised, placebo-controlled trial evaluating the effect of daily consumed 300 mL cranberry juice drink provided by Ocean Spray Inc. (with estimated 100 mg PAC/day) was carried out in a nursing home population of women with a mean age of 78.5 years over a period of 6 months. Bacteriuria with pyuria was found in 28 % of urine samples of the placebo group versus 15 % of the cranberry juice group. The data on the baseline measurements of the study participants, in particular on the history of previous urinary tract infections, show that the incidence of previous UTI in the 6 and 12 months prior to the intervention was 25 and 33 % in the placebo group, but only 7 and 17 % for the cranberry juice group. The lack of adequate randomisation and the high drop out rates in this study considerably limit its value as a source of evidence to support the claimed effect.

The Panel noted that in the other 3 pertinent human studies there were significant limitations, including use of different cranberry formulations from that in the application, poor study design e.g. small numbers of subjects, the lack of a control group, short duration of study, as well as high drop-out rate in some of the studies, that considerably limit their value as a source of evidence to substantiate the claimed effect.

The Panel considers that the provided studies do not establish that the anti-adherence effects of cranberry products in urine shown *in vitro* are predictive of the occurrence of a clinically relevant bacterial anti-adherence effect within the urinary tract under the conditions of use proposed for the claim.

The Panel concludes that the evidence provided is not sufficient to establish a cause and effect relationship between the consumption of Ocean Spray cranberry products® and the reduction of the risk of UTI in women by inhibiting the adhesion of certain bacteria in the urinary tract.

Key words: Cranberry juice, proanthocyanidins, PAC, bacterial adhesion, E. *coli*, urinary tract infection, UTI

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BACKGROUND

Regulation (EC) No 1924/20062 harmonises the provisions that relate to nutrition and health claims and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of that Regulation and are authorised in accordance with this Regulation and included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Articles 14 to 17 of that Regulation lay down provisions for the authorisation and subsequent inclusion of reduction of disease risk claims and claims referring to children's development and health in a Community list of permitted claims.

According to Article 15 of that Regulation, an application for authorisation shall be submitted by the applicant to the national competent authority of a Member State, who will make the application and any supplementary information supplied by the applicant available to European Food Safety Authority (EFSA).

Steps taken by EFSA:

- The application was received on 11/02/2008.
- The scope of the application was proposed to fall under a health claim referring to disease risk reduction.
- During the check for completeness[3] of the application, the applicant was requested to provide missing information on 04/04/2008.
- The applicant provided the missing information on 18/08/2008.
- The scientific evaluation procedure started on 15/09/2008.
- During the meeting on 22/01/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to Ocean Spray cranberry products and urinary tract infections in women.

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16 of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to Ocean spray cranberry products and urinary tract infection in women.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of Ocean spray cranberry products, a positive assessment of its safety, nor a decision on whether Ocean spray cranberry products is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

[2] European Parliament and Council (2006). Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. Official Journal of the European Union OJ L 404, 30.12.2006. Corrigendum OJ L 12, 18.1.2007, p. 3–18.

[3] In accordance with EFSA "Scientific and Technical guidance for the Preparation and Presentation of the Application for Authorisation of a Health Claim".

It should also be highlighted that the scope, the proposed wording of the claim and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 17 of Regulation (EC) No 1924/2006.

ACKNOWLEDGEMENTS

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1. Information provided by the applicant

Applicant's name and address: Ocean Spray International Services (UK). Limited Laser House 75-79 Guildford Street Chertsey Surrey KT16 9AS.

The application includes confidential and proprietary data. The applicant claimed confidentiality and proprietary rights for the information indicated in section 1.3.4 and 1.3.5 of the dossier. The applicant's claim for proprietary rights include studies conducted with Ocean Spray products and studies sponsored or partially funded by the applicant.

1.1. Food/constituent as stated by the applicant

Ocean Spray cranberry products containing typically 80 mg cranberry proanthocyanidins per serving.

Drink range:
Ambient range: Cranberry Classic and Classic Light
Chilled range: Growers Select; Select Light; Select Cranberry & Orange; Select Cranberry & Blueberry; Select Cranberry & Pomegranate.

Dried range: Craisins® (sweetened dried cranberries).

1.2. Health relationship as claimed by the applicant

The cranberry proanthocyanidin (PAC) content at typically 80 mg per serving in Ocean Spray products possibly together with other factors present in cranberry, have properties that inhibit the adhesion of p-fimbriated E. *coli* bacteria to uroepithelial cells, acting to reduce a risk factor for urinary tract infection. Cranberry PAC have been shown to have a relatively rare A-type linkage that is important in this anti-adhesion phenomenon.

1.3. Wording of the health claim as proposed by the applicant

Regular consumption of 2 servings per day of an Ocean Spray product each containing typically 80 mg cranberry proanthocyanidins helps reduce the risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract.

1.4. Specific conditions of use as proposed by the applicant

A serving of an Ocean Spray cranberry product containing typically 80 mg cranberry PAC should be taken morning and evening. The serving size will be specified for each Ocean Spray product. For example, a typical serving size for Ocean Spray drinks will be 250 mL; for sweetened dried cranberries (Craisins®) the serving size will be 40 g. The target population proposed by the applicant is able-bodied women from the age of 16.

1.5. Similar claims as proposed/authorized by other entities

In its assessment of 2003, AFSSA considered that the submitted cranberry products could be efficient but, based on the limited number of studies performed at that time, considered the proposed wording "health of the urinary tract" as too general and not substantiated (AFSSA 2003).

In 2004, AFSSA accepted a new proposed wording "contributes to decrease the adhesion of some bacteria on the urinary tract". The claim was accepted for the product used in the clinical studies with a minimum amount of 36 mg proanthocyanidin/day (AFSSA, 2004a). AFSSA also

accepted an extension of this wording to some other products containing cranberry, while for some cranberry products the extension was not granted due to the absence of appropriate studies (AFSSA, 2004b).

2. Assessment

2.1. Characterisation of the food/constituent

The foods that are the subject of the health claim are Ocean Spray cranberry products (juice drinks and sweetened dried berries Craisins®) containing typically 80 mg cranberry proanthocyanidins per serving. Only the fruit of the North American cranberry plant, *Vaccinium macrocarpon* Aiton is used by contracted growers who supply cranberries to the manufacturer for production of juice extract. The botanical description of *V. macrocarpon* has been published in the American Herbal Pharmacopeia and Therapeutic Compendium monograph. The major commercial *V. macrocarpon* cultivars have been DNA fingerprinted providing additional means of identification and validation of the raw material used by the manufacturer. The applicant has provided full description of the manufacturing process where the juice is extracted according to GMP and the sweetened dried cranberries are produced. Each of the drinks includes 25 % cranberry juice. Serving size of the drinks is 250 mL and for sweetened dried cranberries 40 g. The applicant has provided nutrition information (energy, protein, carbohydrates, fat, fibre, sodium) on cranberry drinks and sweetened dried cranberries (Craisins®) as well as analytical data on the constituents of different cranberry juice drinks including sugars (fructose, glucose, sucrose), acids (quinic, citric, malic, benzoic), ascorbic acid, and different phenolic compounds including proanthocyanidins. The proanthocyanidin content has been determined using an updated dimethylaminocinnamaldehyde method (DMAC) taking advantage of the selective colorimetric reaction between PACs and DMAC after open column gel chromatography on LH-20. Analytical data on the proanthocyanidin amount in dried cranberries is not provided apart from the statement that 40 g of sweetened dried cranberries (Craisins®) typically contain 80 mg of cranberry PAC.

The proanthocyanidins constitute a group of flavan-3-ols ranging from dimers to polymers. The monomeric flavan-3-ols (such as catechin and epicatechin) are not considered PACs. There are differences in the linkages (A- or B-type) between the monomeric units. Analysis of the proanthocyanidin fraction isolated from cranberries (*Vaccinium macrocarpon* Ait) identified a mixture of epicatechin oligomers of various molecular weights with activity associated with A-type linkages (Foo et al., 2000a; 2000b).

The Panel considers that Ocean Spray cranberry drinks and sweetened dried cranberries (Craisins®) containing typically 80 mg cranberry proanthocyanidins per serving are sufficiently characterised.

2.2. Relevance of the claimed effect to human health

The claimed effect is “helps reduce the risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract”. The target population indicated by the applicant is healthy women from the age of 16 years.

Apart from respiratory tract infections, urinary tract infection (UTI) is the most common infection in girls and women with the incidence rising with age and sexual activity. In adult women UTI includes uncomplicated, sporadic or recurrent cystitis and acute pyelonephritis, complicated UTI and asymptomatic bacteriuria (Stamm and Hooton, 1993). Between 40-50 % of women will develop a UTI in their lifetime (Kunin, 1994) and between 20-40 % of women

will develop a recurrent UTI (Maybeck, 1972). It is estimated that between 10-15 % of women over 60 years of age have frequent UTI recurrences (Romano and Kaye, 1981).

UTI refers to the presence of bacteria in the urinary tract. Symptomatic UTI are usually accompanied by bacteriuria at levels of $\geq 10^5$ /mL urine (WHO, 2006). Uropathogenic strains of E. *coli* bacteria cause up to 95 % of UTIs (Ronald 2003; WHO, 2006). Bacterial adherence to mucosal surfaces is generally considered to be an important prerequisite for colonisation and infection with bacteriuria (Harber and Asscher, 1985). Adherence is facilitated by fimbriae which are proteinaceous fibers on the bacterial cell wall (Beachey et al., 1981; Duguid et al., 1955). Preventing adhesion facilitates urinary flushing of the causative bacteria, preventing bacterial colonisation of the urinary tract (Foo et al., 2000a). The Panel notes that bacterial adherence precedes an infection and therefore inhibition of bacterial adhesion might result in a reduction for the risk of symptomatic UTI with bacteriuria $\geq 10^5$ cfu/mL.

The Panel considers that the claimed effect "helps reduce the risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract" is beneficial to human health.

2.3. Scientific substantiation of the claimed effect

A PubMed database was used in literature search. The applicant has indicated a total of 21 pertinent studies with inclusion and exclusion criteria given. These include 12 human studies, 8 *ex vivo / in vitro* studies and one animal study. In addition the applicant provided two meta-analyses on studies of the effect of cranberry products in the prevention of urinary tract infections.

To determine the effects of cranberry in the anti-adherence of uropathogenic organisms, the applicant indicates 8 studies where urine from human female volunteers *ex vivo* was subsequently assayed *in vitro* for bacterial anti-adhesion to uroepithelial cells. In these studies urine from female subjects (number of subjects ranged from 4 to 39) having consumed cranberry drink, cranberry concentrate, cranberries, or dried cranberries in a single dose or during a few days was found to contain bacterial anti-adhesion activity (Di Martino et al., 2006; Greenberg et al., 2005; Howell and Foxman, 2002b; Howell et al., 2005; Schmidt and Sobota, 1988; Sobota 1984). All of these studies were performed with foods provided by the applicant.

A dose-response effect was reported by Di Martino et al. (2006) in a double-blind, randomised, placebo-controlled, cross-over trial. This study was designed to examine the presence of an *ex vivo* inhibitory activity of the urine samples from 10 female and 10 male healthy volunteers after consumption of cranberry juice on the adherence of 6 uropathogenic E. *coli* strains to human T24 uroepithelial cells. Urine samples from the volunteers were incubated together with E. *coli* bacteria on T24 monolayer cell cultures and counted after incubation and washing steps. The bacterial adherence in the urine samples from volunteers having received 250 mL and 750 mL of cranberry juice (containing 27 % cranberry concentrate) was reduced by 45 % and 62 %, respectively. The decrease of the adhesion activity was measured by counting the average number of bacteria per cell determined by examining 100 cells. The cranberry preparations administered were based on a proprietary formula of Ocean Spray Cranberry Inc., USA.

Anti-adherence activity on uropathogenic E. *coli* strains was also detected in urine samples in a study with 65 healthy women, aged 19 to 28 years, after consumption of 1200 mg (but not after 400 mg) dried cranberry juice in capsule form for 8 weeks (Valentova et al. 2007).

The applicant provides further dose-response data from 6 *ex vivo* studies with urine from subjects fed with different cranberry fruit products (juice, concentrate, capsules) at 11, 23, 45,

86, 89, 142, and 179 mg PAC content per serving. (Howell and Winterbottom, 2001; unpublished, proprietary data). The results demonstrated an anti-adhesion effect of the urine in a dose-dependent manner from the lowest dose of PAC consumed, and seems to level off at doses higher than 86 mg PAC.

Another study (Howell 2007, unpublished) shows that anti-adhesion activity in urine occurs at a later time (4-6 hours after consumption) in 6 out of 8 healthy middle-aged subjects consuming 40 g of sweetened dried cranberries (Craisins®) as compared to 240 mL of cranberry juice cocktail (2-4 hours).

Also, other mechanistic and animal data were provided by the applicant in support of the inhibition of cranberry products of bacterial adherence to mucosal surfaces (Foo et al., 2000a; Fo et al., 2000b; Howell et al., 1998; Howell et al., 2001; Howell 2002; Ofek et al., 1991; Ofek et al., 1996; Zafriri et al., 1989).

The Panel considers that these studies demonstrate an *in vitro* anti-adherence effect of urine on uropathogenic E. *coli* strains following consumption of cranberry products. However, these studies do not establish the validity of such anti-adherence effects shown *in vitro* to predict the occurrence of a clinically relevant bacterial anti-adherence effect within the urinary tract.

Six of a total of 12 human studies claimed to be pertinent by the applicant, were carried out on patients suffering from neurogenic bladder (Foda et al., 1995; Lee et al., 2006; Schlager et al., 1999), part of them children (Foda et al. 1995, Schlager et al. 1999), or patients with spinal cord injury (Linsenmeyer et al., 2003; Reid et al., 2001; Waites et al., 2004). In another study (Stothers 2002), the daily dose (1000 mg PAC, *est*) consumed was approximately 6 times higher than the use levels proposed by the applicant for the present claim (160 mg PAC/day). The Panel considers that these 7 studies are of limited relevance for the claim targeted to healthy women from the age of 16 years at the proposed levels of use. The Panel considered the other 5 human studies to be pertinent to the claimed effect.

In an open labelled intervention pilot study, Bailey et al. (2007) investigated the ability of cranberry to prevent UTI for three months in 12 women (25 - 70 years) with a history of recurrent UTI (patients with ≥ 6 occurrences in the previous 12 months). The intervention was 2 x 200 mg capsules of dried cranberry extract standardised to 30 % phenols (≥ 25 % minimum proanthocyanidins) equivalent to a daily intake of approximately 100 mg cranberry proanthocyanidins. Outcome measures were monthly urine analysis by microscopy to detect bacteriuria and pyuria and symptoms of UTI as assessed by questionnaire. At the start of the study all subjects were free of symptomatic and asymptomatic UTI. None of the subjects developed a symptomatic UTI during the study compared to 24 UTI occurrences predicted on the basis of the previous 12-months history of the study population. The Panel notes the limitations of the study design, including the small number of subjects, the lack of a control group, the short duration of the study and the intervention matrix (capsules) differing from the foods specified in this application.

The effect of the consumption of cranberry juice for 4 weeks on bacteriuria in 38 elderly hospitalised patients (9 men, 29 women, mean age 81 years) was investigated in a randomised cross-over study (Haverkorn and Mandigers, 1994). In this study provided as a "letter to the editors", only 17 patients out of the original 38 subjects completed the study. In another "letter to the editor", 19 women (mean age 37 years) with a history of recurring UTI were given once daily either a capsule containing 400 mg cranberry solids or a placebo capsule for three months in a randomised, crossover study. Outcome measures were diagnosed symptomatic UTI and bacteriuria. Only 10 subjects completed the study (Walker et al., 1997). The small number of subjects, the high drop out rates and the short duration of these studies considerably limit their value as a source of evidence to support the claimed effect.

McMurdo et al. (2005, proprietary data) studied the effects of a daily consumption of 300 mL undiluted cranberry juice (provided by Ocean Spray Inc., 100 mg PAC/day, *est*) in 376 elderly (121 men, 255 women, mean age 81 years) hospitalised patients for 18 days in a placebo-controlled, double-blind intervention trial. A total of 115 of the participants withdrew from the study, 62 of the 189 in the placebo group and 53 from the 187 in the cranberry juice group. A total of 5.6 % of the participants developed a symptomatic UTI (primary outcome), 14 of the 189 in the placebo group and 7 from the 187 in the cranberry juice group. The between-group differences were not significant [relative risk (RR) of 0.51, 95 % CI 0.21 – 1.22, $P = 0.122$]. As the actual infection rate was lower than anticipated, the authors concluded that the study was underpowered, and had less than 50 % power to detect a significant difference between the groups. Although there were significantly fewer infections with *Escherichia coli* in the cranberry group (4 out of 7 infections in the cranberry group versus 13 out of 14 infections in the placebo group, RR 0.31, 95% CI 0.10–0.94, P =0.027), the identity of the bacteria responsible for the remaining infections was not provided and the authors concluded that this finding should be interpreted with caution as it was a secondary outcome The short duration and lack of statistical power of this study considerably limit its value as a source of evidence to support the claimed effect.

A randomised, double-blind, placebo controlled trial was carried out in a nursing home population of women with a mean age of 78.5 years over a period of 6 months (Avorn et al. 1994; proprietary data). Urine samples from 153 out of originally 192 recruited women with a daily consumption of either 300 mL of a low-calorie cranberry juice drink (provided by Ocean Spray Inc., 100 mg PAC/day, *est*) or of a placebo drink were analysed monthly for bacteriuria ($\geq 10^5$ organisms/mL urine) and pyuria. A total of 121 subjects completed the 6 months of study (60 in the cranberry group, 61 in placebo). In total 818 urine samples were collected and investigated. Bacteriuria with pyuria was found in 28 % of urine samples of the placebo group versus 15 % of the cranberry juice group. An odds ratio of 0.42 was calculated for the cranberry juice group relative to the control subjects (95 % CI: 0.23 – 0.76, $P = 0.004$). The data on the baseline measurements of the study participants, in particular on the history of previous urinary tract infections show that the incidence of previous UTI in the 6 and 12 months prior to the intervention was 25 and 33 % in the placebo group, but only 7 and 17 % for the cranberry juice group. Two letters to the editors of the publishing journal commented on these differences and inferred that the randomisation and/or blinding scheme had failed (Hopkins et al., 1994; Katz, 1994). The lack of adequate randomisation and the high drop out rates in this study considerably limit its value as a source of evidence to support the claimed effect.

A Cochrane study (Jepson et al., 2004) selected two intervention trials (Stothers, 2002; Kontiokari et al., 2001) for inclusion in a meta-analysis. The Panel considers these two studies are not pertinent to the claimed effect under the proposed conditions of use. The daily dose (1000 mg PAC, *est*) used in Stothers (2002) was approximately 6 times higher than the use levels proposed by the applicant for the claim. In the study by Kontiokari et al. (2001), 50 mL juice daily were consumed (formulated by Maija, Marli, Finland) which contained 7.5 g cranberry concentrate and 1.7 g lingonberry concentrate. Also the applicant indicated the latter study as not pertinent for the substantiation of the claim. Thus, the outcome of this meta-analysis has limited value as a source of evidence to support the claimed effect.

A recent meta-analysis by Jepson and Craig (2007) included 4 human intervention studies (Kontiokari et al.; 2001; McMurdo et al., 2005; Stothers, 2002; Waites et al., 2004), three of which (Kontiokari et al.; 2001; Stothers, 2002; Waites et al., 2004) were considered by the Panel as not pertinent to the claimed effect as indicated above. Thus, the outcome of this meta-analysis has limited value as a source of evidence to support the claimed effect.

The Panel considers that the human intervention studies provided have considerable limitations and do not establish that the anti-adherence effects of cranberry products in urine shown *in vitro* are predictive of the occurrence of a clinically relevant bacterial anti-adherence effect within the urinary tract under the conditions of use proposed for the claim.

The Panel considers that the evidence provided is not sufficient to establish a cause and effect relationship between the consumption of Ocean Spray cranberry products and the reduction of the risk of UTI in women by inhibiting the adhesion of certain bacteria in the urinary tract.

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The foods that are the subject of the health claim (i.e., Ocean Spray cranberry drinks® and sweetened dried cranberries = Craisins®) containing typically 80 mg cranberry proanthocyanidins per serving) are sufficiently characterised.
- The claimed effect is "helps reduce the risk of urinary tract infection in women by inhibiting the adhesion of certain bacteria in the urinary tract". The target population indicated by the applicant is healthy women from the age of 16 years. The claimed effect is beneficial to human health.
- The Panel concludes that the evidence provided is not sufficient to establish a cause and effect relationship between the consumption of Ocean Spray cranberry products and the reduction of the risk of UTI in women by inhibiting the adhesion of certain bacteria in the urinary tract.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Ocean Spray cranberry products and urinary tract infections in women pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0037-UK). August 2008. Submitted by Ocean Spray International Services (UK).

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GLOSSARY / ABBREVIATIONS

Bacteriuria	The presence of bacteria in the urine, typically $\geq 10^5$ /mL
E. coli	*Escherichia coli*
DMAC	Dimethylaminocinnamaldehyde
GMP	Good Manufacturing Practice
PAC	Proanthocyanidins
Pyuria	The presence of leucocytes in the urine, typically ≥10 /mL
Recurrent UTI	The frequent reoccurrence of UTI
Symptomatic UTI	A clinical manifestation of UTI
UTI	Urinary Tract Infection