SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to glucosamine hydrochloride and reduced rate of cartilage degeneration and reduced risk of development of osteoarthritis pursuant to Article 14 of Regulation (EC) No 1924/2006[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following an application from GP International Holding B.V. submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to glucosamine hydrochloride and reduced rate of cartilage degeneration and reduced risk of development of osteoarthritis.

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

The food constituent that is the subject of the proposed claim is glucosamine hydrochloride. Glucosamine is a well characterised amino monosaccharide where a hydroxyl group is replaced with an amino group. Glucosamine is usually formulated as the hydrochloride salt or as glucosamine sulphate and can be quantified in foods by established methods. The Panel considers that the food constituent, glucosamine hydrochloride, that is the subject of the claim is sufficiently characterised.

The claimed effect is "slowing down/reduce the destruction process of cartilage of the musculoskeletal system and consequently reduce the risk of osteoarthritis". The target population is males and females older than 40 years. Osteoarthritis is a disease characterised by erosion of articular cartilage. Cartilage degeneration may proceed to clinical osteoarthritis, and slowing cartilage degeneration in individuals without osteoarthritis may reduce the risk of development of the disease. The Panel considers that a reduced rate of cartilage degeneration in individuals without osteoarthritis might be beneficial to human health by reducing the risk of development of osteoarthritis.

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1 On request from GP International Holding B.V., Question No EFSA-Q-2009-00412 adopted on 15 October 2009.

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3 Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims for the preparation of this opinion: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen.

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The applicant identified a total of 19 publications as being pertinent to the health claim (13 randomised controlled trials, two meta-analyses, one systematic review, two animal studies, and one *in vitro* study).

Ten of the human studies on the effects of glucosamine (either as glucosamine hydrochloride or as glucosamine sulphate) on joint health (e.g. joint pain, structure or function) have been conducted in patients with clinical diagnosis of primarily knee osteoarthritis. Two human studies have been carried out in patients with temporomandibular joint disorders/osteoarthritis. Each of the two meta-analyses comprised 15 human studies and reported on the efficacy of glucosamine for the treatment of (mainly knee) osteoarthritis.

The Panel considers that the evidence provided does not establish that patients with osteoarthritis are representative of the target population with regard to the status of joint tissues, or that results obtained in studies on subjects with osteoarthritis relating to the treatment of symptoms of this disease (e.g. erosion of articular cartilage, reduced mobility of joints) can be extrapolated to the target population. The available scientific evidence indicates that normal cells and tissues are genetically and functionally different from osteoarthritic cells and tissues and therefore may respond differently to intervention with exogenous substances. Therefore, no scientific conclusions can be drawn from the studies mentioned above for the substantiation of the claimed effect.

One human study reported on the bioavailability of two different formulations of glucosamine sulphate, but no endpoints related to cartilage degeneration were measured.

The two animal studies are not pertinent as they were not performed with glucosamine alone and therefore no scientific conclusions can be drawn from these studies for the substantiation of the claim. The evidence provided in the *in vitro* study does not establish that an effect of glucosamine on the degeneration of collagen *in vitro* can predict an effect on cartilage degeneration in humans.

In weighing the evidence the Panel took into account that no studies were provided on the effect of glucosamine on cartilage degeneration in individuals without osteoarthritis, the lack of evidence that patients with osteoarthritis are representative of the target population, and the lack of evidence that the *in vitro* study can predict an effect on cartilage degeneration in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of glucosamine hydrochloride and a reduced rate of cartilage degeneration in individuals without osteoarthritis.

KEY WORDS

Glucosamine, joints, cartilage, osteoarthritis, health claims.

TABLE OF CONTENTS

Summary 1
Background as provided by the European Commission 4
Steps taken by EFSA 4
Terms of reference as provided by the European Commission 4
EFSA disclaimer 4
Information provided by the applicant 6
Assessment 6
1. Characterisation of the food/constituent 6
2. Relevance of the claimed effect to human health 6
3. Scientific substantiation of the claimed effect 7
Conclusions 8
Documentation provided to EFSA 8
References 8

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1924/2006[4] 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 the European Food Safety Authority (EFSA).

STEPS TAKEN BY EFSA

- The application was received on 20/02/2009.
- The scope of the application was proposed to fall under a health claim referring to disease risk reduction.
- During the check for completeness[5] of the application, the applicant was requested to provide missing information on 25/03/2009.
- The applicant provided the missing information on 18/05/2009.
- The scientific evaluation procedure started on 15/06/2009.
- During the meeting on 15/10/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to glucosamine hydrochloride and reduced rate of cartilage degeneration and reduced risk of development of osteoarthritis.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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: glucosamine hydrochloride and reduced rate of cartilage degeneration and reduced risk of development of osteoarthritis.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of glucosamine hydrochloride, a positive assessment of its safety, nor a decision on whether

[4] 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.

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

glucosamine hydrochloride 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.

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 authorization procedure foreseen in Article 17 of Regulation (EC) No 1924/2006.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: GP International Holding B.V., Am Roda-Ring 39, 6460 HA Kerkrade, The Netherlands.

Food/constituent as stated by the applicant

Glucosamine hydrochloride

Health relationship as claimed by the applicant

The applicant claims that glucosamine hydrochloride is part of cartilage and has been shown to protect/reduce the destruction of cartilage of the musculoskeletal system.

Wording of the health claims as proposed by the applicant

Slowing down/reduce the destruction process of cartilage of the musculoskeletal system and consequently reduce the risk of osteoarthritis.

Specific conditions of use as proposed by the applicant

The target population is mainly males and females older than 40 years.

One tablet (600 mg glucosamine hydrochloride) per day orally with some water, at least for 6 months.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the proposed claim is glucosamine hydrochloride. Complete specifications, manufacturing process, bioavailability and stability information have been provided.

Glucosamine is a well characterised amino monosaccharide where a hydroxyl group (-OH) is replaced with an amino group (-NH2) (2-amino-2-deoxy-D-glucose). Glucosamine is usually formulated as the hydrochloride salt or as glucosamine sulphate and can be quantified in foods by established methods.

The Panel considers that the food constituent, glucosamine hydrochloride, that is the subject of the claim is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect is "slowing down/reduce the destruction process of cartilage of the musculoskeletal system and consequently reduce the risk of osteoarthritis". The target population is males and females older than 40 years.

Osteoarthritis is a disease characterised by erosion of articular cartilage. Cartilage degeneration may proceed to clinical osteoarthritis, and slowing cartilage degeneration in individuals without osteoarthritis may reduce the risk of development of the disease.

The panel considers that a reduced rate of cartilage degeneration in individuals without osteoarthritis might be beneficial to human health by reducing the risk of development of osteoarthritis.

3. Scientific substantiation of the claimed effect

The applicant performed a literature search in MEDLINE using the search terms "osteoarthritis, treatment of osteoarthritis, joint pains, degeneration of cartilage of musculoskeletal system". Pertinent publications were selected using the inclusion criteria: knee pain or low back pain for at least six months, elimination of functional mobility. Studies which reported on injuries, on the use of anti-inflammatory medication, and on people with prominent patellar symptoms were excluded.

The applicant identified a total of 19 publications as being pertinent to the health claim (13 randomised controlled trials (RCT), two meta-analyses, one systematic review, two animal studies, and one *in vitro* study).

Ten of the human studies on the effects of glucosamine (either as glucosamine hydrochloride or as glucosamine sulphate) on joint health (e.g. joint pain, structure or function) have been conducted in patients with clinical diagnosis of primarily knee osteoarthritis (Braham et al., 2003; Cibere et al., 2004; Clegg et al., 2006; Houpt et al., 1999; Leffler et al., 1999; Pavelka et al., 2002; Qiu et al., 1998, 2005; Reginster et al., 2001; Usha and Naidu, 2004). Two human studies have been carried out in patients with temporomandibular joint disorders/osteoarthritis (Thie et al., 2001; Nguyen et al., 2001). Each of the two meta-analyses comprised 15 human studies and reported on the efficacy of glucosamine for the treatment of (mainly knee) osteoarthritis (McAlindon et al., 2000; Richy et al., 2003).

The Panel considers that the evidence provided does not establish that patients with osteoarthritis are representative of the target population with regard to the status of joint tissues, or that results obtained in studies on subjects with osteoarthritis relating to the treatment of symptoms of this disease (e.g. erosion of articular cartilage, reduced mobility of joints) can be extrapolated to the target population. The available scientific evidence indicates that normal cells and tissues are genetically and functionally different from osteoarthritic cells and tissues and therefore may respond differently to intervention with exogenous substances (FDA, 2004). Therefore, no scientific conclusions can be drawn from the studies mentioned above for the substantiation of the claimed effect.

One human study reported on the bioavailability of two different formulations of glucosamine sulphate (Basak et al., 2004), but no endpoints related to cartilage degeneration were measured.

Two animal studies were concerned with the effect of a combination of glucosamine hydrochloride/ chondroitin sulphate/manganese ascorbate on collagen-induced autoimmune arthritis in rats (Beren et al., 2001) and a combination of glucosamine hydrochloride/chondroitin sulphate on synovitis in dogs (Canapp et al., 1999), respectively. As they were not performed with glucosamine alone, no scientific conclusions can be drawn from these studies for the substantiation of the claimed effect.

One *in vitro* study reported the effect of glucosamine hydrochloride and glucosamine sulphate on collagen degradation induced by calcium ionophore-activated chondrocytes (Tiku et al., 2007). The Panel considers that the evidence provided does not establish that an effect of glucosamine on the degeneration of collagen in this *in vitro* model can predict an effect on cartilage degeneration in humans.

In weighing the evidence the Panel took into account that no studies were provided on the effect of glucosamine on cartilage degeneration in individuals without osteoarthritis, the lack of evidence that patients with osteoarthritis are representative of the target population, and the lack of evidence that the *in vitro* study can predict an effect on cartilage degeneration in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of glucosamine hydrochloride and a reduced rate of cartilage degeneration in individuals without osteoarthritis.

CONCLUSIONS

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

- The food constituent, glucosamine hydrochloride, that is the subject of the claim is sufficiently characterised.
- The claimed effect is "slowing down/reduce the destruction process of cartilage of the musculoskeletal system and consequently reduce the risk of development of osteoarthritis". The target population is males and females older than 40 years. A reduced rate of cartilage degeneration in individuals without osteoarthritis might be beneficial to human health by reducing the risk of development of osteoarthritis.
- A cause and effect relationship has not been established between the consumption of glucosamine hydrochloride and a reduced rate of cartilage degeneration in individuals without osteoarthritis.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on glucosamine hydrochloride and reduced destruction process of cartilage and reduced risk of osteoarthritis pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0241_DE). May 2009. Submitted by GP International Holding B.V.

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