

## SCIENTIFIC OPINION

### Calcium + Vitamin D3 chewing tablets and bone loss

**Scientific substantiation of a health claim related to Calcium plus Vitamin D3 chewing tablets and reduction of the risk of osteoporotic fractures by reducing bone loss pursuant to Article 14 of Regulation (EC) No 1924/2006<sup>1</sup>**

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

**(Question No EFSA-Q-2008-721)**

**Adopted on 2 July 2009**

#### PANEL MEMBERS

Jean-Louis Bresson, Albert Flynn, Marina Heinonen, Karin Hulshof, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Hildegard Przyrembel, Seppo Salminen, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Henk van den Berg, Hendrik van Loveren and Hans Verhagen.

#### SUMMARY

Following an application from Abtei Pharma Vertriebs GmbH 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 Calcium + Vitamin D3 chewing tablets and reduction of the risk of bone loss and osteoporotic fractures.

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 claim is chewing tablets containing calcium or calcium and vitamin D as active ingredients. Both calcium and vitamin D are well recognised nutrients and are measurable in foods by established methods. Calcium occurs naturally in foods in many forms which are generally well utilised by the body. This opinion will apply to all forms of calcium and vitamin D naturally occurring in foods and those forms authorised for addition to foods and for use in food supplements from all sources with appropriate bioavailability. The Panel considers that the food constituents calcium and vitamin D are sufficiently characterised.

The claimed effect is “improves bone density” and “reduces the risk of osteoporotic fracture”. The target group is women 50 years and older. The Panel considers that limiting the reduction

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of BMD in postmenopausal women might be beneficial to human health by reducing the risk of osteoporotic fractures.

A total of 53 publications were considered by the applicant as pertinent to the claim, including 43 randomized controlled trials (RCT) in humans and 10 meta-analyses of RCTs in which calcium, vitamin D or calcium in combination with vitamin D were used to prevent bone fracture and osteoporotic bone loss. Excluded were trials that studied calcium/vitamin D naturally present in the diet.

The Panel considers that, taken together, the meta-analyses consistently support a cause and effect relationship between the supplementation with calcium alone, or the combined supplementation with calcium and vitamin D, and reduction in the loss of BMD and reduction of the risk of vertebral and non-vertebral osteoporotic fractures in post-menopausal women. The Panel further considers that reducing the loss of BMD in postmenopausal women by supplementation with calcium alone or combined supplementation with calcium and vitamin D may contribute to a reduction in the risk of bone fractures.

In the meta-analyses of the studies on the effect of calcium, alone supplementation with calcium was in the range of 500-1600 mg/d in addition to diet, while in the meta-analyses of the studies on the effect of calcium and vitamin D, combined supplementation with calcium and vitamin D was in the range of 200-1200 mg/d and 200 - 800 IU/d, respectively, in addition to diet. The Panel notes that in the evidence provided there is limited information about the dose-response relationship of calcium and vitamin D and BMD or osteoporotic fractures.

The Panel concludes that, on the basis of the data provided, a cause and effect relationship has been established between the intake of calcium, either alone or in combination with vitamin D, and reducing the loss of BMD in postmenopausal women. Reducing the loss of BMD may contribute to a reduction in the risk of bone fractures.

The following wordings reflect the scientific evidence: “Calcium may reduce the loss of bone mineral in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic bone fractures” and “Calcium and vitamin D may reduce the loss of bone mineral in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic bone fractures”.

The Panel considers that the information provided is insufficient to establish conditions of use for the claims.

**Key words:** calcium, vitamin D, cholecalciferol, osteoporosis, bone mineral density, osteoporotic fractures, health claim.

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**BACKGROUND**

Regulation (EC) No 1924/2006<sup>2</sup> 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. Article 13(5) of that Regulation lays down provisions for addition of claims (other than those referring to the reduction of disease risk and to children's development and health), which are based on newly developed scientific evidence or include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

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 21/10/2008.
- The scope of the application was proposed to fall under a health claim referring to disease risk reduction and including a request for the protection of proprietary data.
- During the check for completeness<sup>3</sup> of the application, the applicant was requested to provide missing information on 13/11/2008.
- The applicant provided the missing information on 09/02/2009.
- The scientific evaluation procedure started on 09/02/2009.
- During the meeting on 30/06/2009, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to Calcium + vitamin D3 chewing tablets and reduction the risk of bone loss and osteoporotic fractures.

**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: calcium + vitamin D3 and "improves bone density" and "reduces the risk of osteoporotic fracture".

**EFSA DISCLAIMER**

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of calcium + vitamin D3 chewing tablets, nor a decision on whether calcium +

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<sup>2</sup> 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.

<sup>3</sup> In accordance with EFSA "Scientific and Technical guidance for the Preparation and Presentation of the Application for Authorisation of a Health Claim"

vitamin D<sub>3</sub> chewing tablets 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 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:** Abtei Pharma Vertriebs GmbH, Abtei 1, 37696 Marienmünster, Germany.

### **1.1. Food/constituent as stated by the applicant**

Chewing tablets with calcium (1000 mg) and vitamin D<sub>3</sub>(800 IU).

### **1.2. Health relationship as claimed by the applicant**

Calcium plays a critical structural role, comprising a substantial proportion of the skeleton, supported by vitamin D which enhances the efficiency of intestinal calcium absorption along the small intestine and controls the blood calcium concentration.

In aging persons an increase in bone loss is observed, probably caused by negative calcium balance and the resulting secondary hyperparathyroidism. Calcium plus vitamin D may slow bone loss and reduce the risk of falls. The impact of vitamin D might be explained by the observed improvement in musculoskeletal function. This vitamin appears to have a beneficial effect on muscle strength and balance mediated through highly specific receptors in the muscle tissue.

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

Chewing tablets with calcium and vitamin D improves bone density in women 50 years and older. Thus chewing tablets may reduce the risk of osteoporotic fractures and it could demonstrate (in a 7 year-lasting supplementation study by 36,000 women) that the risk of hip fractures can be reduced (up to 29% if taken regularly).

### **1.4 Specific conditions of use as proposed by the applicant**

The recommended daily dose is one chewing tablet per day corresponding to 1000 mg elemental calcium and 800 IU (20 µg) cholecalciferol (vitamin D<sub>3</sub>). The target group is women 50 years and older.

## **2. Assessment**

### **2.1. Characterisation of the food/constituent**

The food constituent that is the subject of the claim is chewing tablets containing calcium and vitamin D as active ingredients. Both calcium and vitamin D are well recognised nutrients and are measurable in foods by established methods. Calcium occurs naturally in foods in many forms which are generally well utilised by the body. Different forms of calcium are authorised for addition to foods (Annex II of the Regulation (EC) No 1925/2006). Vitamin D occurs naturally in foods as vitamin D<sub>3</sub> (cholecalciferol). Both vitamin D<sub>3</sub> and vitamin D<sub>2</sub> (ergocalciferol) are authorised for addition to foods (Annex II of the Regulation (EC) No 1925/2006) and for use in food supplements (Annex II of the Regulation (EC) No 1925/2006 and Annex I of Directive 2002/46/EC). This opinion will apply to all forms of calcium and vitamin D naturally occurring in foods and those forms authorised for addition to foods and for use in food supplements from all sources with appropriate bioavailability.

The Panel considers that the food constituents calcium and vitamin D are sufficiently characterised.

## 2.2. Relevance of the claimed effect to human health

The claimed effect is “improves bone density” and “reduces the risk of osteoporotic fracture”. The target group is women 50 years and older.

Bone mineral density (BMD) is an indirect marker of bone quantity ( $\text{g}/\text{cm}^2$ ), but does not necessarily reflect bone quality in terms of micro-architectural deterioration (Krieg et al., 2008; Kanis et al., 2008, Li et al., 2004). Reduced BMD in older adults is predictive of the risk of osteoporotic fractures. However, increasing BMD or limiting the reduction of BMD in post-menopausal women has not been consistently shown to reduce the risk of osteoporotic fractures.

The Panel considers that limiting the reduction of BMD in postmenopausal women might be beneficial to human health by reducing the risk of osteoporotic fractures.

## 2.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in PubMed [MEDLINE] to identify human intervention studies and meta-analyses of randomised controlled trials (RCTs) in which calcium, vitamin D or calcium in combination with vitamin D were used to prevent bone fracture and osteoporotic bone loss using combinations of the key words calcium, vitamin D, and hip fracture. Animal studies, diagnostic studies, pharmacological studies, non-randomized trials, epidemiological studies, and duplicate studies were excluded. The search was supplemented by reviewing guidelines, text books and review articles, and by hand searching. The studies concerned the use of calcium and/or vitamin D taken as dietary supplements. Excluded were trials that studied calcium/vitamin D naturally present in the diet.

A total of 43 RCTs and 10 meta-analyses of RCTs investigating the effects of either calcium, vitamin D, or calcium and vitamin D intake on BMD or on incident bone fracture were identified by the applicant as being pertinent to the claim.

### *Calcium and vitamin D*

Among the studies identified as being pertinent by the applicant were four meta-analyses of RCTs assessing the effects of the combination of calcium and vitamin D on changes in BMD or incidence of osteoporotic bone fractures (Homik et al., 1998; Avenell et al., 2005; Tang et al., 2007; Boonen et al., 2007).

The meta-analysis by Homik et al. (1998) was performed to determine the efficacy of calcium and vitamin D supplementation in the prevention and treatment of steroid-induced osteoporosis in adults (older than 18 years). The Panel considers that this study group is not representative of the general population and these studies are not a suitable source of data to substantiate the claimed effect.

The meta-analysis by Tang et al. (2007) included 29 RCTs with a total of 63,897 participants (92% women) which investigated whether calcium (16 trials, 6,517 subjects, calcium supplement 500-1600 mg/d in addition to diet), or calcium in combination with vitamin D (13 trials, 46,108 subjects, calcium supplement 200-1200 mg/d and vitamin D supplement 200-800 IU in addition to diet), had an effect in the prevention of bone fracture and osteoporotic bone loss in subjects aged 50 years and older. When the trials reporting on bone fractures were considered (17 trials, 52,625 subjects), treatment with calcium (calcium supplement 750-1600 mg/d in addition to diet) or with calcium plus vitamin D (calcium supplement 500-1,200 mg/d and vitamin D supplement 400-800 IU in addition to diet) was associated with a significant 12% risk reduction in bone fractures of all types (RR = 0.88, 95% CI 0.83–0.95). When the trials reporting on BMD were considered (23 trials, 41,419 subjects), treatment with

calcium (calcium supplement 500-1600 mg/d in addition to diet) or with calcium plus vitamin D (calcium supplement 200-1200 mg/d and vitamin D supplement 200-800 IU in addition to diet) was associated with a significant lower rate of bone loss at the hip (-0.54%, 95% CI -0.35; -0.73%) and lumbar spine (-1.19%, 95% CI -0.76; -1.61%). A significant reduction in bone loss was observed in most of the individual studies considered. The reduction in fracture risk was significantly greater (by 24%) in trials reporting a compliance rate >80% (n = 8). The treatment effect was significantly greater in subjects with low dietary calcium intake (< 700mg/d), in subjects with low serum vitamin D concentrations (25-(OH)-vitamin D<sub>3</sub> <25 nmol/L), in subjects receiving ≥ 1200 mg calcium/d, in subjects receiving ≥ 800IU of vitamin D (among those receiving calcium plus vitamin D supplementation). The effect was consistent irrespective of sex, fracture sites, or history of previous fracture. Although the addition of vitamin D to calcium did not change the treatment effect significantly, the authors attribute this fact to the relatively low number of subjects receiving supplementation with vitamin D (in addition to calcium) ≥ 800 IU. The treatment effect was greater with calcium doses of 1200 mg or more than with doses less than 1200 mg (0.80 vs. 0.94; p=0.006), and with vitamin D doses of 800 IU or more than with doses less than 800 IU (0.84 vs. 0.87; p=0.03). The Panel notes the large number of subjects included in this meta-analysis, the consistency of results obtained across trials, and that the authors could not identify significant publication bias. The Panel, however, notes that there were relatively few trials (13) that investigated the effects of supplementation with both calcium and vitamin D. Furthermore, dietary intake of calcium was not provided for some studies.

The Cochrane systematic review and meta-analysis by Avenell et al., (2005) had the objective of determining the effects of vitamin D<sub>3</sub> or vitamin D<sub>3</sub> analogues, with or without calcium, in the reduction of incidence of vertebral, hip, and other non-vertebral fractures in older people (postmenopausal women and men over 65 years of age). Seven RCTs including 10,376 participants reported on the effects of vitamin D plus calcium versus placebo or no treatment. Pooled data from these trials showed a statistically significant reduction in the incidence of hip fracture (RR 0.81, 95% CI 0.68 to 0.96) and in the incidence of non-vertebral fracture (RR 0.87, 95% CI 0.78 to 0.97). The Panel notes that, although the target population, women, for the claim was not considered separately in any sub-group analysis, all the studies included in the meta-analysis had recruited mostly or exclusively post-menopausal women.

The meta-analysis by Boonen et al. (2007) was conducted with the aim of defining the need for additional calcium supplementation in individuals receiving vitamin D<sub>3</sub> for the prevention of hip fractures (Bischoff-Ferrari et al., 2005). The meta-analysis included nine RCTs on the effects of vitamin D<sub>3</sub> with or without calcium supplementation vs. placebo or no treatment in postmenopausal women and/or older men (over 50 years) specifically reporting on hip fracture risk. Based on four RCTs (9,083 patients), the pooled relative risk (RR) of hip fracture for subjects supplemented with vitamin D alone (400 IU/d in two trials, 700-800 IU in two trials) was 1.10 (95% CI 0.89-1.36, non significant compared to placebo/no treatment). In the six RCTs (45,509 subjects) that used supplementation with vitamin D<sub>3</sub> (400 IU/d in one trial, 700-800 IU in five trials) in combination with calcium (500 mg/d in one trial, 1000 mg/d in three trials, 1200 mg/d in two trials), the pooled RR of hip fracture for the group supplemented with vitamin D<sub>3</sub> and calcium was 0.82 (95% CI 0.71-0.94, statistically significant compared to placebo/no treatment). Measurement of BMD was not reported in the meta-analysis. The Panel notes that, although the target population, women, was not considered separately in any sub-group analysis, the majority of subjects included in the RCTs considered in the meta-analysis were women (from 62% to 85% of total subjects depending on the study).



Relatively few studies have specifically investigated the effect of age on the relationship between calcium and vitamin D supplementation and fracture risk. Jackson, et al. (2006) randomised 36,282 postmenopausal women aged 50 to 79 years to consume 1000 mg of calcium as calcium carbonate with 400 IU of vitamin D<sub>3</sub> daily or placebo. The follow-up period was 7 years. In the intention-to-treat (ITT) analysis, no significant differences were observed between the intervention and placebo groups in fracture risk (calculated as hazard ratio) at any skeletal site. When follow-up data for non-compliant participants were excluded from the analysis, a lower risk of hip fracture was observed in the intervention group as compared to placebo (RR = 0.71, 95% CI = 0.52-0.97). Loss of BMD during follow-up at the hip was also significantly lower in the intervention than in the placebo group (ITT). The Panel notes that in the subgroup of women aged 50-59 years, the effect of supplementation on risk of hip fracture was not seen (2.17, 95% CI = 1.13-4.18).

### *Calcium*

One meta-analysis on calcium supplementation for the prevention of postmenopausal osteoporosis was presented (Shea, et al., 2002). This meta-analysis included 15 trials (1,806 subjects) published before 2000 that used calcium ( $\geq 400$  mg/d), either alone or combined with vitamin D ( $\leq 400$  IU/d – 2 studies) against placebo. The endpoints measured were BMD and incidence of fractures. Five of those studies (including 576 women) reported vertebral fractures as an outcome. The pooled RR indicated a non significant trend toward reduction in vertebral fractures in the calcium group (RR 0.77, 95% CI 0.54–1.09,  $p = 0.14$ ). The two trials that reported non-vertebral fractures had very few events, and the CI on the pooled estimate is very wide (RR 0.86, 95% CI 0.43–1.72,  $p = 0.66$ ). The impact of calcium on BMD at several sites was examined - total body (4 studies), lumbar spine at 2 years (9 studies), lumbar spine at 3 or 4 years (2 studies), hip (8 studies) and distal radius (6 studies). Calcium showed a statistically significant effect on BMD of about 1.6 – 2 % increase over 2 years at all sites except for the lumbar spine. The authors conclude that calcium supplementation has a relatively small, but possibly important effect on BMD in postmenopausal women. The weaknesses included large number of drop-outs during follow-up in most studies and the unexplained heterogeneity of results across studies.

The effects of calcium supplementation alone on BMD and bone fracture incidence in older subjects were also addressed in a more recent meta-analysis described above (Tang et al., 2007), where calcium supplementation alone showed a significant increase in BMD and a significant decrease in fracture risk.

### *Vitamin D*

Five meta-analyses on the effects of vitamin D in the prevention of bone fractures and bone loss were submitted (Bischoff-Ferrari et al, 2004; Bischoff-Ferrari et al., 2005; Izaks, 2007; Jackson et al., 2007; Papadimitropoulos et al., 2002).

The aim of the meta-analysis performed by Bischoff-Ferrari et al. (2004) was to assess the effectiveness of vitamin D in preventing an older person from falling. The observed endpoints did not include measurements of bone loss or fracture. The Panel therefore considers this meta-analysis does not provide evidence to support the claimed effect.

Papadimitropoulos et al. (2002) in their meta-analysis of 25 studies evaluated the effect of vitamin D (4 studies also included additional calcium supplementation) on bone density and fractures in postmenopausal women. RCT studies with doses of vitamin D greater than 400 IU/d and with follow-up of at least 1 year were taken into consideration. In 8 studies (1,130 patients) the incidence of fractures was measured. The use of vitamin D

supplementation reduced the incidence of vertebral fractures (RR 0.63, 95% CI, 0.45– 0.88,  $p=0.01$ ) but not the incidence of non-vertebral fractures (RR 0.77, 95% CI 0.57–1.04,  $p=0.09$ ). The effect of vitamin D supplementation on BMD was measured in 14 studies. The results showed heterogeneity depending on the type of vitamin D taken – standard vitamin D (vitamin D<sub>3</sub>) or vitamin D analogues. In the case of standard vitamin D, the differences reached statistical significance only for lumbar spine at the 1st year and for the femoral neck at 2nd year of intervention. The Panel notes that most of the studies included in this meta-analysis were performed with the use of analogues of vitamin D, so their relevance to the claimed effect is limited.

Effectiveness of vitamin D supplementation in preventing hip and non-vertebral fractures in older ( $\geq 60$  yr) persons was evaluated in a meta-analysis by Bischoff-Ferrari et al. (2005). Seven double-blind RCT studies (9,820 subjects) investigated the effects of oral vitamin D supplementation (4 trials also included calcium supplementation) with a minimum follow-up of 1 year. When all studies were considered together, and when only trials ( $n=2$ ) using 400 IU/d of vitamin D were considered, the effects of vitamin D supplementation on hip fracture risk were not significant. However, a statistically significant reduction in the risk of hip fracture was observed when trials ( $n=3$ ) using 700 to 800 IU/d were considered. The pooled RR for any non-vertebral fracture for any vitamin D dose was 0.83 (95% CI, 0.70-0.98). Taking into account only the five trials (6,098 subjects) using high vitamin D doses (700 – 800 IU/d), the pooled RR was 0.77 (95% CI, 0.68-0.87), suggesting that these doses reduced non-vertebral fracture risk by 23%. The dose of 400 IU/d revealed no significant benefit on total non-vertebral fracture risk.

The meta-analysis by Izaks (2007) included 7 studies from the meta-analysis by Bischoff-Ferrari et al. (2005) plus four additional RCTs, which used calcium 500 – 1200 mg/d in addition to vitamin D. A funnel plot was used to explore the possibility of publication bias. For any non-vertebral fracture, the funnel plot was asymmetrical because two small RCTs showed a large positive effect. This effect was not found for hip fracture. Low doses of vitamin D (<400 IU daily) were not effective in reducing fracture risk. In contrast to the Bischoff-Ferrari et al. (2005) meta-analysis, however, the effect of high dose vitamin D ( $\geq 700$  IU daily) seemed to be dependent on the target population. For any non-vertebral fracture, the pooled RR was 0.80 (95% CI, 0.70–0.90) in institutionalised persons, and 0.88 (95% CI, 0.75–1.04) in the general population; for hip fracture, pooled RR were 0.72 (95% CI, 0.59 to 0.88) and 1.04 (95% CI, 0.72–1.50), respectively. It was concluded that the inconsistency between previous meta-analysis and the recent trials might be owing to publication bias and differences in target populations. Nevertheless vitamin D at doses  $\geq 700$  IU daily was still effective in reducing fracture risk, at least in institutionalised persons.

In the meta-analysis performed by Jackson et al., (2007), which included nine studies in post-menopausal women, the effect of cholecalciferol (vitamin D<sub>3</sub>) given in a dose of 400 – 800 IU/d on the risk of fracture was evaluated. Studies with complementary calcium supplementation were excluded. Men aged 65 years and over were included only where they were a part of a study in which results for men and women were not presented separately. The Panel notes that differences between intervention and control groups regarding non-vertebral and vertebral fractures were not statistically significant.

The Panel considers that, taken together, the meta-analyses described above consistently support a cause and effect relationship between the supplementation with calcium alone or the combined supplementation with calcium and vitamin D and reduction in the loss of BMD and reduction of the risk of vertebral and non-vertebral osteoporotic fractures in post-menopausal women. The Panel further considers that reducing the loss of BMD in

postmenopausal women by supplementation with calcium alone or combined supplementation with calcium and vitamin D may contribute to a reduction in the risk of bone fractures.

In the meta-analyses of the studies on the effect of calcium, alone supplementation with calcium was in the range of 500-1600 mg/d in addition to diet, while in the meta-analyses of the studies on the effect of calcium and vitamin D combined supplementation with calcium was in the range of 200-1200 mg/d in addition to diet and with vitamin D in the range of 200 - 800 IU/d in addition to diet. The Panel notes that in the evidence provided there is limited information about the dose-response relationship of calcium and vitamin D and BMD or osteoporotic fractures as most of the studies focused on the effect of supplemental intake of calcium and/or vitamin D in addition to dietary intake which was not provided for some studies. Furthermore, studies on the effect of calcium and vitamin D naturally present in the diet were excluded.

The Panel concludes that a cause and effect relationship has been established between the intake of calcium, either alone or in combination with vitamin D, and reducing the loss of BMD in postmenopausal women. Reducing the loss of BMD may contribute to a reduction in the risk of bone fractures.

#### **2.4 Panel's comments on the proposed wording**

Taking into account the scientific evidence presented, the Panel considers that the following wordings reflect the scientific evidence:

“Calcium may reduce the loss of bone mineral in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic bone fractures”.

“Calcium and vitamin D may reduce the loss of bone mineral in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic bone fractures”.

#### **2.5 Conditions and restrictions of use**

The applicant proposed as conditions of use 1000 mg of calcium and 800 IU of vitamin D in a daily dose (taken as dietary supplement).

In the evidence provided there is limited information about the dose-response relationship of calcium and vitamin D and BMD or osteoporotic fractures. Most of studies focused on the effect of supplemental intake of calcium and/or vitamin D in addition to dietary intake which was not provided for some studies. Furthermore, studies on the effect of calcium and vitamin D naturally present in the diet were excluded.

The Panel considers that the information provided is insufficient to establish conditions of use for the claims.

### **CONCLUSIONS AND RECOMMENDATIONS**

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

- The food constituents, calcium and vitamin D, that are the subject of the health claim are sufficiently characterised.
- The claimed effect is “improves bone density” and “reduces the risk of osteoporotic fracture”.
- A cause and effect relationship has been established between the intake of calcium, either alone or in combination with vitamin D, and reducing the loss of bone mineral

density. Reducing the loss of BMD may contribute to a reduction in the risk of bone fractures.

- The following wording reflects the scientific evidence:
- “Calcium may reduce the loss of bone mineral in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic bone fractures”.
- “Calcium and vitamin D may reduce the loss of bone mineral in post-menopausal women. Low bone mineral density is a risk factor in the development of osteoporotic bone fractures”.
- The target population is women 50 years of age and older.
- The information provided is insufficient to establish conditions of use for the claims.

#### **DOCUMENTATION PROVIDED TO EFSA**

Health claim application on calcium + vitamin D<sub>3</sub> chewing tablets and reduction the risk of bone loss and osteoporotic fractures pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0225\_DE). October 2008. Submitted by Abtei Pharma Vertriebs GmbH.

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## GLOSSARY / ABBREVIATIONS

BMD	Bone Mineral Density
CI	Confidence Interval
DXA	Dual-energy X-ray Absorptiometry
IU	International Units
RCT	Randomized controlled trial
RR	Relative Risk