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Abtei comments on the Scientific Opinion of the EFSA NDA Panel on the

**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**

Abtei welcomes the EFSA opinion on the health claim related to Calcium and Vitamin D3 chewing tablets and the reduction of the risk of osteoporotic fractures by reducing bone loss. Abtei agrees with the assessment confirming that a cause-effect relationship has been described between the supplementation of Calcium and Vitamin D and reduction in the loss of BMD and reduction of the risk of osteoporotic fractures in postmenopausal women.

**Regarding conditions and restrictions of use** Abtei is slightly concerned that EFSA only seems to consider that the “evidence provided there is limited information about the dose-response relationship of Calcium and Vitamin D and BMD or osteoporotic fractures”.

*Firstly* the range in the meta-analysis by **Tang et al. (2007)** of combined supplementation of Calcium has to be corrected to

**500 mg** - 1200 mg Calcium and from **500 IU** - 800 IU Vitamin D .

The study of Christian Meier (2004) was wrongly reported in the meta-analysis with a dosage of 200 mg Calcium and 200 IU Vitamin D.

That shows all studies cited had been carried out with **an additional supplementation of minimum 500 mg Calcium and minimum 500 IU Vitamin D.** (1, 4)

The main focus and power of the studies is clearly on supplemental dosages with 1000 mg Calcium and 400 IU – 800 IU Vitamin D<sub>3</sub>. (table1, figure1)

Furthermore *Tang et al. (2007)* reported that the treatment effect of reduction in fracture risk was greater with Calcium doses of 1200 mg or more than with doses less than 1200 mg (0,80vs.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). (1)

Secondly **Bischoff-Ferrari et al. (2005)** showed in a meta-analysis for trials (n = 2) using 400 IU/d of Vitamin D the effectiveness of Vitamin D supplementation on hip fracture risk was not significant. However, a statistically significant reduction in the risk of hip fracture was observed when trials (n = 3) using 700 IU/d to 800 IU/d were considered. (1) (figure 4)

Thirdly **Kevin D Cashman et al. (2009)** observed clear dose-related increments ( $p < 0,0001$ ) in serum 25-hydroxyvitamin D with increasing supplemental Vitamin D3 intakes. (5) (figure 2, 3)

This is particularly important because this underlines the dose-response relationship between supplemental intake and Bone Mineral Density (BMD).

Finally the studies should show generally the additional benefit through supplementation on the dietary intake.

Therefore *post-menopausal* women need to be provided with the appropriate supplement levels to reduce risk of osteoporotic bone fractures effectively. This reflects also the recent views, as expressed by health organizations like the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO).

**They recommend a minimum daily amount of 1000 mg Calcium and 800 IU Vitamin D per day (2, 3).**

In view and summarizing of the above stated matter, Abtei is firmly convinced that there is sufficient information and therefore it is necessary to define specific conditions of use like

**“Recommended daily dose is 1000 mg Calcium and 800 IU Vitamin D3”**

or at least

**“Recommended daily dose is minimum 500 mg Calcium and minimum 400 IU Vitamin D3”.**

This would help and provide post-menopausal women with appropriate supplement levels to reduce the risk of osteoporotic bone fractures.

## ANNEX

Table 1: (Tang et al.)

### Effect of calcium and vitamin D on fracture risk

"Of the 17 trials reporting fracture as an outcome (n=52 625), calcium and calcium in combination

with vitamin D were associated with a 12% risk reduction in fractures of all types"

references	calcium [mg]	vitamin D [IU]	RR [95% CI]	n
Dawson-Hughes-1	500	700	0,46	389
Peacock	750		0,81	261
Chevalley	800		0,96	156
Fujita	900		0,31	19
Reid-1	1000		0,4	122
<b>Larsen</b>	<b>1000</b>	<b>400</b>	<b>0,84</b>	<b>9605</b>
Harwood	1000	800	0,49	150
<b>RECORD-1</b>	<b>1000</b>		<b>0,94</b>	<b>2638</b>
<b>RECORD-2</b>	<b>1000</b>	<b>800</b>	<b>0,94</b>	<b>2643</b>
<b>Porthouse</b>	<b>1000</b>	<b>800</b>	<b>0,96</b>	<b>3314</b>
<b>Jackson</b>	<b>1000</b>	<b>400</b>	<b>0,97</b>	<b>36282</b>
<b>Reid-2</b>	<b>1000</b>		<b>0,92</b>	<b>1471</b>
<b>Chapuy-1</b>	<b>1200</b>	<b>800</b>	<b>0,75</b>	<b>2790</b>
Recker	1200		0,85	197
Chapuy-2	1200	800	0,85	583
Prince-1	1200		0,87	1460
Riggs	1600		0,89	236

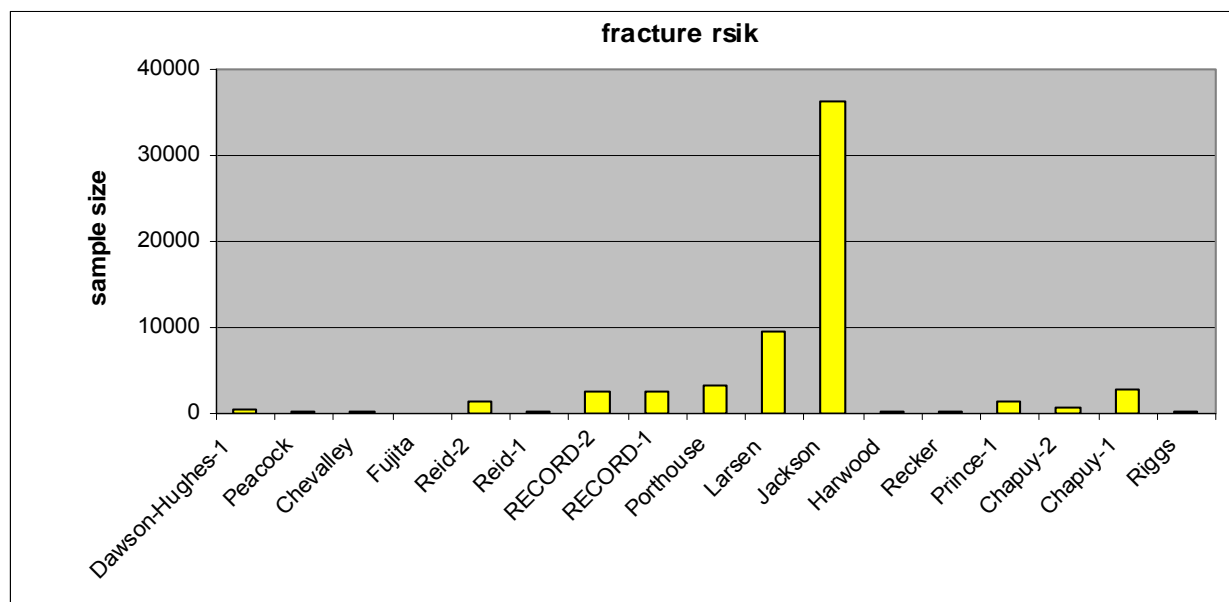
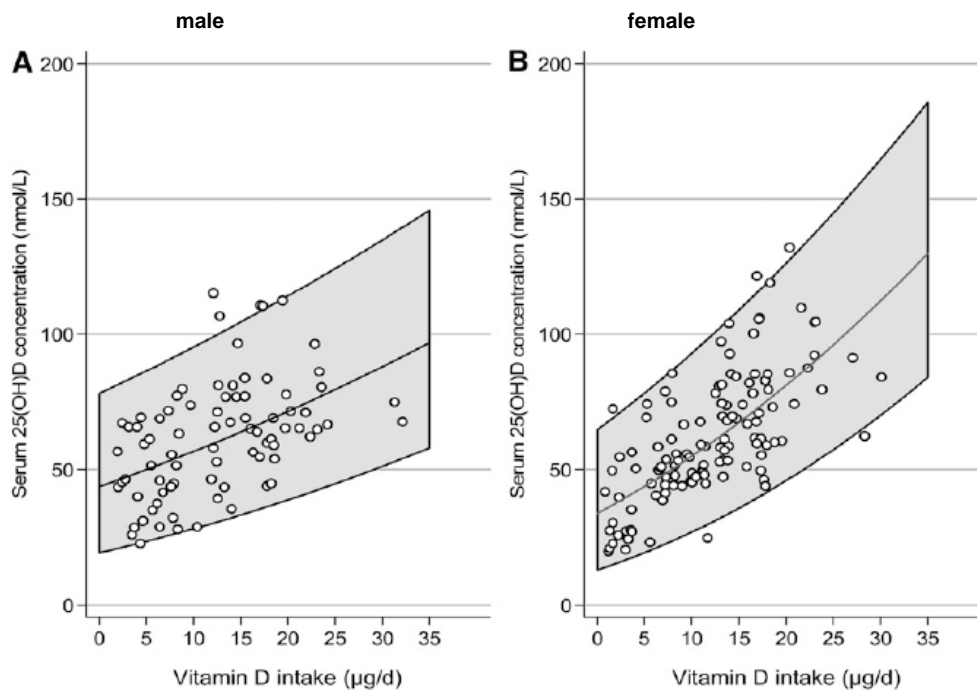


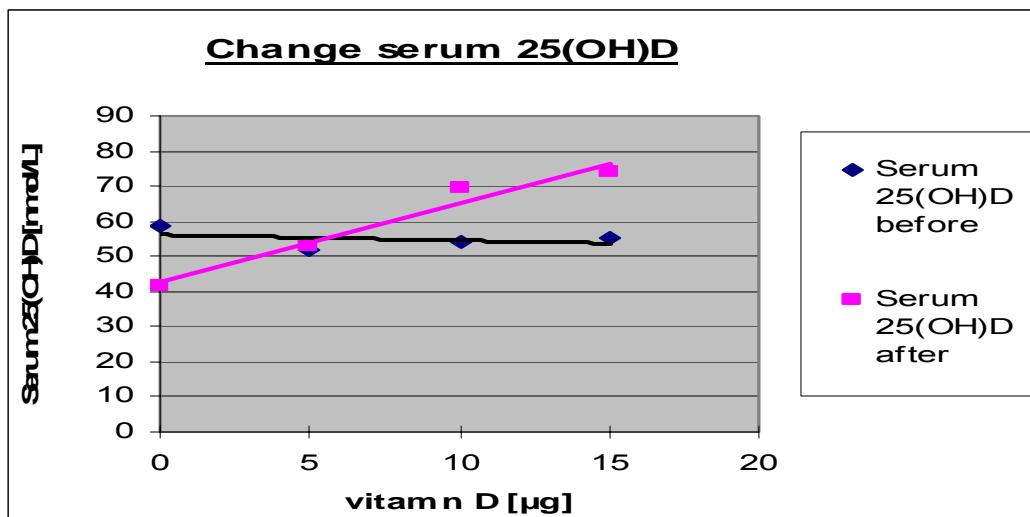
Figure1: main focus and power of the studies



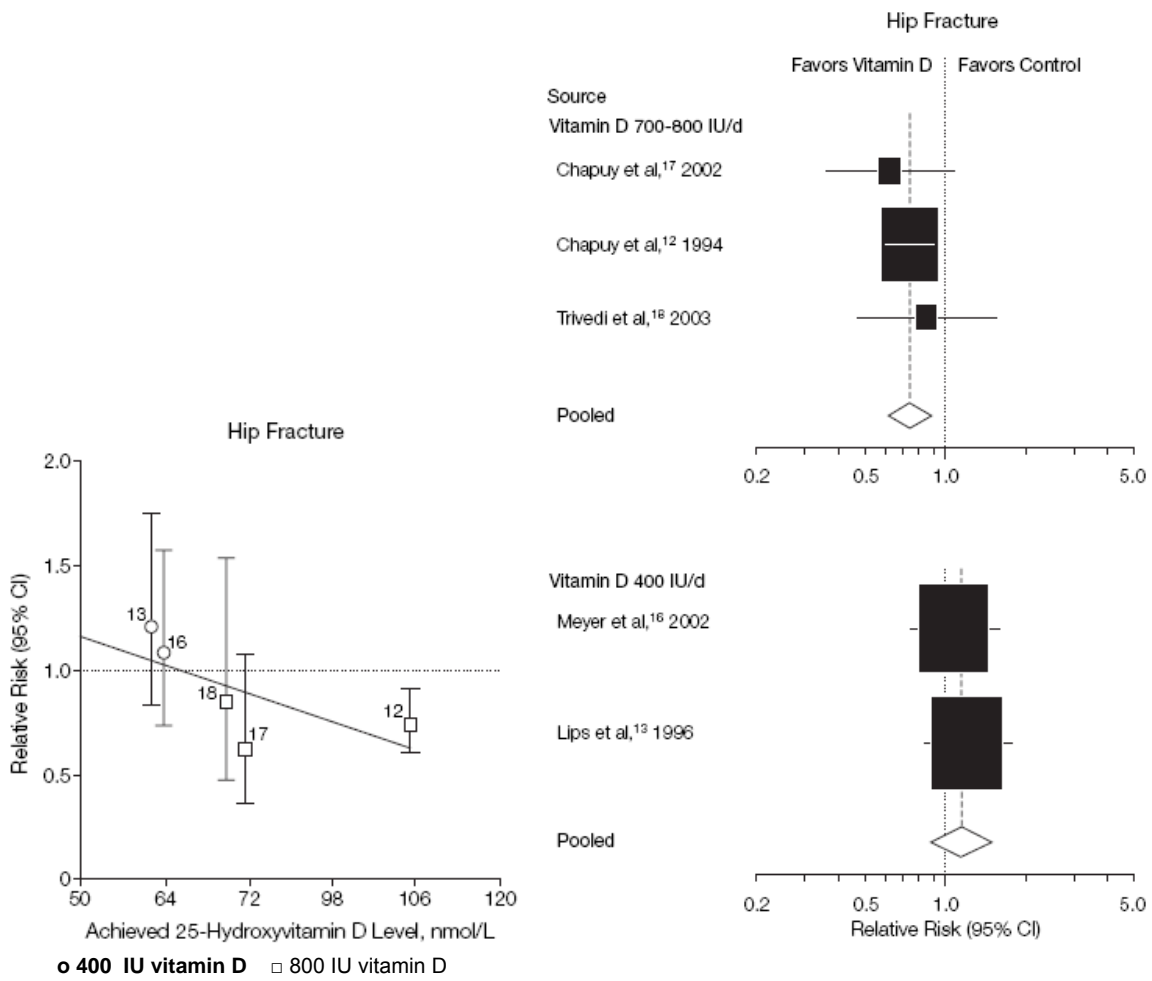
**FIGURE 2.** Relation between mean serum 25-hydroxyvitamin D [25(OH)D] concentrations (in late winter, 2008) and total vitamin D intake (diet and supplemental) in healthy men (A;  $n = 82$ ) and women (B;  $n = 122$ ) aged  $\geq 64$  y living at northerly latitudes (51 and 55°N). The shaded areas represent 95% CIs.

**Change serum 25(OH)D (nmol/L)**

vitamin D [ $\mu\text{g}$ ]	Serum 25(OH)D before	Serum 25(OH)D after	n
0	58,8	41,6	55
5	51,8	53,2	48
10	54,3	69,5	53
15	55,1	73,8	48



**Figure 3: dose-related increments ( $p < 0,0001$ ) in serum 25-hydroxyvitamin D with increasing supplemental Vitamin D intakes.**



**Figure 4: fracture prevention with vitamin D supplementation (Bischoff-Ferrari)**

reference: H.A.Bischoff-Ferrari, W.C.Willett, J.B.Wong, E.Giovannucci, T.Dietrich, and B.Dawson-Hughes. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. JAMA, 293 (18):2257-2264 (2005)

## **Reference list**

1 **efsa** Journal (2009) 1180, 1-13

2 **esceo** the European society for clinical and economic aspects of osteoporosis and osteoarthritis

3 **Kanis** I.A., Burlet N., Cooper C., Delmas P.D., Reginster I.Y., Borgstrom F., Rizzoli R. European guidance for diagnosis and management of osteoporosis in postmenopausal women, position paper, Osteoporos Int 2008

4 **Meier** et al. Supplementation with oral Vitamin D3 and Calcium during winter prevents seasonal bone loss, Journal of bone and mineral research Volume 19, Number 8, 2004

5 **Kevin D Cashman** et al. Estimation of dietary requirement for vitamin D in free-living adults  $\geq 64$  y of age, Am J Clin Nutr 2009; 89:1366-74