AGENCE FRANÇAISE DE SÉCURITÉ SANITAIRE DES ALIMENTS

Maisons-Alfort, 28 January 2009

OPINION

of the French Food Safety Agency on models for setting maximum vitamin and mineral levels in fortified foods and food supplements

LA DIRECTRICE GÉNÉRALE

On 17 December 2008, the Directorate General for Competition, Consumer Affairs and Fraud Control requested the French Food Safety Agency (Afssa) to assess the models for setting maximum vitamin and mineral levels in fortified foods and food supplements, in the context of Regulation (EC) No 1925/2006 on the addition of vitamins and minerals and of certain other substances to foods.

Context and work objectives

European Regulation (EC) No 1925/2006 on the addition of vitamins and minerals to foods has been in force since 1 July 2007[1]. It provides for the setting of maximum fortification levels at European level. In this regard, Afssa was requested on 11 September 2007 to assess the scientific data available for setting maximum vitamin and mineral levels (2007-SA-315).

As part of this request, Afssa had recommended a probabilistic assessment approach for testing the safety of the maximum fortification limits obtained by the different mathematical models put forward (Flynn *et al.*, 2003; Domke, 2004a; Domke, 2004b; Rasmussen *et al.*, 2006; Richardson, 2007). This resulted in an opinion being produced on 13 October 2008 (Afssa, 2008).

The approach and tool developed by Afssa were presented at meetings held at the end of 2008 with European Member States. During the last meeting in December 2008, the European Commission recommended the adoption of two models for setting two series of maximum levels independently: one for fortified foods (expressed for 100kcal) according to the new Flynn model (2008) and the other one for food supplements (expressed in daily intake), based on the model developed by the ERNA[2] (Richardson, 2007). The new request has been made within this context: with a view to testing the new series of maximum levels obtained by these 2 models by varying the different model parameters.

The simulation work involves simultaneously testing, on the basis of recent French consumption data (national INCA2[3] survey 2006-2007), the maximum vitamin and mineral fortification levels in the foods that are likely to be fortified and the maximum vitamin and mineral levels for food supplements. This probabilistic simulation approach developed by Afssa is based upon the previous approach put forward for fortified foods only, without account taken of food supplements (Afssa, 2001). The tool reveals whether or not the maximum levels set independently for fortified foods and food supplements, but introduced simultaneously into the simulation tool, lead to the tolerable upper intake level being exceeded.

For each nutrient, the distributions of total vitamin and mineral intakes (via base diet, fortified foods and food supplements) are studied according to the different scenarios in adults and children. The tolerable upper intake levels are then compared with the intake distributions to identify any risks of their being exceeded.

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[1] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins, minerals and of certain other substances to foods. JO L 404 of 30.12.2006 :26.38

[2] European Responsible Nutrition Alliance

[3] Second National Individual Study of Food Consumption.

Methods

Data used: the INCA2 2006-2007 consumption study and the CIQUAL[4] 2008 food composition table

The second National Individual Study of Food Consumption (INCA2) was conducted from 2006 to 2007. In order to take account of dietary changes through the seasons, it was carried out on three separate occasions over more than twelve months. It involved 4,079 participants aged between 3 and 79 years old (including 2,624 adults aged 18-79 and 1,455 children aged 3-17) living in mainland France. The participants were selected using a three-stage cluster sampling technique stratified on region and size of urban area. The random selection of households was made from the 1999 national population census and the bases of new housing built between 1999 and 2004.

A weighting was allocated to each participant to ensure that the sample was representative at national level in line with socio-demographic criteria. Moreover, under-reporters (participants who said they consumed less than their requirements) were excluded from the analyses. The sample of non-under-reporting adults included 1,918 people and that of children: 1,444.

The INCA2 study gathers all of the participants' dietary intakes, using food diaries filled in over 7 consecutive days by the participants (food and drinks consumed at each meal and between meals). Portion size is estimated from a photo album (SU.VI.MAX, 1994). If they also consumed food supplements, the study participants filled in a separate food supplement diary during the same week of the study.

Calculating nutritional intakes by simulations

The simulation carried out involves calculating total dietary intakes from the three possible sources (base diet, fortified foods and food supplements) based on detailed and nationally representative consumption data and by integrating the maximum safe levels for fortified foods (MSL_f) and maximum safe levels for supplements (MSL_s). Moreover, several hypotheses of the market shares of fortified foods (among those likely to be fortified) are tested: 0% (no fortification), 10%, 25% and 50%.

The simulations carried out concern vitamin D, vitamin B6 and iron. Prior to simulation, the MSL_f expressed for 100kcal and MSL_s expressed in daily intake are calculated for each nutrient. These calculations are based on Flynn's (2008) and Richardson's (2007) models respectively.

Setting the MSL_f

The MSL_f (expressed for 100kcal) are calculated using Flynn's model (2008) according to the following formula:

$$\mathbf{MSL_f(/100kcal)=[UL-(CI+SI)_{95}]/[EFF_{95}/100]}$$

With **UL :** Tolerable upper intake level

$(CI+SI)_{95}$: 95th percentile intake level from base diet and food supplements

EFF_{95} : Energy intake for the nutrient from fortified food at the 95th percentile

Irish data were favoured for taking account of a mature market as regards the development of fortified food and food supplement consumption. In accordance with the choices recommended by the European Commission, the MSL_f were calculated using the values for 3 to 10 year-old children in the parameters of Flynn's model (2008). It was also decided to carry out several MSL_f calculations by making hypotheses on possible market trends. Accordingly, 3 options were tested:

Option 1: 50% increase in $(CI+SI)_{95}$

Option 2: 50% increase in EFF_{95}

[4] Food Quality Information Centre

Option 3: 50% increase in $(CI+SI)_{95}$ **and** EFF_{95}

Option 0, corresponding to the strict application of the formula without upwardly adjusting one or more parameters, was also tested.

Table 1: MSL_f calculations (mg or µg/100kcal) for fortified foods from Irish consumption data of 5-10 year-old children[5]

						MSL_f (mg or µg/100kcal)			
Nutrient	UL[1]	$(CI+SI)_{95}$[3]	EFF_{95}[4]	$(CI+SI)_{95}$+ 50%	EFF_{95}+ 50%	**Option 0**	**Option 1**	**Option 2**	**Option 3**
Vitamin D (µg/d)	25	4	115	6	172.5	**18.3**	**16.5**	**12.2**	**11.0**
Vitamin B6 (mg)	7	2.3	200	3.45	300	**2.4**	**1.8**	**1.6**	**1.2**
Iron[2] (mg)	14	10.6	200	15.9	300	**1.7**	**0**	**1.1**	**0**

[1] UL Vitamin D: EFSA-SCF value in 4-10 year-old children (SCF, 2002); UL vitamin B6: EFSA-SCF value in 4-6 year-old children (SCF, 2000)[6]
[2] No UL for iron by the SCF, value used: the one recommended by Denmark for 4-6 year-old children (DG Sanco presentation on 15/10/2008)
[3] Dietary intake data for 5-10 year-old children from the Ireland Food Consumption Survey 2003-2004, except for vitamin D, value for 3-10 year-old children in INCA2 2006-2007
[4] Values based on the Irish data; values provided for adults applied to children in kcal

Setting the MSL_s

The MSL_s (expressed in daily intake) are calculated using Richardson's model (2007) according to the following formula:

$MSL_s(vit)=UL-MHI*150\%$
$MSL_s(min)=UL-[(MHI*110\%)+IW]$

With **UL :** Tolerable upper intake level
MHI : Base level intake at the 97.5th percentile from food and fortified food
IW : Base level intake at the 97.5th percentile from water

The MSL_s are calculated separately for adults and children. This is because food supplements are either intended specifically for adults or for children.

[5] It is recommended to use the data for 3-10 year-old children, although the Irish survey focuses on 5-12 year-old children. The data used are therefore those concerning 5-10 year olds.
[6] When there are several ULs within the 3-10 year-old age group, the lowest value is selected.

Table 1: MSL_s calculations (in daily intake) for food supplements from Irish and French consumption data

	Nutrient	UL[1]	MHI[4]	IW	MSL_s (mg or µg/d)	MSL_s rounded values[5]
CHILDREN	Vitamin D (µg)	25	4.5	-	**18.3**	
	Vitamin B6 (mg)	7	2.5	-	**3.3**	
	Iron[3] (mg)	14	17.4		**0.0**	
ADULTS	Vitamin D (µg)	50	11.2	-	**33.2**	**35**
	Vitamin B6 (mg)	25	5.9	-	**16.2**	**20**
	Iron[2] (mg)	45	26.4	0.4	**15.6**	**18**

1 UL Vitamin D: EFSA-SCF values for adults and 4-10 year-old children (SCF, 2002); UL vitamin B6: EFSA-SCF values for adults and 4-6 year-old children (SCF, 2002)
2 UL Iron adults: no EFSA-SCF value; value used: US-IOM
3 UL Iron children: no EFSA-SCF value; value used: the one recommended by Denmark for 4-6 year-old children (DG Sanco presentation on 15/10/2008)
4 Adult values: 18-64 year-old men - Ireland Food Consumption Survey 1997-1999; Children values: 3-10 year olds INCA2 2006-2007 study (for child data from the INCA2 study, only breakfast cereals are considered to be fortified foods)
5 Rounded values put forward by Richardson (from calculations on Irish and UK data) in his note dated 17/09/2008

Scenarios to test with Afssa's tool on INCA2 data

Finally, two series of scenarios were tested.

- The first series applies to children: 4 scenarios combine the maximum levels calculated for food supplements on the basis of "children" data with those calculated for fortified foods according to the 4 options selected.
- The second series applies to adults: 4 scenarios combine the maximum levels calculated for food supplements on the basis of "adult" data with those calculated for fortified foods according to the 4 options selected.

Table 3: Summary for each nutrient of the maximum levels (for fortified foods and supplements) tested according to the different scenarios.

		Vitamin D (µg)	**Vitamin B6 (mg)**	**Iron (mg)**	
Scenario 9-0	MSL_f-option 0	18.3	2.4	1.7	Results to be compared with the ULs for 3-10 year-old children
	MSL_s children	18.3	3.3	0	
Scenario 9-1	MSL_f-option 1	16.5	1.8	0	
	MSL_s children	18.3	3.3	0	
Scenario 9-2	MSL_f-option 2	12.2	1.6	1.1	
	MSL_s children	18.3	3.3	0	
Scenario 9-3	MSL_f-option 3	11	1.2	0	
	MSL_s children	18.3	3.3	0	
Scenario 10-0	MSL_f-option 0	18.3	2.4	1.7	Results to be compared with the ULs for adults
	MSL_s adults	35	20	18	
Scenario 10-1	MSL_f-option 1	16.5	1.8	0	
	MSL_s adults	35	20	18	
Scenario 10-2	MSL_f-option 2	12.2	1.6	1.1	
	MSL_s adults	35	20	18	
Scenario 10-3	MSL_f-option 3	11	1.2	0	
	MSL_s adults	35	20	18	

For iron, the results obtained in options 1 and 3 are the same in children. Iron intake from base diet exceeds the tolerable upper intake level for this nutrient and the MSL_f and MSL_s calculated are therefore invalid. In adults, options 1 and 3 are also the same and result in only supplements, without food fortification, being tested as the MSL_f are invalid.

Results and comments

The table below presents the results obtained in adults and children for the 3 nutrients tested according to the 4 scenarios in the median and theoretically realistic hypothesis, whereby the proportion of fortified foods for a consumer would represent 25% of foods that are likely to be fortified, excluding all unprocessed foods in particular. Three other hypotheses were also tested: 0%, 10%, and 50%. The results of these other three hypotheses are presented in the annex.

Table 4: Percentile (Pn) of dietary intake beyond which the tolerable upper intake level may be exceeded: summary of the results for vitamins D and B6 and iron in adults and children according to the 4 scenarios in the event that the market share of fortified foods is 25%.

		Tolerable upper intake level	Option 0	Option 1	Option 2	Option 3
CHILDREN 3-10 years old	**Vitamin D**	25 µg	P5	P5	P10	P20
	Vitamin B6	7 mg	P20	P40	P50	P70
	Iron	14 mg	P40	P90	P60	P90
ADULTS	**Vitamin D**	50 µg	P30	P40	P50	P60
	Vitamin B6	25 mg	P80	P90	P90	P90
	Iron	45 mg	-	-	-	-

Reading example: 30% of 3-10 year-old children risk exceeding the tolerable upper intake level set in this age group for vitamin B6 (7mg) in the scenario corresponding to option 3 (calculating the MSLf with a safety factor of 50% applied to $(CI+SI)_{95}$ and to EFF_{95}). This proportion is 10% in adults for which the tolerable upper intake level is 25mg.

In 3-10 year old children, for the 3 nutrients considered, the simulations carried out with the maximum levels calculated according to the basic formula (option 0) result in very high risks of the tolerable upper intake levels being exceeded (for 60 to 95% of 3-10 year olds depending on the nutrient considered). Adjusting the parameters integrated in the model for setting MSL_f (options 1 to 3) upwards reduces the risk of the ULs being exceeded, although this still remains high in the case of vitamin D (80%). Regarding iron, the maximum levels obtained with options 1 and 3 (corresponding to a diet without any fortified foods or food supplements) already lead to the tolerable upper intake level being exceeded with base diet for 10% of 3-10 year-old children.

For adults, the risks of exceeding the tolerable upper intake levels are higher for vitamin D than for vitamin B6, irrespective of the option selected. Accordingly, even in option 3, which is the most protective, 40% of adults are likely to exceed the tolerable upper intake level for vitamin D. Concerning iron, there is no risk of the tolerable upper intake level used for these simulations being exceeded.

Choosing a fortified food market share of 50% (high hypothesis) instead of 25% leads to higher risks of the tolerable upper intake levels being exceeded for all the options in adults and children (annex).

In the event of fortification for only 10% of the foods that are likely to be fortified, the risks of exceeding the tolerable upper intake levels are lower in option 3 (the most protective). That said, in children, the tolerable upper intake level for vitamin D is exceeded for 30% of them (annex).

Conclusion

This study simulated the impact on dietary intakes of the simultaneous application of maximum vitamin and mineral levels in fortified foods and food supplements, calculated on the basis of Flynn's model (2008) and Richardson's model (2007).

The simulation method had already been assessed in Afssa's opinion dated 13 October 2008 (2007-SA-0315), which was presented to the DG SANCO "vitamins and minerals" working sub-group[7] in October and November 2008.

The options and parameters of this simulation largely come from the choices made by this group: choice of nutrients, consideration of children, definition of tolerable upper intake levels, options of possible change in intake in the future.

Both adults and children have been observed to exceed the tolerable upper intake levels for vitamins D and B6. For iron, this has only been observed for children, even in option 3 in Flynn's model (2008) where the lowest tolerable upper intake levels were defined. These exceeded tolerable upper intake levels are even observed in the low hypothesis where a person would consume 10% of fortified foods among fortifiable foods.

In Afssa's opinion of 13 October 2008, other models for setting maximum vitamin and mineral levels in fortified foods and food supplements had been tested for 10 nutrients for adults alone. Afssa had concluded that the two most protective scenarios for consumers were (i) the one combining the maximum fortification levels from the Danish model (DFVR) and the maximum levels for food supplements set by the French regulations, and (ii) the one combining the maximum levels for fortified foods and food supplements of the German model (Bfr), (except for vitamin B9 for which the levels put forward did not completely do away with the risk of the tolerable upper intake level being exceeded).

To conclude, the maximum levels of vitamins B6, D and iron in fortified foods (MSL_f) and food supplements (MSL_s), set independently according to the two models recommended by the European Commission, result in dietary intakes that may exceed the tolerable upper intake levels. As a result, irrespective of the options tested to date, the levels defined using these models are not protective enough for consumers.

[7] " Ad hoc working group on food supplements and on the addition of vitamins and minerals and of certain other substances to foods "

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Key words: vitamins, minerals, food supplements, fortified foods, simulations, models

Annexes. Percentile (Pn) of dietary intake beyond which the tolerable upper intake level may be exceeded: results for vitamins D and B6 and iron in adults and children according to the 4 scenarios for the marketing shares 0%, 10% and 50%.

Market share =0%

		UL	Option 0	Option 1	Option 2	Option 3
CHILDREN	**Vitamin D**	25µg	-	-	-	-
	Vitamin B6	7 mg	-	-	-	-
	Iron	14 mg	P90	P90	P90	P90
ADULTS	**Vitamin D**	50µg	-	-	-	-
	Vitamin B6	25 mg	-	-	-	-
	Iron	45 mg	-	-	-	-

Market share =10%

		UL	Option 0	Option 1	Option 2	Option 3
CHILDREN	**Vitamin D**	25µg	P50	P50	P70	P70
	Vitamin B6	7 mg	P80	P90	P90	P95
	Iron	14 mg	P70	P90	P80	P90
ADULTS	**Vitamin D**	50µg	P70	P80	P80	P90
	Vitamin B6	25 mg	P95	P95	P95	-
	Iron	45 mg	-	-	-	-

Market share =50%

		UL	Option 0	Option 1	Option 2	Option 3
CHILDREN	**Vitamin D**	25µg	<P2.5	<P2.5	<P2.5	<P2.5
	Vitamin B6	7 mg	<P2.5	P5	P5	P20
	Iron	14 mg	P10	P90	P30	P90
ADULTS	**Vitamin D**	50µg	P2.5	P5	P10	P10
	Vitamin B6	25 mg	P70	P80	P80	P80
	Iron	45 mg	P95	-	-	-