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# OPINION

## of the French Food Safety Agency (Afssa) on the estimation of vitamin and mineral levels for fortified foods and supplements: synopsis of a risk assessment tool based on vitamins and minerals intakes from the INCA 2 data, according to different scenarios

THE DIRECTOR GENERAL

On September 11th, 2007, the French Food Safety Agency (Afssa) received a request from the Directorate General for Health, Directorate General for Food and Directorate General for Competition, Consumer Affairs and Fraud Control to set maximum levels of vitamins and minerals for fortified foods and supplements in the context of Regulation (EC) No 1925/2006 on the addition of vitamins and minerals and certain other substances to foods.

### *Context*

European Regulation (EC) No 1925/2006 on the addition of vitamins and minerals to foods has been in force since July 1st, 2007[1]. It consists of establishing a harmonised Community basis on such practices in order to guarantee both consumer safety and free movement of goods. This regulation defines the objectives, scope and conditions for adding vitamins and minerals and gives a list of substances that may be added to foods. The main difficulty is setting maximum levels of nutrient for fortification (article 6 of the regulation) which take into account the tolerable upper intake levels (UTL), the vitamins and minerals intakes from other food sources and the population reference intakes.To the end, proposals from the Commission can be submitted by 19 January 2009.

Afssa has already proposed a probabilistic risk assessment approach for testing the safety of maximum levels of vitamins and minerals for fortification (Afssa, 2001). This work has been used as a validation tool by Flynn et al. (2003). Besides, a public health approach has been suggested to evaluate relevance of vitamins and minerals usual food fortification. Moreover, foods contributing the most to vitamins and minerals needs has been defined (Afssa, 2004; Touvier et al., 2006).

In this context, Afssa has been requested to assess the scientific information available for determining maximum levels of vitamins and minerals in foods. Particularly, Agency's opinion on the mathematical models proposed for setting maximum levels is expected. Different models have been developed to estimate and propose maximum levels of vitamins and minerals in foods, as well as in food supplements (FSs) (Flynn et al., 2003; Rasmussen et al., Richardson, 2007; Domke, 2004a; Domke, 2004b). Discussions in this regard and on methodological development were held in the "Fortification of common foods with vitamins and minerals" working group of the "Human Nutrition" Afssa Scientific Panel, which validated those conclusions by correspondence on 6 October 2008.

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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 and minerals and of certain other substances to foods. JO L 404 of 30.12.2006 :26.38.

### *Objectives*

The simulation work involves **simultaneously testing, on the basis of recent French consumption data** (national INCA2[2] survey 2006-2007), **the maximum levels of vitamins and minerals for fortification** in certain foods **and the maximum levels of vitamins and minerals for food supplements** (levels estimated by various published European models). This test is based on a probabilistic simulation developed by Afssa and derived from the approach for fortified foods only, without taking into account of the consumption of food supplements (Afssa, 2001). The different series of levels obtained from the different models lead to several scenarios.

For each nutrient, the distributions of adults vitamin and mineral intakes (via usual foods, fortified foods and food supplements) are studied according to different scenarios and then compared to existing UTL.
The approach adopted is based on protective assumptions since it systematically takes into account the maximum amounts consumed foods that are likely to be fortified and for food supplements.

### *Population and methods*

Data used: the INCA2 2006-2007 consumption survey and the CIQUAL[3] food composition table 2008
The French National Dietary Survey INCA2 was carried out between 2006 and 2007. In order to take into account dietary changes through the seasons, the survey was carried out over more than twelve months. It involved 4,079 participants aged between 3 and 79 years old (including 2,624 adults aged 18-79) living in mainland France. The participants were selected using a multistage cluster sampling technique stratified by region and size of urban area. The random selection of households was made from the 1999 national 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 underestimate their intakes compared to their needs) were excluded from the analyses. The sample of non-under-reporting adults includes 1,918 people.

The INCA2 survey gathers all of the participants dietary intakes, using a 7-day open-ended food record (food and drinks consumed at each main meal and between meals). Portion size are estimated from a photographic booklet (SU.VI.MAX, 1994). In the end, the survey will also accurately identify fortified foods (thanks to the names and brands of products collected and an ad hoc nutritional composition table). During the week in which they filled in the food diary, the participants also filled in a food supplement diary, if they consumed such products.

The foods consumed in the INCA 2 survey were matched with foods described in the French food composition databank CIQUAL, using a food list drawn up specifically for INCA 2. By codifying the foods gathered in the diaries according to this list, each food could be linked to a nutritional composition vector containing 12 vitamins and 11 minerals.

Methodology: calculating nutritional intakes by simulations

Nutritional intakes in the population have to take into account 3 components : conventional or common foods, fortified foods and food supplements.

- The estimation of nutritional intakes by common foods does not pose any particular problems: it is obtained by linking consumption data with the CIQUAL composition table.
- Since we have no precise data on fortified foods, the method developed to estimate nutritional intakes via this source is as follows: first of all, a list of foods consumed in the INCA 2 survey that could be fortified is drawn up (non-processed foods such as eggs,

[2] Second Individual and National Enquiry on Food Consumption.
[3] Food Quality Information Centre.

meat and poultry, offal, fruit, vegetables, water and alcoholic drinks are fully excluded from this list, which contains 55% of the foods on the INCA 2 list). Then, for each individual, foods are randomly selected from the list of foods that could be fortified based on a theoretically defined market share of the fortifiable foods. Market shares of 10% and 25% appear to be rational and realistic choices given existing information on fortification and 50% represents a high assumption for the share of fortified foods that does not seem possible to exceed. The maximum authorised level of fortification is applied to these random selected foods. According to this method, each participant in the INCA 2 survey would therefore consume, in theory, some fortified foods and others non-fortified throughout the week. For "fortified" foods, the nutritional intake is calculated using the maximum safe level (MSL) for fortified food (different depending on the model tested).

- Intakes through food supplements only concern consumers of such products. The vitamin and mineral concentrations in food supplements are defined by the maximum daily amount (different depending on the model tested). Intakes from food supplements are added to intakes from common foods and fortified foods.

The method therefore involves calculating the overall nutritional intakes obtained from the three possible sources of intake by analysing detailed, nationally representative, data of food supplements and food consumption, and by integrating the maximum limits obtained by the different models for fortified foods and food supplements. The main assumptions are about the market shares of fortified foods for categories of fortifiable foods.

For fortified foods, three series of maximum values have been obtained from the ILSI model[4] (Flynn et al., 2003), the DFVR model[5] (Rasmussen et al., 2006) and the Bfr model[6] (Domke, 2004a; Domke, 2004b), to which a fourth series has been added (assumption of fortification up to 15% of the RDIs for 100 kcal of food, which is a minimum assumption from a regulatory point of view). For food supplements, two series of values obtained from the ERNA/EPHM[7] (ERNA/EHPM, 2004) and Bfr (maximum daily intake) models exist, as well as French regulatory values from the regulation of May 9th, 2006[8].

Twelve combinations are possible between the 4 series of maximum values set for fortified foods and the 3 series of maximum daily intakes recommended for food supplements. To illustrate the results obtained by the method, 5 scenarios were selected to begin with, summarised in the table below (*Table 1*): the model presented by the Bfr, setting maximum levels for both fortified foods and food supplements, is a scenario in itself (scenario 4); the combination of the ILSI's fortification levels and the ERNA/EPHM's levels in food supplements is a scenario presenting high levels in both cases (scenario 1); lastly, with no data on food supplements, it was agreed to combine the other 3 models setting fortification levels with the values set by the French regulations in 2006 for food supplements (scenarios 2, 3 and 5). Other scenarios may be tested at a later date.

Moreover, for each of the 5 scenarios, assumptions must be made on the market share of fortified foods among those that are likely to be so; 4 market shares will be tested: 0%, 10%, 25% and 50%. This fairly wide range of market shares integrates certain consumers behaviour tending to favour systematically fortified foods.

Once the overall nutritional intakes have been estimated, they are compared to the existing UTL.

[4] International Life Sciences Institute.
[5] Danish Institute for Food and Veterinary Research.
[6] Federal Institute for Risk Assessment.
[7] European Responsible Nutrition Alliance - European Federation of Associations of Health Product Manufacturers.
[8] Order of 9 May 2006 on nutrients that can be used to manufacture food supplements. JO of 28 May 2006.

*Table 1:* **S***elected Scenarios combining maximum values for fortified foods and food supplements*

| **Supplements** / **Fortification** | ERNA/EHPM | BfR | French regulations – order of 09/05/06 |
|---|---|---|---|
| ILSI | **Scenario 1** | | **Scenario 2** |
| DFVR | | | **Scenario 3** |
| BfR | | **Scenario 4** | |
| 15% of RDIs | | | **Scenario 5** |

***Results and discussion:***

Among the micronutrients studied, 5 vitamins (retinol, vitamin D, vitamin E, vitamin B6 and vitamin B9) and 5 minerals (calcium, copper, iodine, selenium and zinc) have a UTL defined by the Scientific Committee on Food[9] (SCF, 2000a, SCF, 2000c, SCF, 2002b, SCF, 2000b, SCF, 2002a, SCF, 2002d, SCF, 2003b, SCF, 2003a, SCF, 2002c, SCF, 2003c). For these 10 nutrients, it is possible to find out the adult population proportion of the at risk of exceeding those UTL, according to the different scenarios and for a given market share. Afssa insists that these simulations do not refer to specific populations. Nutrient specific warning points for these populations may be proposed, on a case-by-case basis in the final opinion concluding this request.

The table below (*Table 2*) summarises the results obtained for the 10 nutrients according to the 5 scenarios, in the event that fortified foods would account for 25% of fortifiable foods. This median, realistic assumption corresponds to a consumer for whom 25% of the foods that could be fortified are effectively fortified. Three other assumptions were also tested: 0%, 10%, and 50%.

*Table 2: Summary of scenarios in the event that the market share of fortified foods = 25%: percentile beyond which the UTL may be exceeded*

| | | **UTL** | **Scenario 1** | **Scenario 2** | **Scenario 3** | **Scenario 4** | **Scenario 5** |
|---|---|---|---|---|---|---|---|
| **Vitamins** | **Retinol** | 3000 µg | P95 | P95 | P95 | P95 | P90 |
| | **Vitamin D** | 50 µg | P70 | P80 | - | - | - |
| | **Vitamin E** | 300 mg | P10 | P10 | - | - | - |
| | **Vitamin B6** | 25 mg | P60 | P70 | - | - | - |
| | **Vitamin B9** | 1000 µg | P70 | P80 | - | P60 | - |
| **Minerals** | **Calcium** | 2500 mg | P90 | - | - | - | P95 |
| | **Copper** | 5 mg | P20 | P20 | - | - | P90 |
| | **Iodine** | 600 µg | P40 | P40 | - | - | - |
| | **Selenium** | 300 µg | P70 | P80 | - | - | - |
| | **Zinc** | 25 mg | P40 | P40 | P90 | - | P70 |

[9] Quoted in EFSA (2006) Tolerable upper intake levels for vitamins and minerals. Parme.

We observe that the first two scenarios (taking into account of ILSI's maximum values for fortified foods) are those for which the UTL are exceeded the quickest, at variable percentile levels depending on the nutrient. Scenarios 3 (maximum limits in fortified foods set by the DFVR model and maximum amounts for supplements by the French regulation) and 4 (maximum limits set by Bfr for fortified foods and supplements) are those which incur the least risk of exceeding the UTL for all 10 nutrients. Scenario 5 has fairly similar results to scenarios 3 and 4.

To be more exact, in terms of vitamins, with the scenarios 1 and 2 the UTL may be exceeded by 20 to 30% of the population for vitamin D, by 90% of the population for vitamin E, by 30 to 40% of the population for vitamin B6 and by 20 to 30% of the population for vitamin B9 intakes.
In terms of minerals, for the same scenarios, the UTL set for copper intakes may be exceeded by 80% of the population, for iodine intakes by 60% of the population, for selenium intakes by 20 to 30% of the population and for zinc intakes by 60% of the population.
Opting for a 50% market share instead of 25% leads to the same classification within the different scenarios, depending on their more or less conservative options.

A new model based on the ILSI model has recently[10] been presented by the CIAA[11] for calculating maximum limits, by now integrating intakes by consuming food supplements (which was not the case in the initial model). It will be entirely possible to test new series of maximum limits with the simulation tool presented here, as soon as these series will be available (as a 6th scenario). For its part, Afssa will not be able to provide data on the consumption of fortified foods (unpublished data) to use in this model within the near future. However, even if this data were available, it would not be realistic in the context of European deliberations to calculate maximum limits by using data from a country like France, where current consumption of fortified foods is low, as this would result in maximum limits that are too high. In order to calculate maximum limits, it is necessary to use data from countries that have already widely promoted fortification.

***Conclusion***

The discussions conducted at European level deal with a new and complex reality. The fortification conditions laid down by Regulation (EC) No 1925/2006 may result in a very wide range of foods being fortified, which may add to the intake of vitamins and minerals from common foods and food supplements. Afssa believes that a rational risk assessment approach is essential and that, given the often sparse nature of available data, data from countries which already have a significant share of fortified foods should be considered. This approach is essential to protect all consumers from the risk of exceeding the UTL (general population and specific populations).

The simulation work conducted by Afssa gives a clearer insight into this new situation. These simulations do not concern specific populations. Afssa assessed the maximum vitamin and mineral levels in foods and food supplements from different models developed by other institutes.
Two scenarios are the most protective in public health terms. One comprises maximum fortification limits from the DFVR model and maximum levels in food supplements set by the French regulation; the other combines the maximum fortification levels and maximum amounts of food supplements from the Bfr model. The maximum level for fortification set by the Bfr for vitamin B9 do not, entirely, eliminate the risk of exceeding the UTL.

This risk assessment approach by simulating vitamin and mineral intakes may subsequently be applied to any proposal of maximum vitamin and mineral fortification limits. Given the deviations observed between the various models tested to date, Afssa recommends paying particular attention to the validation of available models in European discussions, so as to ensure that they protect consumer health sufficiently.

[10] This new model was presented on 27 June 2008 during the meeting of the Expert Group on Food Supplements and the Addition of Vitamins, Minerals and Other Substances to Foods of the European Commission.

[11] Confederation of the Food and Drink Industries of the EU.

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