6.

BACKGROUND AND REGULATION ON ZINC FORTIFICATION LEVELS

Sofia V. Amarra, Ph.D.
International Life Science Institute

ABSTRACT

WHO suggested the following preliminary considerations when planning micronutrient fortification programs and establishing appropriate levels of fortification: 1) Health authorities looking to initiate a micronutrient fortification program should not do so without first collecting food intake data, supported by ancillary information such as biochemical data on nutritional status; 2) Food intake information is necessary for the following reasons: to justify the fortification program; to make an informed choice about the types and amounts of specific nutrients to include; to understand which foods would make suitable vehicles for fortification. Finally, it should be kept in mind that the goal of zinc fortification is to ensure adequate intakes of zinc by the targeted individuals, without imposing a risk of excessive intake on the rest of the population.

Keywords : fortification, food

A. BACKGROUND

In February 2000, the Asian Development Bank convened the Manila Forum 2000 to accelerate efforts to fortify common basic foods in Asia and the Pacific with essential micronutrients. During subsequent workshops in 2001 and 2002, consensus statements were signed by eight countries on wheat flour and cooking oil fortification.

The workshops set out a vision that all flour used in the preparation of staple foods such as leavened and unleavened breads, noodles, pastas, biscuits and other flour products, and consumed by at-risk populations in the region, should be fortified (1).

The participants from Indonesia, Thailand, Vietnam, India and China agreed on regional guidelines for flour fortification. The recommended fortification package for flour was 30 ppm zinc (as zinc oxide) for both white and brown flours, and included iron, folic acid, riboflavin and thiamin (Table 6.1).

Table 6.1 Basic Recommended Fortification Package for Flour

Nutrient	White flour (ppm)	Brown flour (ppm)
Folic acid	2.0	2.0
Iron	60.0	60.0
Riboflavin	4.0	
Thiamin	2.5	
Zinc	30.0	30.0

Source: Asian Development Bank. Food Fortification in Asia: Improving Health and Building Economies. Nutrition and Development Series. June 2004.

At present, Indonesia is the only Asian country that undertakes mandatory zinc fortification (2). Other developing countries with mandatory zinc fortification laws are shown in Table 6.2.

B. GOAL OF FORTIFICATION

The desired outcome of any fortification program is to improve a population's nutritional status by improving nutrient intake. In the *Guidelines on Food Fortification with Micronutrients* (3), the dietary goal of fortification is formally defined as: "*to provide most (97.5%)*

of individuals in the population group(s) at greatest risk of deficiency with an adequate intake of specific micronutrients, without causing a risk of excessive intakes in this or other groups". Hence, fortification should aim to shift the distribution of usual nutrient intakes of a target population upwards so that:

Table 6.2 Countries with Zinc Fortification Regulations.

Country	Mandate	Product	Mandated level (mg/kg)
Mexico	Gentlemen's agreement between industry and government 1998	Wheat flour	16.0-26.0
		Corn flour	20.0
Malawi	MS34: 2002 (draft)	Maize flour	7.5
South Africa	Act 54, 1972, April 2003	Maize meal - Super - Special - Sifted - Unsifted	18.90 22.55 26.60 30.20
		Wheat flour - White - Brown	20.70 26.63
		Wheat bread - White - Brown	15.30 20.07
Zambia	Government of Zambia Statutory Instrument No. 90 of 2001	Enriched maize meal	12.0
Indonesia	MOH Decree No. 632/MENKES/SK/ VI/1998 National Standard No. 153/MPP/Kep/5/2001jo 323/MPP/Kep/11/2001	Enriched wheat flour	30.0

Source: Nutriview special issue: Mandatory food enrichment. 2003.

- only a small proportion of the population is at risk of having an *inadequate* intake (i.e., intake defined as being below the Estimated Average Requirement (EAR)); and
- those who consume larger amounts of the food vehicles will not be at risk of an *excessive* intake (i.e., intake defined as being above the Tolerable Upper Intake Level (UL)).

In the case of zinc, the proper level of fortification is that which would "increase the intake of zinc by the targeted individuals, without imposing a risk of excessive intake on the rest of the population".

Table 6.3 shows the estimated risk of zinc deficiency in Southeast Asian countries based on various indicators. Thailand and Malaysia are classified as medium-risk. The rest of the countries are classified as high-risk for zinc deficiency. The cut-off point for inadequate intake beyond which fortification is recommended is 25% of the population at risk (4). The data show that, except for Malaysia, all the other countries need to consider some degree of fortification.

Table 6.3 Estimated Risk of Zinc Deficiency by Country

Country	Zinc (mg/ d)	Pytate (mg/ d)	Pytate : Zn (molar ratio)	% of energy from animal source food	Zinc Density (mg/ 1000 kcal)	Estimated zinc absorption (%)	Estimated % of population at risk, IZiNCG	Prevalence of stunting	Risk category
Cambodia	7.1	1,722	24.0	8.0	3.7	25.5	43.6	53.3	High
ndonesia	10.0	2,859	28.4	4.4	3.5	20.9	34.4	42.4	High
Laos	7.9	2.031	25.6	6.6	3.6	24.0	35.7	47.3	High
Malaysia	10.3	1,534	14.7	20.2	3.6	24.1	14.1	26.6	Medium
Myanmar	9.3	2,612	27.9	3.9	3.4	21.7	34.6	41.6	High
Filipina	7.8	1,344	17.1	14.0	3.4	26.5	31.9	32.7	High
Thailand	8.1	1,610	19.7	12.7	3.4	25.2	41.6	16.0	Medium
Vietnam	9.2	2,008	21.6	9.5	3.7	23.2	27.8	38.7	High

Source: IZiNCG. 2004.

C. ESTIMATED AVERAGE REQUIREMENT (EAR) AND TOLERABLE UPPER INTAKE LEVEL (UL)

The EAR and UL are among the reference values that comprise the Dietary Reference Intakes (DRIs) established by the U.S. Food and Nutrition Board, Institute of Medicine (5). These reference values specify levels of adequacy for each nutrient in specific population groups.

Estimated Average Requirement

A requirement is defined as the lowest continuing intake level of a nutrient that, for a specific indicator of adequacy, will maintain a defined level of nutriture in an individual. The Estimated Average Requirement (EAR) for a micronutrient is defined as the average daily intake that is estimated to meet the requirements of half of the healthy individuals in a particular life stage and gender subgroup. The EAR is usually the lowest intake level that will sustain physiologic function in an individual, as determined by clinical trials. As illustrated in Figure 6.1, EAR is the point where the risk of inadequacy of intake for a nutrient is 0.5. The Recommended Dietary Allowance (RDA) is derived from EAR values. The RDA is an estimate of the minimum daily average intake level that meets the requirements of 97 to 98 percent of all healthy individuals in a population, hence the risk of inadequacy is lower (around 0.2 to 0.3).

Tolerable Upper Intake Level

On the other hand, the Tolerable Upper Intake Level (UL) is the highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase. The UL is considered the most appropriate reference value for determining whether or not the micronutrient intakes of population subgroups are safe (3). At intakes between the RDA and UL, the risk of inadequacy and of excess are both estimated to be close to zero. Ideally, fortification programs should seek to maintain population intakes of nutrients within these levels.

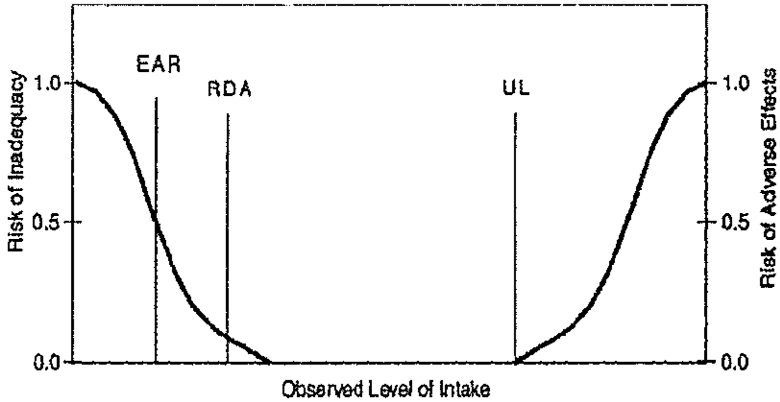

Figure 6.1. Dietary Reference Intakes - EAR and UL.

Source: National Academy of Sciences. 2002. Dietary Reference Intakes for Energy, Carbohydrates, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids (Macronutrients).

D. PREVIOUS STRATEGIES TO DETERMINE MICRONUTRIENT FORTIFICATION LEVELS

Strategies that have been used to determine zinc fortification levels are the following (3):

1. Based on levels used elsewhere - this has been done mostly in situations where food intake data are not available, yet there was a strong desire to move ahead with fortification;

2. Based on the average amount of food consumed by individuals in the target population - fortification is planned to supply a specific fraction of the recommended dietary intake, and levels were based on the average amount of food consumed by individuals in the target population (eg., the amount needed to supply 1/3 or 30% of the RDA).

The disadvantages of these strategies are that fortification levels used in one location may be inappropriate in another location due to differences in environmental conditions, dietary patterns, and the food matrix. Furthermore, the impact of current levels of fortification on nutrient intake and nutritional status have not been evaluated extensively. Hence, these levels cannot be recommended universally (3).

WHO (3) emphasized that unless food and nutrient intake data are used as the basis of program design and evaluation, it cannot be known whether a) those at greatest risk of deficiency in a specific nutrient (and who have the lowest pre-fortification intakes) will consume enough of the fortified food to improve their nutrient intake significantly, and b) whether those who have the highest pre-fortification intakes will be at risk of excessive intakes after fortification.

E. ESTIMATED AVERAGE REQUIREMENT (EAR) CUT-POINT METHOD TO DETERMINE MICRONUTRIENT FORTIFICATION LEVELS

A recommended strategy to determine appropriate micronutrient fortification levels is the Estimated Average Requirement (EAR) cut-point method developed by WHO (3). The method determines micronutrient levels to be added to a specific food based on the distribution of intakes in specific population groups, and hence, based on each country's specific needs. Estimates are based on food consumption data, and the amount of fortificant is determined that will bring about an upward shift in the distribution of usual intakes. The goals of the EAR cut-point method are to ensure the safety of consumers by making sure that those who eat fortified foods do not exceed the tolerable upper level, and to shift the usual distribution of intakes upwards so that only a small proportion (2-3%) of the population is at risk of having an inadequate intake (Figure 6.2).

An example of a usual intake distribution in which 2.5% of the group have intakes below the EAR (the recommended approach)

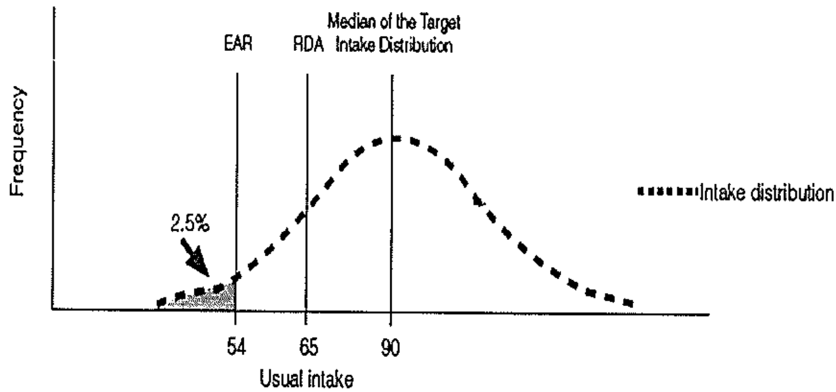

Figure 6.2 An example of a Usual Intake Distribution

The EAR cut-point method consists of the following steps:

1. Examine the prevalence of inadequate intakes of each nutrient in specific population groups, based on the distribution of usual intakes;
2. Identify which population groups have the highest prevalence of inadequate intakes;

3. Estimate the usual consumption of the chosen food vehicle by the target group;
4. Calculate the reduction in the prevalence of inadequate intakes (i.e., what proportion of this group will have intakes below the EAR) and the risk of excessive intakes (i.e., what proportion will have intakes above the UL) that would be expected to occur at different levels of fortification.

After examining the results of the simulation described above, the most appropriate level of fortification of a specific food vehicle can be determined.

Hence, to estimate zinc fortification levels, it would be necessary to estimate the following :

- The prevalence of inadequate zinc intakes based on the *distribution of usual intakes* of zinc from all foods by different population subgroups; and
- The amount of the food vehicle (cereal staples) being consumed by these different segments of the population.

The required data can be obtained from national dietary surveys.

Dietary survey design to estimate the distribution of usual zinc intakes. In order to estimate the distribution of usual zinc intakes, the design of dietary surveys should include the following aspects (4) :

1. Plan to include at least two non-consecutive days of intake data for all individuals in the sample, with at least 200 individuals per population subgroup;
2. Use quantitative measures of food intake (weighed food records or 24-hour recalls);
3. Calculate dietary intakes of zinc using local food composition tables, if available;

4. Correct the resulting distribution of zinc intakes for intra-individual variation (using statistical adjustment methods) to determine "usual" intake.

Determination of usual dietary intake

What do we mean by "usual" dietary intake? In layman's terms, usual means *habitual* or *customary*. In statistical terms, as used by the U.S. National Center for Health Statistics (NCHS), usual means the "long-run daily average", where "long-run" is effectively a year (6). Usual intakes should form the basis of decisions about which micronutrients to add to which foods, and to predict the probable impact of potential fortification interventions (3).

Sources of error in dietary intake data. There are two major sources of error in dietary data: between-individual (or inter-individual) variation and within-individual (or intra-individual) variation. When analyzing dietary data, only the between-person variation is of interest. The within-person variation should be removed, as the variation of "usual" intakes is of interest (6). One way to reduce errors due to within-person variation is to increase the number of days of data collection. A study among Malawian women estimated that, in order to obtain an accurate measurement of zinc intake that is within 20% of the true mean 95% of the time, at least 11 days of food recall measurements are needed per subject (4). The large number of days necessary would make any dietary survey extremely expensive.

Statistical adjustment to estimate usual intake. A method for statistical adjustment to estimate usual nutrient intake has been developed by USDA and Iowa State University (ISU) which makes use of data from as little as two independent or non-consecutive days of 24-hour recalls or food records. Statistical transformations remove within-person or day-to-day variability in nutrient intake, which accounts for a large portion of error, and normalize skewness in data, making the distribution symmetrical and more robust for analysis. The method is available in a software package called SIDE (Software for Intake Distribution Estimation) at ISU. Table 6.4 outlines the steps in the method (6).

Table 6.4. Outline of Steps in The Method Developed At Iowa State University for Estimating Usual Nutrient Intake Distributions

1. Initial data adjusments
   - A. Shift of data away from zero
   - B. Initial power (or log) transformation
   - C. Regretion adjusment for nuisance effect
   - D. Homogenization of subsequent intake days to match distribution of first day
   - E. Creation of equal-weight sample
   - F. Back transformation to original scale
2. Measurement error model
   - A. Full transformation to normal scale (power transformation followed by grafted polynomial
   - B. Estimation of within and between individual variances
   - C. Test for heterogeneity of within individual variances and consequent adjusments of variances component estimates
   - D. Estimation of usual intake distribution in normal scale
   - E. Bias adjusted back transformation to original scale of a representative sample from the intake distribution
3. Estimation of usual intake distribution in original scale

Source: Guenther, et.al. 1997. Development of an approach for estimating usual nutrient intake distributions at the population level. J Nutr. 127:1106-1112.

If some form of adjustment for variability is not made, the prevalence of inadequacies could be incorrectly estimated because the distribution does not reflect the usual intakes of the individuals in the group. Adjusting for day-to-day variation narrows the intake distribution, with fewer individuals below the EAR and above the UL. Once the distribution of usual intakes has been established, the data can now be used to determine the prevalence of inadequate intakes of different subgroups (i.e., intakes below the EAR), and to identify the intake of potential food vehicles by these subgroups.

Table 6.5 illustrates the resulting prevalence of adequate intakes for nutrients obtained from the distribution of usual intakes in a sample population, after adjustment of mean one-day and three-day intake data (6).

The next step in the EAR cut-point method is to simulate the effect of adding different levels of each micronutrient to specific foods on the prevalence of inadequate and excessive intakes. The following steps are taken:

- Calculate the total amount of a nutrient that will be consumed by different population subgroups after fortification of each potential food vehicle;
- From the information above, calculate the reduction in the prevalence of inadequate intakes and the risk of excessive intakes that would be expected to occur at different levels of fortification.

Table 6.5. Comparison of The Prevalence of Adequate Intakes based on 1-D, 3-D, And Usual Intake Distributions.

Estimated proportion of the population recommende intake levels for selected nutrients on 1 d, on 3 d and the estimated proportion whose usual intake meets the recommendation in populations of men and women 20 y and older, 1989-91

Population group	Nutrient	Recommended level	Proportion meeting recommended level		
			One day	Three day	Usual[1]
Men	Fat [2]	30% of energy	0.28	0.21	0.14
	Folate	200 μg/d	0.59	0.65	0.76
	Vitamin A	1000 μg RE/d	0.37	0.40	0.49
Women [3]	Fat [2]	30% of energy	0.33	0.28	0.22
	Folate	180 μg/d	0.49	0.53	0.61
	Vitamin A	800 μg RE/d	0.36	0.42	0.49

[1] Adjusted for day of week, month of year, and sequence of surveyed days
[2] Individual who fasted on one the three reported intake days excluded
[3] Pregnant and lactating women excluded

Source : U.S. Departement of Agriculture, Continuing Survey of Foof Intakes by Individuals (1996) (3,38$_1$ men; 462$_1$ women In Guenther, et.al. 1997. Development of an approach for estimating usual nutrient intake distributions at the population level. J Nutr. 127:1106-1112.

Table 6.6 illustrates how the EAR cut-point method was applied to a hypothetical country to determine the appropriate vitamin A fortification level. Prior to fortification, 65% of adult women (the target group) were found to have inadequate intakes of vitamin A, and the proportion of women who were at risk of exceeding the tolerable upper level (UL) was negligible. Simulating the effects of vitamin A fortification at 3 mg/kg and at 5 mg/kg gave the following results:

- At a fortification level of 3 mg/kg, the prevalence of inadequate intakes fell from 65% to 15%, and the proportion of women at risk of excessive intakes was around 2%;
- At a fortification level of 5 mg/kg, the prevalence of inadequate intakes decreased further to 8%, but the proportion at risk of excessive intakes rose to 6%.

Given this scenario, WHO (3) suggested that it would be better to select the 3 mg/kg fortification level and use another delivery mechanism such as supplementation to meet the shortfall in vitamin A intake in the 15% of women whose intakes remain inadequate.

Table 6.6 Example Using EAR Cut-Point Method to Determine Vitamin A Fortification Level in A Population

Predicting the effect on the intake distributions of adult women of fortifying wheat flour different level of vitamin A

Percentile	Distribution of usual wheat consumption (g/day)	Distribution of vitamin A intake from all sources (µg/day)			Vitamin A intake in relation to the EAR and the UL		
		Before fortification	After fortification at a level of 3 mg/kg	After fortification at a level of 5 mg/kg	Before fortification	After fortification at a level of 3 mg/kg	After fortification at a level of 5 mg/kg
Group at risk deficiency							
5	30	120	210	270	-	-	-
10	45	160	295	385	-	-	.
25	120	200	560	800	-	.	.
50	180	240	780	1140	-	.	.
Group at risk of excess							
75	240	6000	1320	1800	.	.	.
90	300	1000	1900	2500	.	.	.
95	360	1250	2330	3050	.	.	-
Resulting prevalence of inadequacy and risk of toxicity							
Proportion of women with intakes below the EAR (%)					65	15	8
Proportion of women with intakes above the UL (%)					0	2	6

Intake is below the EAR : Intake is above the EAR but below the UL; intake above the UL for vitamin A and EAR of 357 µg/day is assumed. This is derived from the FAO/WHO RNI for this vitamin 500 µg/day to which a conversion factor of 1.4 has been applied (see Annex C). The UL is 3000 µg/day. If β Caroten were used rather than preformed vitamin A (retinol) there would be no.

Source : WHO. 2006. Guidelines on food fortification with micronutrients.

F. SUMMARY

WHO (3) suggested the following preliminary considerations when planning micronutrient fortification programs and establishing appropriate levels of fortification:

1. Health authorities looking to initiate a micronutrient fortification program should not do so without first collecting food intake data, supported by ancillary information such as biochemical data on nutritional status;
2. Food intake information is necessary for the following reasons:
   - To justify the fortification program;
   - To make an informed choice about the types and amounts of specific nutrients to include;
   - To understand which foods would make suitable vehicles for fortification.

Finally, it should be kept in mind that the goal of zinc fortification is to ensure adequate intakes of zinc by the targeted individuals, without imposing a risk of excessive intake on the rest of the population.

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