An Updated Model for Establishing Salt Iodization Standards

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Introduction

In 1996, WHO/UNICEF/ICCIDD convened a technical consultation to discuss recommended iodine levels in salt[1]. It was proposed that at the point of production, the iodine content in salt should be within the range of **20-40 mg I/kg** if the adult daily consumption of salt was 10 g/d. This recommendation replaced those of 1993 that considered salt intakes of 5 and 10 g/d, as well as weather conditions and size of packaging[2]. **Table 1** shows the 1993 recommended levels at the point of production.

Table 1.
Recommended average levels of iodine in salt (mg I/kg salt) at the point of production by WHO/UNICEF/ICCIDD[¶]

Climate	Salt consumption = 10 g/d		Salt consumption = 5 g/d	
	Bulk (sacks)	**Retail (Plastic bags)**	**Bulk (sacks)**	**Retail (Plastic bags)**
Warm moist	50	40	100	80
Cool dry	40	30	80	60

[¶] Levels were also suggested for salt at retail sale, which were 66% to 75% of the values at point of production after considering losses during transportation and storage.
Source: WHO/UNICEF/ICCIDD. *Indicators for assessing iodine deficiency disorders and their control programmes.* Document WHO/Nut/93.1. 1993.

Although the 1996 recommendation reduced the risk of excessive iodine intakes because it specified lower iodine levels, and it was simpler than the recommendations of 1993, it lacked of details for modifications to different salt consumption patterns, as well as for introducing needed adjustments because of different iodine stability conditions due to climate, packaging type, and qualities of salt. The 1996 recommendations made easier the implementation of salt iodization programs, but they have created difficulties in the enforcement practices and, which is worse, have introduced unreasonable criteria to qualify the epidemiological success of the salt iodization programs. Thus in 2007, in the most recent edition of the WHO/UNICEF/ICCDD[3] "Assessment of iodine deficiency disorders and monitoring their elimination", it has been stated that "the percentage of food-grade salt with iodine content of between 20 and 40 ppm[a] in a representative sample of <u>households</u> must be <u>equal to or greater than 90%</u> as determined by RTK and by titration in a sub-sample"; this is an inappropriate use of the recommendation for the iodine content in salt at the point of production because it is also being applied to households but without considering the many factors that affect determination of iodine levels in salt from factories to homes.

The recommendations for enacting salt iodization standards have evolved during the years based on the accumulated experience and information in the implementation of the salt iodization programs worldwide. Now, after 15 years of additional work since 1996, it is time to make a critical review of the concepts, principles, and calculations that support these recommendations, as well as the criteria to qualify the epidemiological performance of the salt iodization programs.

[a] Part per million (ppm) is equivalent to mg/kg.

This article is going to cover four main topics:

- Iodine provision at households to satisfy the nutritional needs;
- Estimation of the average iodine content of salt at households;
- Specifications of the iodine content to use in salt standards; and
- Important methodological factors to incorporate in salt iodization standards.

In the preface of the WHO/UNICEF/ICCIDD report of 1993 appeared the following statement: "The assessment of IDD is constantly evolving and so also is the science of indicators of IDD. This report will certainly not be the last word on the subject". The same assertion is also applicable here. A few years from now, new approaches and procedures might be introduced based on future lessons learned from the implementation of salt iodization programs in the countries.

Iodine Provision at Households to Satisfy the Biological Needs

The WHO/UNICEF/ICCIDD recommendation is aimed to provide 150 µg/d of iodine to adults in addition to the iodine supply by the diet. The 150 µg I/d is the Recommended Nutrient Intake (RNI)[b] for this age group, which is calculated by adding two standards deviation to the Estimated Average Requirement (EAR)[c] of 95 µg I/d[4]. This position of selecting the RNI value of iodine for adults as the based for the salt iodization programs is supported by the following assumptions:

1. The RNI satisfies the iodine intakes of almost all individuals of the population(97.5 %; i.e. mean of the population requirement plus two standard deviations);
2. Other age groups would receive sufficient iodine based on the fact the RNI value of adults is the largest if requirements of pregnancy and lactation are not included; and
3. Supply of iodine by the diet is negligible.

In practice, the value of 150 µg/d of iodine has been used as a cut-off point, i.e. most intakes should be above 150 µg I/d. As consequence most adult individuals of the population are targeted to have iodine intakes much larger than their daily requirements, based on the fact that half of them are satisfied with 95 µg I/d or less (the EAR value). If the cut-off point is switched from RNI to EAR, most individuals of the population are still going to receive larger than required iodine intakes, as shown in **Figure 1**. A small proportion of individuals, equivalent to the intersection between the curve of risk of inadequacy and the predicted intake curve, are going to have iodine intakes slightly lower than the requirement. However, the proportion of individuals with iodine intakes lower than their requirements is going to be smaller or even eliminated if the iodine supply from the diet is taken in consideration. The use of EAR over RNI for micronutrients with EAR values and small variation of intake among individuals, such as the case of iodine, has been proposed for assessing and designing dietary programs for populations. In summary, it is preferable to set the nutritional goal of the iodine program in EAR values rather than RNI values. An additional advantage of this change is reducing the risk of providing unnecessary excessive iodine intake levels.

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[b] The Recommended Nutrient Intake (RNI) is the daily intake that meets the nutrient requirements of almost all apparently healthy individual in an age- and sex/ specific population group.

[c] The Estimated Average Requirement (EAR) is the average (near to the median) daily nutrient intake level estimated to meet the need of half the healthy individuals in a particular age and gender group.

The goal of any micronutrient intervention is to keep the population intake between the EAR and the Tolerable Upper Intake Level (UL)[d] values.

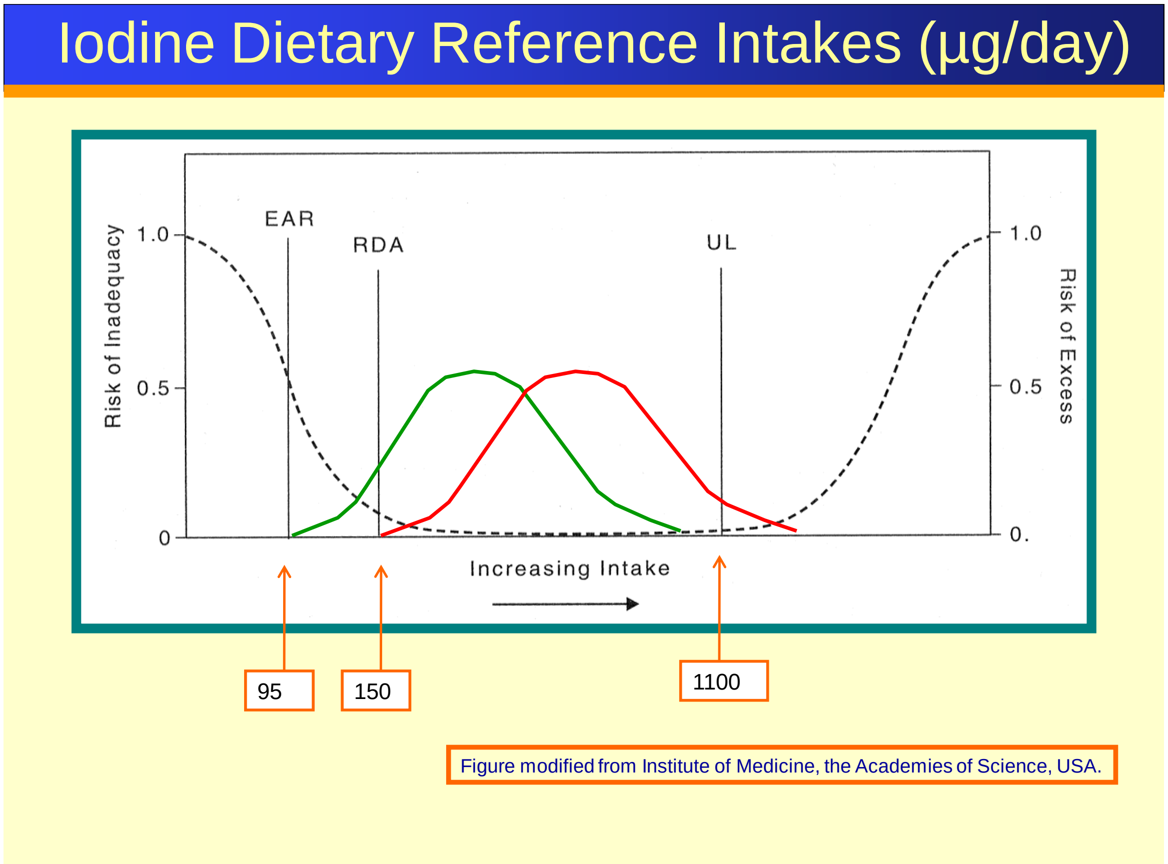

Figure 1
Dietary Reference Intakes (DRI) of iodine for adults accordingly with the Institute of Medicine of the National Academies of Science of the USA.

Nevertheless, the fact that adults are receiving sufficient amounts of iodine does not mean that other age-, sex-, and physiological stage- groups of the population are equally covered. Excepting children younger than 24 months of age, the diet is commonly the same for all members of the family. Therefore, the iodine provision of the diet at households should be one that is low enough to avoid excessive intakes (above the UL values), but sufficiently high to satisfy the nutritional need (above the EAR values) of all members of the family. In order to estimate the "household" provision of iodine in the diet, a comparison of the iodine requirement per energy requirement of the members of the family could help. The calculation is based on the assumption that iodine intake is going to be proportional to the energy intake, which is very applicable for iodine either supplied in the natural ingredients of the usual diet or coming through addition of iodized salt to the meals.

[d] The Tolerable Upper Intake Level (UL) is the highest average daily nutrient intake level unlikely to pose risk of adverse effects to almost all apparently healthy individuals in an age- and sex-specific population group.

Table 2 shows the EAR values of iodine for the different population groups, and it also shows the estimation of these values in terms of 100 kcal of energy intake. The larger the latter value the highest the susceptibility to have iodine inadequacy, because the diet must have a larger iodine density. The three groups at the highest risk to suffer of iodine deficiency are lactating women, pregnant women, and children younger than 3 years of age. Based on the values of the table, the diet should supply at least **7.5 µg I/100 kcal** to satisfy the iodine requirements of all members of the population. If the adult females (19-30 year old) are used as the reference for estimating the "household" need, the minimum iodine intake by this group should be **178 µg/d** (95 x 7.5/4.0). It means that the adult females should receive 88% and 19% more iodine than their corresponding EAR and RNI values. This additional intake is required in order to assure that women during pregnancy and lactation (and the non-breast feed children younger than 3 years of age) are receiving sufficient iodine through the diet. It is interesting to notice here, that if those at risk groups are excluded, the "household" iodine need (using the adult women as the reference) would only be **109 µg/d**. It means that the current goal of the cut-off intake of 150 µg/d, is high for covering the iodine requirements for most members of the family, but it is still insufficient for covering the iodine requirements of pregnant and lactating women, and young children. Here, it is important to point out that the RDA (RNI) values recommended by the IOM during pregnancy and lactation are 220 µg/d and 290 µg/d, respectively. WHO/UNICEF/ICCIDD adopted 250 µg/d as the RNI for both groups.

Table 2.

Iodine EAR value of the different age-, sex-, and physiological stage- groups, and the iodine density per 100 kcal to satisfy the EAR¶

Parameters	Children (years)		Females (years)								Males (years)							
	1-3	4-8	9-13	14-18	19-30	31-50	50-70	≥70	Pregn.	Lact.	9 - 13	14-18	19-30	31-50	50-70	≥70	Max. Value	Prop. 19-30y Women
Iodine EAR (µg/d)	65	65	73	95	95	95	95	95	160	209	73	95	95	95	95	95		
Energy intake (k/d)	1062	1400	2069	2488	2400	2350	2350	2100	2637	2804	2360	3225	3050	2950	2450	2450		
Iodine density (µg in 100 kcal)	6.1	4.6	3.5	3.8	4.0	4.0	4.0	4.5	6.1	7.5	3.1	2.9	3.1	3.2	3.9	3.9	7.5	1.87

Conclusion: EAR based on adult females (19-30 y)should be : 95 x 1.87 = **178** **µg I/d**

If excluding pregnant and lactating women, and children younger than 3 year old : 95 x 1.15 = **109** **µg I/d** | 4.6 | 1.15 |

¶ EAR values are from the Institute of Medicine of the USA; and the energy requirements from FAO (human energy requirements, 2004). Energy requirements during pregnancy (second trimester, as the average) and lactation are from Butte and King; *Pub. Health Nutr.* 2005; **8**(7A):1010-1027. Energy requirement during the third trimester of pregnancy is similar to that during lactation.

Table 3 shows a similar type of calculations as Table 2 but for the UL values. In this case, the groups with the lowest UL/100 kcal values are the most at risk of suffering adverse effects due to excessive iodine intakes, because higher iodine densities in the diet would supply excessive amounts of that micronutrient. The group at the highest risk is children 1-3 year old, who receive most of the iodine through breast milk. The diet should supply less than **19.0 µg I/100 kcal** to be safe for all members of the population. If the adult females (19-30 year old) are used as the reference for the "household" iodine safety, the maximum iodine intake by this group should be **451 µg/d**; i.e. 41% of the recommended UL iodine value for this group. This lower safe intake is required in order to assure that children younger than 3 years of age and other susceptible groups are not receiving excessive amounts of iodine through the diet. It is important to point out that WHO/UNICEF/ICCIDD have recommended that pregnant and lactating women should not receive more than 500 µg I/d, which is slightly higher to the calculated values.

Table 3.

Iodine UL value of the different age-, sex-, and physiological stage- groups, and the iodine density per 100 kcal to avoid the UL[¶]

Parameters	**Children (years)**		**Females (years)**								**Males (years)**							
	1-3	4-8	9-13	14-18	19-30	31-50	50-70	≥70	Pregn.	Lact.	9 - 13	14-18	19-30	31-50	50-70	≥70		
Iodine UL (µg/d)	200	300	600	900	1100	1100	1100	1100	1100	1100	600	900	1100	1100	1100	1100		
Energy intake (k/d)	1062	1400	2069	2488	2400	2350	2350	2100	2637	2804	2360	3225	3050	2950	2450	2450	Min. Value	Prop. 19-30y Women
Iodine density (µg in 100 kcal)	19	21	29	36	46	47	47	52	42	39	25	28	36	37	45	45	19	0.41

Conclusion: UL based on adult females (19-30 year old) should be : 1100 x 0.41 = **451 µg I/d**

¶ Same sources as in Table 2.

In summary, in order that every member of the family receives efficacious and safe iodine levels, the diet should supply between 7.5 and 19.0 µg I/100 kcal. If these daily iodine densities in the diet were assessed by the iodine intakes of adult females, they are equivalent to the cut-off points of 178 and 451 µg I/d, respectively. In other words, the cut-off values (minimum and maximum) of the "household-intakes" of iodine, measured through the intake of adult females (19-30 year old), should be 178 and 451 µg I/d. Round numbers can be applied, and be less strict in the upper intake level based on the fact that the intake distributions are shifted toward the high values. Thus for example, it would be appropriate to say that the **"household" intake goal of the iodine intake should be between 180 and 500 µg I/d** based on the intake of adult females (19-30 year old), which is near to the family per capita intake.

One hundred kilocalories are usually given by 25 grams of solid foods (1 gram of solid foods provides about 4 kcal). Therefore the iodine densities of 7.5-18.0 µg I/100 kcal are roughly equivalent to 0.30-0.72 µg I/g. This iodine density in foods, as summarized in the annex about "Iodine in the Diet and the Environment" is only given by marine fish (1.45 µg I/g) and dairy products coming from cows fed with iodine-rich grasses or feeds. The iodine density of fluid human and cow milk is 0.08-0.09 µg I/mL, but if the milk is transformed in a powder form to be comparable to solid foods, the iodine density increases about ten times, i.e to 0.8-0.9 µg I/g. Therefore, if the diet is poor in marine fish and dairy products, it is very difficult that it is going to provide sufficient iodine for satisfying the requirements of this nutrient to human populations. This analysis explains why iodine deficiency is widespread in the world, and supports the almost universal use of iodine fortification of the human diet.

As corollary of the analysis done in the prior paragraph, both the meals prepared with natural ingredients, as well as the processed foods manufactured by the industry should be enriched with iodine in order to reach the iodine density of 7.5-18.0 µg I/100 kcal or 0.30-0.72 µg I/g. In the case of industry-made products, this iodine density is more or less equivalent to 6% to 15% of the Nutrient Reference Value (NRV)[e] of iodine (150 µg/d) per serving size, under the supposition that most common serving size are 30 grams and provide 120 kcal. In summary, the food industry should be requested to manufacture products with an iodine content equivalent to 6-15% NRV per serving size. The added iodine could come from iodized salt or by incorporating iodine into the micronutrient premixes that the food industry may already be using.

Estimation of the average iodine content of salt at households

In addition to incorporate iodine to processed foods, it is important to add iodine into the meals prepared with natural ingredients at homes. This process has already been done for many years through the use of iodized salt. This is indeed the first case of "home-fortification", in which a premix containing iodine (the iodize salt) is added to the home-prepared foods.

The WHO/UNICEF/ICCIDD publication of 1996 about "*Recommended iodine levels in salt and guidelines for monitoring their adequacy and effectiveness*" specified that the iodine content in salt at the point of production should be within the range of **20-40 mg I/kg**. These values were calculation using the following assumptions:

1. Goal was to provide at households 150 µg I/d to member of the family having a salt intake of 10 g/d;
2. The only source of additional iodine was household salt (cooking and table salt); and
3. Iodine losses were 20% from factory to retail stores, and 20% from retail stores to homes, i.e. a 44% total loss was calculated.

The calculations done were as follows:

150 µg I/10 g salt = 15 µg I/g salt = <u>15 mg I/kg at households</u>.

15 mg I/kg at households x 1.44 = 21.6 mg I/kg ≈ <u>20 mg I/kg at production sites</u>.

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[e] Nutrient Reference Values (NRV) are dietary reference values defined by the Codex Alimentarius Commission with the aim of harmonizing the labeling of processed foods. It is a value applicable to all members of the family aged 3 years and over. The NRV values are roughly equivalent to the RNI values of the adult males.

The WHO/UNICEF/ICCIDD reference of 1996 did not describe how the value of 40 mg/kg was determined. Here it is interesting to notice that the recommendations of 1993 specified that for salt intakes of 5 g/d, the iodine content should be twice than the content estimated for a 10 g/d salt intake (see Table 1). Therefore, the 20-40 mg/kg recommendation of WHO/UNICEF/ICCIDD already includes the range of 5-10 g/day of salt intake; it is 20 mg I/kg when the salt intake is 10 g/d, and 40 mg I/kg when the salt intake is 5 g/d. For intermediate salt intakes, iodine contents between 20 and 40 mg I/kg should be selected at the point of production. Here it is important to point out that these iodine contents are averages, and neither minimum nor maximum values.

This section focuses on the estimation of the iodine content in salt at households. Estimation of the iodine content at the production sites is done in the following section.

In the prior section, it was calculated that in order to ensure sufficient and safe iodine supply to most members of the family, including pregnant and lactating women, the adult women (19-30 year old) should have a usual iodine intake of 180 to 550 µg/d. Here, it is important to emphasize that this is the usual intake, which means the daily average intake during long periods of time; it is not the strict daily intake. Therefore, the parameter that is important to measure is the average value and not a minimum value.

To simplify the calculations, it is going to be assumed that the normal diet has a negligible amount of iodine, and that iodized salt is the only source of this mineral. The latter assumption remains valid even for salt coming from processed foods, because it is going to replace the salt that used discretionally at homes (cooking and table salt). In other words, both the household salt and the salt supplied through processed foods should be taken in consideration because it is not possible, for the purposes of salt iodization program,s to make the distinction between these two sources of salt. Some individuals are going to have salt intakes only from household salt while others only from processed foods, while the rest are going to have combinations of the two situations. What it is important to realize is that both types of salt are "iodizable", although in the case of processed foods the iodine could be directly incorporate to foods either through iodized salt or by means of a micronutrient that contains iodine.

In order to estimate the iodine density in salt, it is important to know the usual salt intakes (both discretional as well as through processed foods).

Measuring salt intake and its population distribution profile is a very difficult task, and probably the only reliable manner to do is through assessing the 24-h urinary sodium excretion –based on the fact that nearly 90% of the sodium intake is excreted through urine-, and assuming that 10-25% of sodium comes from natural ingredients of the diet, while the rest originates from added salt either through discretional use of salt or through processed foods (see the annex about "Note on the iodization of the salt for industrial food manufacturing, with special reference to bread baking and examples from Europe").

Only one population group might be used as reference for making the estimation of salt intake. The most appropriate group seems to be the women of reproductive age (19-30 year old), because this group may be considered the "average" of the family and among its members are the pregnant and lactating women, which are at the highest risk to be affected by iodine deficiency. The same urine samples could be used to determine 24-h excretion of iodine in order to measure the basal intake of iodine. The same urine samples could also be used to estimate the total 24-h urine volume and the 24-h creatinine excretion, which could be applied later for monitoring the sodium[5] and iodine[6] excretions using casual (spot) urine samples. Introduction of these two parameters as correction factor for approximating 24-h excretion appears to be very useful because, once the absolute iodine values are adjusted using them, comparisons among age-, gender-, and geographical-groups might be possible. Daily urinary volume varies among age, physical activity, and climatic conditions, and hence the absolute urinary iodine content has a very limited interpretation. Furthermore, results from spot samples are useful only for estimating population medians and not the distribution profile of excretion (and intake). Having a method to approximate individual sodium and iodine as 24-h excretion values may permit a better interpretation and assessment of the iodization programs.

For monitoring the effectiveness of salt iodization programs, urinary iodine excretion has been followed in school age children (9-13 year old) in spot sample. This practice might continue but it should be re-examined in order to identify the iodine excretion level that reflects a good iodine intake by pregnant and lactating women. Nevertheless pregnant and lactating women should also be studied.

Regardless the total salt (and sodium) intake as measured in 24-h urine samples, it is always appropriate to determine proportional intake of salt coming from discretionary use at households, industry-manufactured foods, and foods purchased outside home. WHO/PAHO has prepared a review of methods to determine the main sources of salt in the diet[7]. Although the document has not been validated in the field, it provides good recommendations and references for this type of work.

For countries whose salt source is mainly household salt because they have little consumption of processed foods, there is an approximate way to estimate the distribution of salt intake through the analysis of secondary data collected in the Household Income and Expenditure Surveys (HIES). These surveys are carried out periodically and they allow deductions for different strata of the population. The apparent intake of certain foods per household can be calculated by using the reported purchasing (transformed into amounts) in a fixed period of time. Then, the "adult-equivalent" intake could be estimated by dividing the total household intake by the total number of "adult equivalents" in the household. Adult equivalent refers to the proportional energy intake of each member of the family using the adult males as the reference. Thus for example, using the values of Table 2, a 9-13 year old girl is 0.68 adult equivalents (2069/3050), while a 19-30 year old woman is 0.79 (2400/3050). Once the total adult equivalents of the household are computed, the apparent intakes for each age-, gender-, and physiological-group can be estimated by multiplying the "adult equivalent" intake for the corresponding adult equivalent factor of each group. **Table 4** illustrates this procedure applied to 19-30 y.o. women in Uganda; percentiles 10-25 are used as minimum intakes, and percentiles 75-90 as maximum intakes.

Table 4

Apparent salt intakes in Uganda in 2008 estimated from reported household purchases¶

REGION	**COUNTRY**					**RURAL**					**URBAN**				
Percentiles	**10**	**25**	**50**	**75**	**90**	**10**	**25**	**50**	**75**	**90**	**10**	**25**	**50**	**75**	**90**
g salt/d per Ad. Equiv.	1.9	4.0	8.0	13.0	19.1	1.9	4.1	8.3	13.1	19.2	1.7	3.5	7.1	12.4	18.0
g salt/d Females (19-30 y)	1.5	3.2	6.5	10.6	15.5	1.6	3.3	6.7	10.6	15.5	1.4	2.8	5.8	10.1	14.6

Conclusion: Minimum intake of salt = **1.4 – 3.3 g/d** Maximum intake = **10.6 -15.5 g/d** for the adult females.

¶ Data computed by the Ugandan Bureau of Statistics. Estimations include neither salt losses nor uses different to human consumption.

In nutrition studies what is important is the determination of usual intakes, which are calculated by using data from several days or at least one repeated measurement to estimate intra-individual variation. Consequently, the intake distribution is narrower than that calculated using the apparent (only one value) intakes. Values of table 4, are more similar to apparent intakes rather than usual intakes. Therefore, the real low and high intake values might be around percentiles 25 and 75, respectively. In the specific case of Uganda, one can assume 3 g/d and 12 g/d, for the low and high salt intake values, and a national median of 6.5 g/d. The low salt intakes are for urban inhabitants and the high intakes for rural inhabitants, which coincide with the highest energy expenditure –that requires eaten more foods, and therefore salt- by the rural communities.

Table 5 presents the estimations of iodine intake through iodized salt in Uganda. In order to fulfill the objective of providing between 180 µg I/d and 500 µg I/d to this population, salt should contain around 50 mg I/kg at the household level. This is a relative large iodine content but it is needed if indeed the salt intake of the population is as low as it was estimated (3 to 12 g/d for women of reproductive age). Levels as low as 30 mg I /kg will meet with the objective for half of the population (median larger than 180 µg I/d of intake), but they may leave uncovered a still large proportion. The table also illustrates that in order to cover even those individuals with low salt intakes, the average women in Uganda is going to receive 3.4 times the EAR (325/95) and 2.2 times the RNI (325/150) values. The same table also shows that the intake distribution is skewed toward the high values, and therefore the mean is always larger than the median.

Table 5

Estimated iodine intakes through the use of iodized salt in Uganda¶

Household salt	Estimated salt intake in Uganda – 2008 (g/d) Women of reproductive age (19-30 year old)				
	Mean	**SD**	**Low**	**Median**	**High**
	8.0	**7.2**	**3.0**	**6.5**	**12.00**
Iodine (mg/kg)	Estimated intake of iodine (µg/d)				
15	120	108	45	98	225
20	160	144	60	130	240
30	241	216	90	195	360
40	321	288	120	260	480
50*	401	360	150	325	600
60	481	432	180	390	720
80	642	576	240	520	960
120	962	864	360	780	1440

¶ Estimations of salt intake by the Ugandan Bureau of Statistics using data of the Ugandan Household Income and Expenditure Survey of 2008.

* The proposed iodization level for the program in order to fulfill the purpose of supplying near and above 180 µg I/d (green cells) and near or below 500 µg I/d (orange cells).

Adjustments to the iodization level should be done after assessing the urinary excretion of iodine by the reference group (in this case, 19-30 year old women). Here, it is important to point out that it is going to be necessary to have an estimation of the 24-h iodine excretion in order to estimate the population distribution. Only the median value is insufficient. It is highly probable that the iodine content would be reduced, because this model did not consider provision of iodine by other sources in the diet.

The example of Uganda also demonstrates that the program of salt iodization is compatible with the policies of reduction of salt intake, because the salt iodization program at this low salt intake pattern provides sufficient iodine to most individuals, including pregnant and lactating women. If the salt intake is lower, it would only be a matter of increasing the iodine content in the salt, hoping that the values of high salt intake are also reduced. If that were not the case, then the maximum iodine level is going to depend on the individuals with high salt intake. The final decision of the "population" iodine content would be a compromise between the efficacious and the safe intake values.

Using the data of **Table 6**, one can estimate the iodine level for the case of Uganda as follows: For the low salt intake of 3 g/d, the iodine content should be 60 mg/kg, but for the high salt intake of 12 g/d, the safe iodine content should not be larger than 42 mg/kg. Then, a compromise of 50 mg/kg is an appropriate decision as it was done in **Table 5**.

Table 6
Possible iodine contents for different salt consumption patterns

Low and High Salt intakes (g/d) and Required Average Iodization Levels (mg I/kg)				
Low Salt Intake (g/d)	[I] (mg/kg)*	[I] (mg/kg)[§]	High Salt Intake (g/d)	Safe [I] (mg/kg)[¶]
1	109.0	180.0	4	125.0
2	54.5	90.0	6	83.3
3	36.3	60.0	8	62.5
4	27.3	45.0	10	50.0
5	21.8	36.0	12	41.7
6	18.2	30.0	16	31.3
7	15.6	25.7	20	25.0
8	13.6	22.5	22	22.7
9	12.1	20.0	24	20.8
10	10.9	18.0	30	16.7

* For providing an iodine intake of at least 109 µg I/d (i.e. excluding iodine requirements for pregnant and lactating women, and children younger than 3 years of age)
[§] For providing an iodine intake of at least 180 µg I/d
[¶] For providing an iodine intake of no more than 500 µg I/d

Data of **Table 6** also shows that the iodine content of 20 mg I/kg is applicable for a low salt intake of 9 g/d but less than 24-25 g/d, and the iodine content of 40 mg I/kg is applicable for a low salt intake of 4.5 g/d but less than 14 g/d. These calculations demonstrate that the current salt iodine recommendations are providing sufficient iodine to most populations because the actual salt intakes are high worlwide.

If the low salt intake continues reducing but the high salt intake value remains invariable, then the iodine content is going to depend on the individuals with the high salt intake. Under this circumstance, the alternative is to design the program discounting the needs of pregnant and lactating women, and young children, and supplying the additional iodine needs of these groups through supplementation. Excluding those groups, an iodine content of 20 mg I/kg would satisfy the requirements of most members of the family when the adult females have salt intakes as low as 5.4 g/d; and iodine content of 40 mg I/kg would work with intakes as low as 2.7 g/d.

In summary, at decreasing salt intakes, the individuals with the high salt intakes will have a larger influence in the decision for selecting the iodine content in salt, and consequently in the overall design of the program (either including or not iodine supplementation for pregnant and lactating women, and perhaps children younger than 3 years of age if they are not breast fed).

A practical conclusion of this analysis is that under the current salt intakes in most countries, the average salt iodization level at households should be between 20 and 40 mg I/kg –which are the present WHO/UNICEF/ICCIDD recommendations at the production site-. However, it may be necessary considering iodine supplementation during pregnancy and lactation. Furthermore, policies of salt intake reduction could take place without a fear of jeopardizing the iodine delivery to the population, although it would be imperative to monitor periodically the 24-h urinary iodine excretion of adult females, including pregnant and lactating women, to make timely adjustments (up or down) to the iodine content in salt, as well as the probably associate supplementation programs.

The same process illustrated here is applicable to all “iodizable” salt; i.e. combining the salt from processed foods.

Specifications of the iodine content to use in salt standards

Once the iodine content in salt at households has been estimated, the calculations for predicting the specifications at the production site should be done. The process is similar to that used by WHO/UNICEF/ICCIDD in 1996, which defined the level of 20 mg I/kg at factories from the goal level of 15 mg I/kg at homes. However, in the case of iodate as the source of iodine the expected losses are much lower than assumed in those calculations. Arroyave[8] summarized in 1998 evidence from real iodization programs that reported iodine losses of 3.5-10.0% within a period of 8 to 12 months. Thus, using these values, for the case of an iodine content of 30 mg/kg, the estimated **level of addition** of iodine at the production site is:

Level of addition = Household level/stability = 30/(0.9) = 33.3 ≈ 35 mg I/kg at production sites.

The estimated level of addition is valid for any type of salt, as well as for those products that replace salt, such as fish and soy sauce, bouillon cubes, and powder soups, which should contain an amount of iodine that is proportional to the content of salt. Costa Rica has already made official this policy, making compulsory the use of iodized salt in the production of bouillon cubes and powder soups[9]. During the manufacturing of these products some iodine may be lost, but manufacturers should restore the lost amounts in order to maintain the expected supply of iodine to the population.

The factory average, which is the **target level**, is calculated by adding the level of addition to the intrinsic content of the same micronutrient in the unfortified product. In the case of salt, because the natural iodine content is inexistent or negligible in comparison with the added amount of iodine, the target level coincides with the level of addition.

Target level = intrinsic content of iodine + level of addition = 35 mg I/kg.

For quality control purposes, the factory requires parameters for accepting or rejecting a lot based on compliance of specifications. The average iodine content should be very near to the expected target level. Single results should be equally distributed around that mean within certain range of dispersion. The range of dispersion (**tolerable range of heterogeneity**) depends on several factors:

- Physical nature of the fortified product: dispersion is larger in solids than in liquids;
- Particle size of the fortified product: dispersion is larger in coarse than in fine products;
- Form of addition of the fortificant (source of the micronutrient): dispersion is larger if fortificant is applied dry rather than in liquid or spray;
- Size of the sample: dispersion is larger when small amounts of the fortified product are used for the analytical assay than when a larger quantity of the fortified product is used for the chemical determinations (this does not applied to liquids, where the homogeneity in general is very good);
- Number of samples: dispersion is larger when a small number of samples are used to take decisions;
- Performance of the analytical assay: dispersion is larger when equipment or methods have low precision; and
- Quality of the mixing process.

The case of salt is interesting, because very different products receive the same name and are used with the same purpose. Salt could be **refined** (purified, re-crystallized, small particle size, and dried), **washed** (elimination of major contaminant and physical particles, grinded, and dried), or **raw** (coarse, almost without treatment after sea or mine extraction). Therefore, there are at least three different products that receive the name of salt, but they cannot be judged using the same criteria. Diodsay and colleagues[10] collected salt from different countries to study the stability of iodine. Their results showed that regardless the type of salt, iodate was very stable. In the paper, they concluded the opposite, but they were referring to results under very hard conditions (100% relative humidity and 40^{o}C), and which are inexistent or very rare in the world. However, their results showed that after 6 months under still hard conditions (40^{o}C and 60% relative humidity) the average iodine stability was 80%. The importance of these results is that many of them were obtained in salt samples that do not comply with the minimum conditions for being classified as food grade salt by the Codex Alimentarius Standard[11]. In the latter document, it is specified that salt for human consumption should have not less than 97% of sodium chloride on a dry matter basis. Some of the “salt” samples that were studied by Diodsay and colleagues presented insoluble matter in proportions larger than 2.0%, which suggests that these products cannot be categorized as food grade salt. Regrettably, the article did not include the percent of sodium chloride.

The WHO/UNICEF/ICCIDD recommendations for iodized salt are easily applied to refined and washed salt types, but they are unsuitable for raw and coarse salt. Nevertheless, the same criteria have been used to judge the performance of all salt iodization programs. Despite of the “incompliance” of the “universal” standards by the “non-food grade” salts, they have been delivering iodine to needed populations, and it is foreseen that this is going to remain invariable in many countries in the near future. Thus, it is important to produce different standards for each type of salt, as well as to establish appropriate criteria to assess the epidemiological performance (supply of iodine). Ideally, salt iodization programs should be implemented over good quality salts but, until that happens; suitable process indicators should be suggested for the poor-quality salts. Otherwise, many salt iodization programs are going to continue being classified as failures, when they are already having an important role in public health nutrition.

Regardless of the type of salt, the iodine content follows a symmetrical distribution profile (normal curve). This condition allows the use of the normal standard curve for estimating percentiles and proportion of samples within specific compliance criteria. **Figure 2** and **Table 7** summarize important reference points and include the formulas for estimating them. **Table 8** summarizes the iodine content and percentile values of different types of salt from different countries.

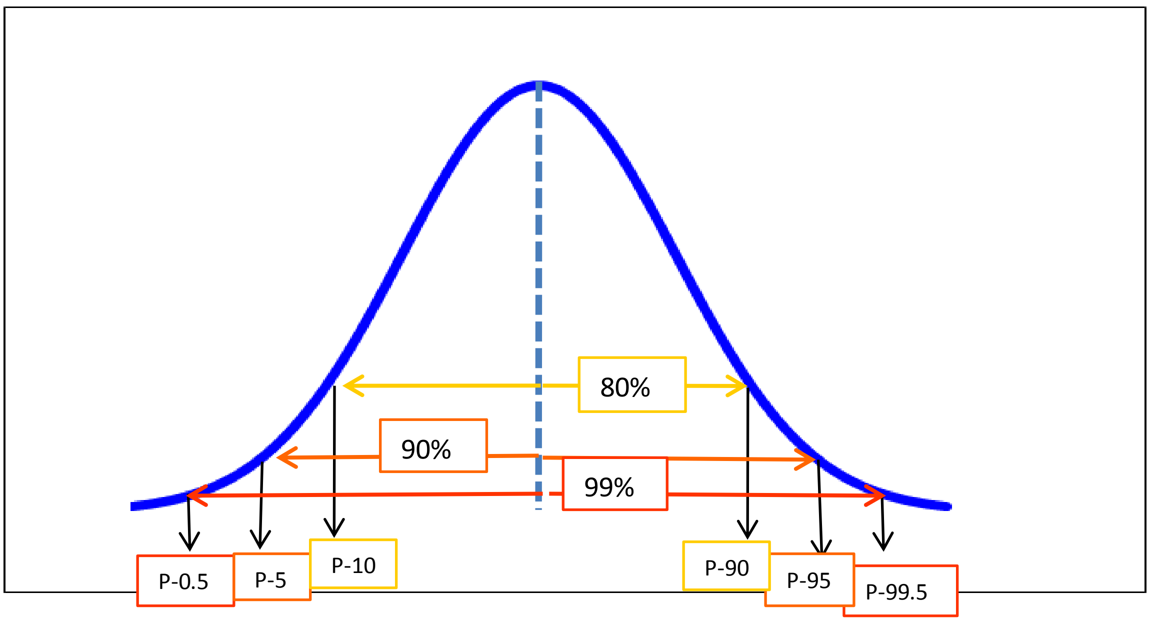

Figure 2
Graphic representation of percentiles and delimited areas under a normal distribution curve.

Table 7
Equations to estimate percentile values and areas under a normal distribution curve using the mean and SD.

FORMULAS **COMPLIANCE**

P-0.5	X - (2.575xSD)
P-5	X - (1.645xSD)
P-10	X - (1.28xSD)
P-90	X +(1.28xSD)
P-95	X +(1.645xSD)
P-99.5	X +(2.575xSD)
C.V.	SD/average x 100
Mean St. Error =	SD/sqr (n)

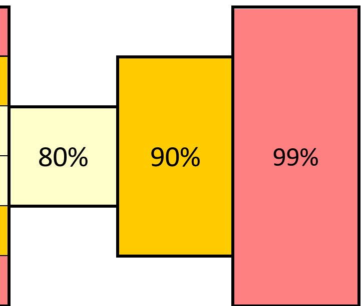

Table 8 Iodine content and distribution of different salt iodization programs.

Country	**Cambodia**[§]	**Guatemala** [Ω]	**Costa Rica**[€]	**West Bank**[¥]
Brand	**-**	**-**	**Brunca-A**	**Dead Sea**
Salt type	Raw-coarse	Raw-ground	Refined	Refined
Premix application	Liquid spray	Dry premix	Liquid spray	Liquid spray
n	192	43	35	15
Average	30.5	26.1	36.5	25.5
St. Deviation	24.9	11.8	5.4	2.6
Mean St. Error	1.8	1.8	1.4	0.7
P-0.5	-33.6	-4.3	22.6	18.7
P-5	-10.5	6.7	27.6	21.2
P-10	-1.4	11.0	29.6	22.1
P-90	62.4	41.2	43.4	28.8
P-95	71.5	45.5	45.4	29.8
P-99.5	94.6	56.5	50.4	32.3
C.V. (%)	81.6 %	45.2 %	14.8 %	10.2 %
% samples < 20 mg/kg	33.7 % %	30.3 %	0.1 %	1.7 %

Sources of data: [§] UNICEF and Government of Cambodia. Report of the National Survey of Iodine Nutrition and Implementation of Universal Salt Iodization. 2008. Only samples positively identified as iodized using a Rapid Test Kit.
[Ω] Liga de Protección al Consumidor (LIDECON), 2009.
[€] National Reference Center of Oral Health, INCIENSA, Costa Rica. 2009.
[¥] Central Public Health Laboratory, MOH, Palestinian Authority. 2010.

Table 8 reveals that the most robust indicator to monitor iodization performance is the mean, because it is independent of the variation of the process and the type of salt. Therefore, the common parameter is the average (the target level), and it should be the indicator to enforce. It is important also to notice that in all cases, the current WHO/UNICEF/ICCDD recommendation of iodized salt is complied, i.e. presenting an iodine content within the range of 20-40 mg I/kg at the production site. However, the data show that determination of this mineral in single samples would be highly variable. For example if the 80% compliance is accepted (i.e. percentiles 10 to 90), the operation in Cambodia would produce values from 0 to 62 mg I/kg; in Guatemala from 11 to 41 mg I/kg; in Costa Rica from 30 to 43 mg I/kg; and in the West Bank from 22 to 29 mg I/kg. The situation would be worse if a more demanding criterion is used (e.g. 90% acceptance, percentiles 5 and 95; or 99% acceptance, percentiles 0.5 and 99.5). This comparison clarifies why the range of 20-40 mg I/kg cannot be applied as technical specification for quality control and inspection, and it also justifies the preparation of at least two different standards, one for the raw and coarse salts, and another for the refined and washed salts. This is the strategy that is being implemented in Honduras.

These results also demonstrate that if the current WHO/UNICEF/ICCIDD recommendation of 20-40 mg I/kg is interpreted as a range of single values, it is rarely applicable, and it is valid only for refined salts. Under this interpretation, the average iodine content should be 30 mg/kg, with a standard deviation of 4.4 mg/kg, for a coefficient of variation equal or lower than 12.5%. If these conditions are not fulfilled the cited range could not be enforced. It is important to point out here that many salt iodization programs have larger coefficients of variation, and therefore they are going to fail the criterion of 20-40 mg I/kg if used as the tolerable range of heterogeneity.

If the range of 20-40 mg I/kg were applied for 90% compliance (i.e. percentiles 5 to 95), the standard deviation should be equal or lower than 6 mg/kg for a coefficient of variation of 20%. This is still a very demanding criterion, and very difficult to be attained using single salt samples collected at retail stores and at homes.

In summary, minimum and maximum levels of the iodine content in salt depend on the overall performance of the iodization operation, and it is highly variable for raw and coarse salts to the point that even at the production sites, there are possibilities to find single samples with very low iodine levels. This is especially true if the coefficient of variation is larger than 30%. For raw and coarse salts, the use of composite samples[f] is required. Refined salt can also take advantage of using composite samples for reducing the number of chemical analysis as it is going to be described in the following section.

Each factory should determine its own performance parameters around the target level. Possibly, it would be appropriate to select range of values for compliances between 80% to 90%, i.e. between P-10 and P-90, and P-5 to P-95, respectively.

For enacting standards, governmental authorities should study the performance characteristics of a few factories with acceptable production practices, and estimate the coefficients of variation of all of them in order to decide for the widest tolerable range of heterogeneity that is still acceptable, and which would be used for checking that the process is continuously controlled. The aim is that the iodine

[f] A composite sample is prepared by mixing 2 or more single samples. The purpose is to identify the minimum number of samples that are needed for reducing the coefficient of variation of the iodine content to less than 30%. Mixing too many single samples would provide the average but it may hide flaws in the control of the process.

content in all factories is around a common average, and the homogeneity –although distinc in each factory- remains within the selected tolerable range of heterogeneity.

In the past, the adoption of the minimum value in food fortification was promoted under the concept that it simplifies the statistical sampling for quality control and inspection, because each sample should conform to a single cut-off point (i.e. a yes or no response). However, experience has shown that this policy is not working, and it should be discouraged. Countries that have based the fortification standards in the compliance of a minimum value have discovered that the industry interprets this figure as the target level, and as consequence many samples fell below this point. Moreover, when food control authorities have enforced the 'minimum", it has been motive of conflicts between the private and the public sector or the industry has added too much, and so increasing the cost of the fortification process and putting the population at risk of having unnecessary excessive intakes.

Standards are also applicable to product in the market, and the same principles can be used to estimate the required iodine content in product collected at retail stores. However, in this case, the tolerable range of heterogeneity should consider reduction in homogeneity due to segregation and losses. **Table 9** illustrates expected values for different target iodization levels (averages) and under distinct conditions of coefficient of variation.

Table 9
Expected percentiles of distribution of the iodine content at different coefficients of variation

For	15	CV (%)	FACTORIES				
Averages	**SD**	**P-0.5**	**P-5**	**P-10**	**P-90**	**P-95**	**P-99.5**
25.0	3.8	15.3	18.8	20.2	29.8	31.2	34.7
35.0	5.3	21.5	26.4	28.3	41.7	43.6	48.5
45.0	6.8	27.6	33.9	36.4	53.6	56.1	62.4
55.0	8.3	33.8	41.4	44.4	65.6	68.6	76.2
65.0	9.8	39.9	49.0	52.5	77.5	81.0	90.1

For	25	CV (%)	RETAIL STORE				
Averages	**SD**	**P-0.5**	**P-5**	**P-10**	**P-90**	**P-95**	**P-99.5**
25.0	6.3	8.9	14.7	17.0	33.0	35.3	41.1
35.0	8.8	12.5	20.6	23.8	46.2	49.4	57.5
45.0	11.3	16.0	26.5	30.6	59.4	63.5	74.0
55.0	13.8	19.6	32.4	37.4	72.6	77.6	90.4
65.0	16.3	23.2	38.3	44.2	85.8	91.7	106.8

For	40	CV (%)	HOUSEHOLDS				
Averages	**SD**	**P-0.5**	**P-5**	**P-10**	**P-90**	**P-95**	**P-99.5**
25.0	10.0	-0.8	8.6	12.2	37.8	41.5	50.8
35.0	14.0	-1.1	12.0	17.1	52.9	58.0	71.1
45.0	18.0	-1.4	15.4	22.0	68.0	74.6	91.4
55.0	22.0	-1.7	18.8	26.8	83.2	91.2	111.7
65.0	26.0	-2.0	22.2	31.7	98.3	107.8	132.0
		99%					
			90%				
				80%			

The salt iodization standards should be completed but not so complicated. Thus, in order to simplify the specifications associated to the iodine content, it is suggested to use the **target level** (average at factories) and the 80% (P-10 to P-90) **tolerable range of heterogeneity** as calculated for product at retail stores, and applying the same values but for 90- 99% compliance at factories. Thus for example, for the target level of 35.0 mg I/kg, if the expected coefficient of variation is 25% at retail stores, the tolerable range of heterogeneity would be 17 to 33 mg I/kg, and which would be enforced for 80% compliance. At factories, the same values would be used for 90-99% compliance, assuming that the coefficient of variation is going to be 15%. Here it is important to emphasize that using 80% compliance, there are still 20%probabilities that single samples of product collected from stores are found outside the tolerable range of heterogeneity. It does not mean that these samples are going to be lacking of iodine, all samples should be iodized.

For **claim level** in the labels, it is suggested to use either the target level or if wishing to be more precise, the intermediate level between the target level and the expected value after considering the maximum losses during the marketing life of the product. For example in the case of a 35.0 mg I/kg target level when losses could go up to 10%, the claim level would be:

Claim level = (35 + 35 x 0.9)/2 = 33.2 ≈ 33 mg I/kg.
In summary, the salt iodization standards should include the following parameters:

1. **Level of addition**: The level of micronutrient that should be added to the product.
2. **Target level:** The average content of the added micronutrient in the product at the production sites that results after considering the intrinsic content of the same micronutrient in the food vehicle.
3. **Tolerable range of heterogeneity:** The allowable dispersion of the micronutrient content in single samples analyzed for checking compliance. It is suggested a range that specified compliance of 80% at retail stores, and which would be used for checking 90-99% compliance at production sites.
4. **Claim level:** It could be either the target level or the expected average level at retail stores after considering expected losses during storage and transportation during the market life of the product.

It is recommended that for purposes of clarity in the interpretation of the standards that each one of the above mentioned parameters are described in different articles or paragraphs of the standard. It is important to emphasize that the goal is to comply with the target level and not with a minimum content.

The bottom section of the **Table 9** shows the theoretical values that the iodized salt would present at households. The coefficient of variation has been assumed to 40%. Although this is the same product that at retail stores might has a coefficient of variation of 25% for the iodine content. At homes, the variation is larger mainly because in most cases a very small amount of salt is analyzed. From samples collected at homes, 1 gram is usually dissolved for the determination of iodine while the analytical methods have been designed for using at least 10 grams for refined salts and 50 grams for coarse salts. The data of **Table 9** illustrates that the criterion that more than 90% (percentile 10) of samples should have a minimum of 20 mg I/kg might happen only if the target level is higher than 40 mg I/kg when the coefficient of variations is 40%. The "incompliance" would be worse if the coefficient of variation is larger, and which is very common for many salt iodization programs in developing countries.

Moreover, at households the indicator that is important is the average content of iodine in the salt and not the minimum content. The latter value has applications only for checking homogeneity in the quality control and inspection actions. At households the focus is on the epidemiological impact of the program, and it should be based on the average iodine supply. Therefore, at households single salt samples should be checked for the presence of iodine using a qualitative test (the Rapid Test Kit, e.g.), and then preparing one or two composite samples per cluster, combining only the single samples with confirmed presence of iodine. These composite samples would be used for the quantitative determination of iodine. If one is interested in determining the average iodine supply including the samples that were found as non-iodized, it could be done easily by multiplying the iodine content of the composite sample for the proportion of samples that were found positive. For example, if 85% of samples are positive, and the iodine content of the composite samples is 30 mg I/kg, then the "average" iodine content in the salt in the cluster would be: 30 x 0.85 = 25.5 mg I/kg.

In summary, the current criteria to classify the success of a salt iodization program should be changed, as for example to say that 90% single samples should be positive for the presence of iodine, and the average content of the salt should coincide with the iodine content that was estimated as efficacious and safe for the specific population group (in the case of Uganda, it should be 50 mg I/kg, if including pregnant and lactating women, or 35 mg I/kg if excluding them).

A note of caution is important to be introduced here. If salt is raw and coarse, the "non-iodization" proportion increases when single samples are checked for the presence of iodine. "Incompliance" as high as 20% may be possible. Therefore, it is important to estimate the tolerable range of variation of this type of salt at households as part of the epidemiological evaluation. It is possible than programs with performances of around 80% of positive samples at households may still be indicative of successful programs.

Important methodological factors to incorporate in salt iodization standards

The Codex Alimentarius model of a standard for food grade salt (CX STAN 150-1985, most recent amend 3-2006) includes the following sections:

1. Scope: Salt for use of human consumption, including as ingredient in food industries as a carrier of nutrients, mainly iodine.
2. Description: Sodium chloride as a food grade.
3. Composition and quality factors: Purity as sodium chloride not less than 97%; other allowable salts depending on the origin; use of potassium iodide or iodate as the fortificant source of iodine.
4. Food additives: If incorporated should be food grade quality.

5. Contaminants: Maximum levels for heavy metals (arsenic, copper, lead, cadmium, mercury).
6. Hygiene: For specifying methods of production, packaging, storage, and transportation for avoiding risk of contamination.
7. Labeling.
8. Packaging, transportation and storage.
9. Methods of analysis and sampling: for assessing purity, allowable accompanying salts, contaminants, and iodide, the latter by titrimetry with sodium thiosulfate.
10. Appendix of sampling for determination of sodium chloride.

Most countries follow a similar structure in their standards for iodized salt. However, in many cases –if not the most- the chemical specifications of the salt that are mentioned in the standards are not checked, and details of sampling and analytical assays are not followed.

In the past, the use of qualitative kits was promoted not only for testing the presence of iodine in the salt but also for quality control. However, during the last ten years, the use of kits for the latter purpose has been discouraged after confirming that the kits are not reliable for determining the iodine content[12]. The main limitation of the kits is the number of false positives for cut-off point values at low levels of iodine. As consequence, compliance can be overestimated. Nevertheless, the sensitivity of the common kits is good (capability to identify presence of iodine above low cut-off points) but the specificity is low (capability to discriminate salt samples with small contents of iodine). These results were confirmed in a small experiment carried out in Cambodia by UNICEF and A2Z (see **Table 10**).

Table 10
Performance of a Rapid Test Kit for iodate in coarse salt samples of Cambodia with low levels of iodine

Performance Parameters	Iodine cut-off points		
	5 mg/kg	10 mg/kg	15 mg/kg
Sensitivity	78 %	100 %	100 %
Specificity	69 %	65 %	62 %
False negatives	15 %	0 %	0 %
False positives	42 %	58 %	67 %

Source: UNICEF-Cambodia and A2Z/USAID.

However, an important characteristic of the qualitative kits has not been fully appreciated, and it is the potential of detecting low levels of iodine (as low as 5 mg/kg) even in salt that is raw and coarse. Having false positives is not a serious flaw, if the use of the kit is combined with the quantitative determination of iodine in composite samples prepared by mixing single samples found as positive for the presence of iodine. The important fact is that the use of the kit allows elimination of all those single salt samples that lack or contain very low iodine levels, and therefore make easier the following analytical work.

Another unfair judgment of the kits is that the uncertainty has been blamed on the kits and not in the nature of the salt. Indeed, the limitation is due to the heterogeneity of the iodine content when using very small amounts of salt, and not to the analytical properties of the chemical reaction of the kits. These arguments are explained below.

Size of the samples for analytical determinations

The titrimetric method that is mentioned in the salt standard of the *Codex Alimentarius* calls for the dissolution of at least 10 grams of refined salt, or at least 50 grams of coarse salt. The main reason is that iodine is present in very small amounts (20 to 60 parts per million; 20-60 mg/kg), and therefore if the reaction occurs with a very small amount of salt, the heterogeneity of the results will be large. The kits provide better results in refined and iodized salt because the iodine content is very homogeneous. The requirement of dissolving adequate amounts of salt has been neglected in the use of a field spectrophotometric method (i.e. the "iodine Chinese checker"). This method might be as good as the titrimetric method, but only if adequate amounts of iodized salt are dissolved before making the chromogenic reaction. Regrettably, the instructions of the use of this method ask for the dissolution of only one gram of salt, which in the case of coarse and raw salts are going to produce unreliable results. The **Figure 3** demonstrates that this is the case.

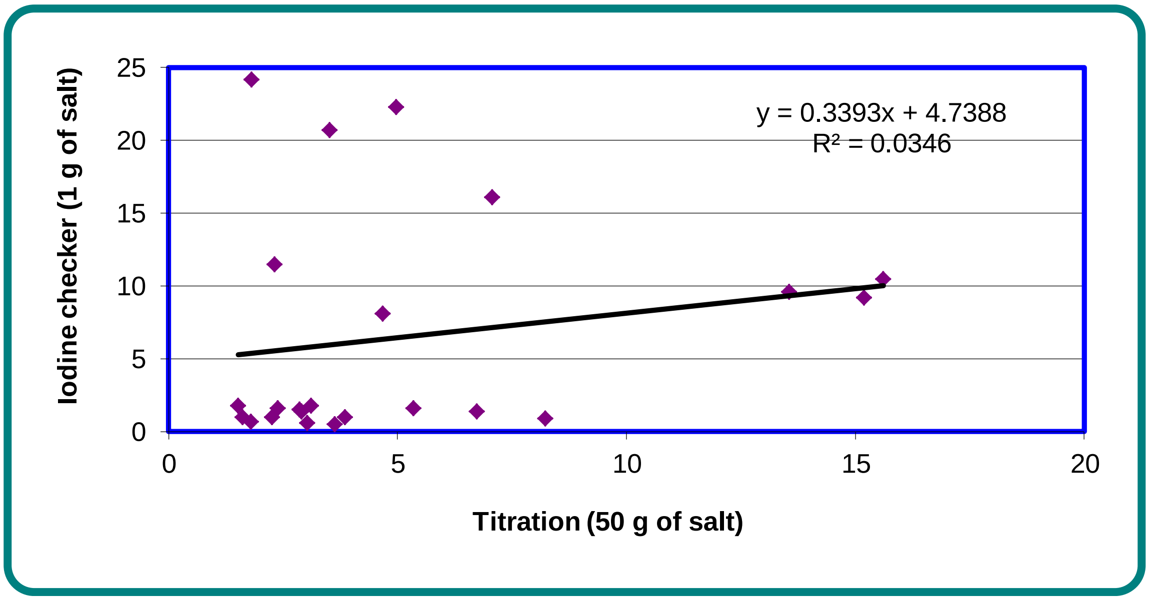

Figure 3. Association between iodine levels determined by titration (50 g of salt) and the "iodine checker" (1 g of salt) using coarse iodized salt from Cambodia.
Source: UNICEF-Cambodia and A2Z/USAID.

If only one gram of coarse salt is used, the performance of the "iodine checker" is similar to the Rapid Test Kit. Like the Rapid Test Kit, the "iodine checker" under this condition is going to produce only qualitative results, with good sensitivity, low specificity, and large proportion of false positive values. Therefore, the standards for iodized salt should include in their annexes specific reference of the sampling procedure, which should include the amounts of salt that should be dissolved for the quantitative determination of iodine.

The requirement of using sufficient quantities of salt for each determination is very difficult to apply for the epidemiological evaluation of the salt iodization program at households. At homes, very small amounts of salt are usually requested, and it would be meaningless to apply a quantitative method on them. This is the main reason of the large coefficient of variation that was assumed in the last section of **Table 9**. Indeed, the variation in most programs based on iodized coarse salt is much larger than 40%, and therefore the criterion of a minimum level for checking performance of the salt iodization program at households does not make sense. At households would be sufficient to check for the presence of iodine with the qualitative kit (which has very good sensitivity) in single samples to determine "coverage", and then to make a quantitative determination of iodine applying a suitable method (titrimetry, spectrophotometry, or any other that produce comparable results) on one or two composite samples per cluster in order to estimate the average content of iodine in salt. The average content will in turn will be used to estimate the supply of iodine to the population after multiplying this value by the salt intake patterns of the population.

Table 11 shows that the use of composite samples is appropriate and practical to estimate average iodine contents in salt. The analytical result obtained in composite samples reproduced very well the arithmetic averages calculated for the iodine contents of each one of the single salt samples that were combined in each composite sample.

Table 11
Comparison of the iodine content estimated chemically in composite samples with the arithmetic average of the iodine content of the single samples¶

Iodine content in single samples (mg I/kg)							Composite Samples	
1-5	6-10	11-15	16-20	10-25	S.D.	Average	[I] (mg/kg)	#
8.22	1.61	6.73	15.61	23.87	8.67	11.21	11.66	1
2.25	1.52	15.19	13.55	3.52	6.60	7.21	7.75	2
2.38	2.85	4.67	17.39	2.31	6.48	5.92	5.93	3
2.90	1.79	1.81	7.06	4.97	2.28	3.71	3.72	4
3.63	3.03	3.85	3.11	5.35	1.64	3.79	5.35	5

¶ Quantitative iodine determinations using the titrimetric method in 50 grams of dissolved salt.
Source: UNICEF-Cambodia and A2Z/USAID.

In summary, the use of composite samples is a useful strategy to determine average content of iodine in salt collected at households; it produces reliable results and, by reducing the number of analytical test, decreases time and cost.

Use of composite samples for quality control

The quantitative determination of iodine in single salt samples is needed on raw and coarse salts for quality control purposes, because the high heterogeneity of the iodine content in that type of salt. **Table 8** shows that for the programs of Cambodia and Guatemala, the criteria for accepting that the program is performing "well" with 80% compliance (i.e. percentiles 10 to 90) should include single samples with no or very low iodine: from 0 to 62 mg/kg, and from 11 to 62 mg/kg, respectively. A standard with these values as the tolerable range of heterogeneity would be unreasonable.

This condition is depending not only on the inadequate nature of the fortified product or the inefficiency of the mixing process, but also on the resolution of the analytical assay. **Table 12** illustrates this situation for the content of fluoride in refined salt in Costa Rica, in the same samples that show a very good homogeneity for iodine.

Table 12
Variation in the iodine and fluoride contents in refined salt of Costa Rica

Premix application	Liquid spray	Dry premix.
Micronutrient	Iodine	Fluoride
n	35	32
Average	36.5	161.4
St. Deviation	5.4	54.9
Mean St. Error	1.4	9.7
P-0.5	22.6	20.0
P-5	27.6	71.1
P-10	29.6	91.1
P-90	43.4	231.7
P-95	45.4	251.7
P-99.5	50.4	302.8
C.V. (%)	14.8 %	34.0 %

Sources of data: [€] National Reference Center of Oral Health, INCIENSA, Costa Rica. 2009.

In the case of fluoride in the Costa Rican salt, the use of single samples is still possible, because a quantitative amount is still possible of being determined, would be estimated, but the tolerable range of heterogeneity is too large for supporting decisions about the quality of the mixing process. For this situation, the use of composite samples is also a good strategy.

The purpose of using composite samples is to reduce the tolerable range of heterogeneity to a level that still allows judging the quality of the mixing process. Thus, the minimum number of single samples to prepare each composite sample should be determined. It is only necessary to reduce the coefficient of variation to less than 30%; blending too many single samples is going to estimate the average content, but may hide errors in the process. In any case, details about when and how to use composite samples should be included in the corresponding standard.

Table 13 shows the results of preparing composite samples for iodized coarse salt in Guatemala. The heterogeneity (assessed through the coefficient of variation) is being reduced at increasing the number of single samples per composite sample. Based on the results of this table, one can conclude that for the Guatemalan coarse salt, each composite sample should be prepared by mixing 5 single samples. Obviously, presence of iodine should be checked in each single sample using a qualitative test before mixing it in the composite sample.

Table 13

Reducing heterogeneity of the iodine content in coarse salt samples by preparing composite samples¶

# Single samples in composite samples	1	2	3	4	5
n	43	21	14	10	8
Average	26.1	26.0	26.0	26.5	26.5
St. Deviation	11.8	10.1	7.8	6.7	4.4
Mean St. Error	1.8	2.2	2.1	2.1	1.6
P-0.5	-4.2	-0.1	5.9	9.1	15.1
P-5	6.8	9.4	13.2	15.4	19.2
P-10	11.1	13.0	16.0	17.9	20.8
P-90	41.2	39.0	36.0	35.1	32.1
P-95	45.5	42.7	38.9	37.6	33.7
P-99.5	56.5	52.1	46.1	43.8	37.8
C.V. (%)	45.2 %	38.9 %	30.0 %	25.5 %	16.6 %
% samples < 20 mg/kg	30 %	28 %	22 %	17 %	7 %

¶ Data from Liga de Protección al Consumidor (LIDECON), Guatemala. 2009.

Although iodization processes with coefficient of variations lower or around 15% do not require the use of composite samples for quality control purposes, they may still take advantage of this strategy to reduce the number of chemical analysis, and at the same time increasing the number of single samples that are tested, because more samples could be checked using a qualitative assay. **Table 14** shows the situation for the Costa Rican salt. This table demonstrates that similar results are obtained by analyzing many single samples or by analyzing a few composite samples; the averages are similar, as well as the mean standard error to interpret them. As in the Guatemalan case, the presence of iodine in each single sample should always be confirmed using a qualitative test.

Table 14

Results of composite samples when single samples are homogeneous¶

# Single samples in composite samples	1	2	3	4	5
n	35	17	11	8	7
Average	36.5	36.2	36.3	36.0	36.5
St. Deviation	5.4	3.4	2.2	2.4	2.0
Mean St. Error	0.9	0.8	0.7	0.9	0.7
C.V. (%)	14.7 %	9.3 %	6.0 %	6.7 %	5.4 %

¶ Data from the National Reference Center of Oral Health, INCIENSA, Costa Rica. 2009.

In summary, use of composite samples allows estimating the most important reference value in food control and inspection: the average content. Nevertheless, detection of the presence of iodine in single samples by using a qualitative test is still needed in order to check that the fortification process is being applied without interruptions. Use of composite samples can make easier and less expensive the food control practices of the salt iodization programs, and they are necessary for coarse salts, or small amounts of samples collected at homes, in which the tolerable range of heterogeneity might be too large for using single samples.

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