Assessment of iodine deficiency disorders and monitoring their elimination

A GUIDE FOR PROGRAMME MANAGERS

Third edition

World Health Organization

unicef

ICCIDD

Assessment of iodine deficiency disorders and monitoring their elimination

A GUIDE FOR PROGRAMME MANAGERS

Third edition

World Health Organization

WHO Library Cataloguing-in-Publication Data

Assessment of iodine deficiency disorders and monitoring their elimination : a guide for programme managers. – 3rd ed.

1.Iodine – deficiency. 2.Nutrition disorders – prevention and control. 3.Sodium chloride, Dietary – therapeutic use. 4.Nutrition assessment. 5.Nutrition policy – standards. 6.Guidelines. I.World Health Organization.

ISBN 978 92 4 159582 7 (NLM classification: WK 250)

This report contains the collective views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization.

Cover photo by Carlos Gaggero
Designed by minimum graphics
Printed in France

Contents

List of tables

List of figures

Abbreviations

BSA	Body surface area
HDPE	High-density polyethylene
HIV	Human immunodeficiency virus
ICCIDD	International Council for Control of IDD
IDD	Iodine deficiency disorders
IIH	Iodine-induced hyperthyroidism
IQ	Intelligence quotient
ISO	International Organization for Standardization
LDPE	Low-density polyethylene
LQAS	Lot quality assurance sampling
MICS	Multiple indicator cluster survey
N	Number
P	Percentile
PAMM	Programme Against Micronutrient Malnutrition
ppm	Parts per million
PPS	Proportionate to population size
RTK	Rapid test kits
SD	Standard deviation
SOWC	State of the world's children
T3	Triiodothyronine
T4	Thyroxin
Tg	Thyroglobulin
TGR	Total goitre rate
TSH	Thyroid stimulating hormone
UI	Urinary iodine
UN	United Nations
UNICEF	United Nations Children's Fund
US	United States of America
USI	Universal salt iodization
WHO	World Health Organization
µg	Micrograms (millionths of a gram)

Preface

Knowledge obtained over the last decade through research and practical use of the *Assessment of Iodine Deficiency Disorders and Monitoring their Elimination* guidelines, edited by WHO in collaboration with UNICEF and ICCIDD, has validated new indicators with public health significance. This progression has necessitated this new, third edition of these guidelines.

New indicators of thyroid function have been included, such as measurement of thyroid volume by ultrasound, as there are new international reference standards, and the measurement of serum thyroglobulin for which thresholds have been validated to differentiate normal status from deficiency. In addition, new iodine requirements for pregnant and lactating women have been provided, which results in an increased median urinary iodine concentration to define a public health problem in pregnant women. Lastly, the programmatic criteria to assess progress towards the elimination of iodine deficiency were revised in light of experience accumulated in the field.

As a first step to revise the guidelines, experts on iodine were commissioned to review and update various sections of the previous version of the document published in 2000. The ensuing updated sections were then used as the background document for an expert technical consultation held in Geneva, Switzerland from 22–23 January 2007, with the objective of conducting a critical analysis of the revised sections, and of subsequently developing a new document. This revised version was then distributed widely; not only to participants in the consultation, but also to other experts in IDD prevention and control whose helpful comments and suggestions are reflected herein.

Salt iodization is currently the most widely used strategy to control and eliminate IDD. However, to be fully effective in correcting iodine deficiency, salt must not only reach the entire affected population (in particular those groups that are the most susceptible, pregnant women and young children) but it also needs to be adequately iodized. This is why these guidelines emphasize process indicators; in particular, those related to the monitoring of iodized salt at the production and/or impor-

tation levels, and iodized salt use in the population. Such monitoring necessarily involves both governments and the salt industry, requiring close collaboration between the public and private sectors.

Impact indicators are meant to assess the magnitude of IDD as a public health problem and to monitor the effects of the intervention on the iodine status of a population. This manual recommends the use of urinary iodine to monitor impact. Blood TSH and thyroglobulin may also be useful for assessing impact, but their use is still limited due to their cost. The measurement of thyroid size by palpation or ultrasound was useful initially, but is less useful once salt iodization is established. For each impact indicator, this manual provides information on biological features, methods of measurement, and criteria for selecting those methods and the interpretation of results. The statistical methodology employed to carry out a survey is also described.

IDD elimination is achieved only if salt iodization can be sustained. The final chapter addresses this issue, and provides criteria to determine whether a programme of IDD control is sustainable.

This document is intended primarily for managers of national programmes dealing with the prevention and control of micronutrient malnutrition, as well as for policy makers. We hope that the information included in this manual will be useful, and that it will contribute to our common goal of the elimination of IDD.

Bruno de Benoist
Coordinator
Micronutrient Malnutrition Unit
Department of Nutrition for Health Development
World Health Organization

Gerald Burrow
Chairman
International Council for Control of Iodine Deficiency Disorders

Werner Schultink
Chief, Nutrition Section
United Nations Children's Fund

1 Introduction

1.1 About this manual

The importance of iodine deficiency disorders (IDD)

Iodine deficiency, through its effects on the developing brain, has condemned millions of people to a life of few prospects and continued underdevelopment. On a worldwide basis, iodine deficiency is the single most important preventable cause of brain damage.

People living in areas affected by severe iodine deficiency may have an intelligence quotient (IQ) of up to 13.5 points below that of those from comparable communities in areas where there is no iodine deficiency (*1*). This mental deficiency has an immediate effect on child learning capacity, women's health, the quality of life in communities, and economic productivity.

On the other hand, IDD are among the easiest and least expensive of all nutrient disorders to prevent. The addition of a small, constant amount of iodine to the salt that people consume daily is all that is needed. The elimination of IDD is a critical development issue, and should be given the highest priority by governments and international agencies.

Recognizing the importance of preventing IDD, the World Health Assembly adopted in 1991 the goal of eliminating iodine deficiency as a public health problem. In 1990, world leaders had endorsed this goal when they met at the World Summit for Children at the United Nations. It was reaffirmed by the International Conference on Nutrition in 1992. In 1993, WHO and UNICEF recommended universal salt iodization (USI)[1] as the main strategy to achieve elimination of IDD (*2*). In 2005, the importance of IDD elimination was again recognized when the World Health Assembly adopted a resolution committing to reporting on the global IDD situation every three years.

Since 1990, there has been tremendous progress in increasing the proportion of dietary salt which is adequately iodized. As a result, many countries have achieved, or are now on the threshold of achieving IDD

[1] Universal salt iodization (USI) is defined as when all salt for human and animal consumption is iodized to the internationally agreed recommended levels.

elimination. In those countries, the emphasis will shift to ensuring that these achievements are permanently sustained.

Objectives of this manual

Progress towards the elimination of IDD can only be demonstrated if it is measured. This requires the selection of appropriate indicators of both process and impact.

Sound techniques are needed in order to reliably measure indicators of IDD, and these techniques must be applied using suitable epidemiological methods that take target population, geographical area, and timing of survey factors into account.

Finally, the results should be presented in a format that is easily interpreted and comparable to those from other regions or countries.

Specifically, the objectives of this manual are to describe:

- The indicators used in assessing the magnitude of IDD at different stages of the USI programme, and in monitoring and evaluating salt iodization and any other interventions for the control of IDD and their impact;
- How to use and apply these indicators in practice;
- How to assess whether iodine deficiency has been successfully eliminated;
- How to judge whether achievements can be sustained and maintained for the decades to come.

Target audience

This book is aimed primarily at IDD programme managers and others in government who are involved in the implementation of IDD control programmes. It is also aimed at the salt industry and all others involved in IDD elimination.

Origins of this book

This is the second revised version of the original document, which was entitled "Indicators for assessing Iodine Deficiency Disorders and their control through salt iodization" (*3*). That document was produced following a consultation held in Geneva in November 1992.

After a considerable amount of new information on the identification, prevention and control of IDD had been generated, and the public health focus regarding this significant problem had shifted to emphasize the importance of the process indicators, a second revision of this book was published in 2001 based on a Consultation held in Geneva in 1999. It involved experts on IDD from all three partner organizations,

WHO, UNICEF, and ICCIDD, representing all regions of the world (see Annex 7).

In 2007, experts and the three partner organizations gathered again for a consultation in Geneva to update the manual to include new knowledge, including new iodine requirements in pregnant and lactating women, refinements in monitoring household iodized salt use, and information on measuring thyroglobulin as an impact indicator.

1.2 Definitions

Iodine deficiency disorders (IDD) refer to all of the consequences of iodine deficiency in a population that can be prevented by ensuring that the population has an adequate intake of iodine. For further details, see Chapter 2.

Indicators are used to help describe a situation that exists, and can be used to track changes in the situation over time. Indicators are usually quantitative (i.e. measurable in some way), but they may also be qualitative.

Monitoring is the process of intermittently collecting and analysing information about a programme for the purpose of identifying problems, such as non-compliance, and taking corrective action so as to meet stated objectives.

Evaluation is a process that attempts to determine as systematically and objectively as possible the relevance, effectiveness, and impact of activities relevant to their objectives (*4*).

1.3 Monitoring and evaluating IDD control programmes

Monitoring of any health intervention is essential to ensure that it is functioning as planned and to provide information needed to take corrective action if necessary. In addition, periodic evaluation of health programmes is necessary to ensure that overall goals and objectives are being met.

Salt iodization programmes, like any other health interventions, therefore require an effective system for monitoring and evaluation. The challenge is to apply the IDD indicators using valid and reliable methods while keeping costs to a minimum. To this end, it is essential to clearly formulate questions to which answers are needed, since the methods used to gather data may be very different. Important questions that will need to be answered include:

- Is all the salt that is being produced or imported iodized to the country's requirements?
- Is adequately iodized salt reaching and being used by the population in countries at risk of iodine deficiency?

- Are there any groups in the population that are not reached by iodized salt, and thus require attention?
- What is the relative contribution to iodine intake from table salt versus iodized salt used in the food industry?
- What impact are salt iodization and other interventions having on the iodine status of the population?

In some countries there is still inadequate information on IDD, and programmes have not yet been implemented. Here the questions may be:

- Have IDD been eliminated as a public health problem?
- What is the prevalence of IDD in specific population groups (pregnant women, infants) based on geographical, administrative, or physiological criteria?
- What steps are necessary to address IDD, such as a salt situation analysis?

Answering these questions requires different approaches to gathering data. It is therefore very important to be quite clear about the purpose of a particular survey. See Annex 6 for guidelines to assess IDD national programmes.

1.4 Indicators described in this manual

This manual describes the various indicators which are used in monitoring and evaluating IDD control programmes. The indicators are divided into three main groups:

1. **Process indicators:** indicators to monitor and evaluate the salt iodization process.

   These indicators reflect monitoring salt iodine content at the production/importation site and at the household level, and in some instances, checking at the retail/wholesale level. Consideration should also be given to assessing the use of iodized salt in the food industry.

2. **Impact indicators:** indicators to assess iodine status and to monitor and evaluate the impact of salt iodization on the population.

   Median urinary iodine is the main indicator to be used to assess iodine status of a population. Goitre assessment by palpation or by ultrasound may be useful in assessing thyroid function, but is difficult to interpret once salt iodization has started. The measurement of thyroid stimulating hormone (TSH) levels in neonates where a screening

programme is in place, and of thyroglobulin in school-age children where feasible are both useful indicators of thyroid function.

Once a salt iodization programme has been initiated, the principal impact indicator recommended is the population median urinary iodine level. Changes in goitre prevalence lag behind changes in iodine status, and therefore cannot be relied upon to accurately reflect current iodine intake.

3. **Sustainability indicators:** indicators to assess whether iodine deficiency has been successfully eliminated and to judge whether achievements can be sustained and maintained for the decades to come.

   This involves a combination of median urinary iodine levels in the population, availability of adequately iodized salt at the household level, and a set of programmatic indicators which are regarded as evidence of sustainability (see Chapter 6).

2 IDD and their control, and global progress in their elimination

2.1 The iodine deficiency disorders

Recommended iodine intake

UNICEF, ICCIDD (*5*), and WHO (*6*) recommend that the daily intake of iodine should be as follows:

- 90 μg for preschool children (0 to 59 months);
- 120 μg for schoolchildren (6 to 12 years);
- 150 μg for adolescents (above 12 years) and adults;
- 250 μg for pregnant and lactating women.

The iodine deficiency disorders

Iodine deficiency occurs when iodine intake falls below recommended levels. It is a natural ecological phenomenon that occurs in many parts of the world. The erosion of soils in riverine areas due to loss of vegetation from clearing for agricultural production, overgrazing by livestock, and tree-cutting for firewood results in a continued and increasing loss of iodine from the soil. Groundwater and foods grown locally in these areas lack iodine.

When iodine intake falls below recommended levels, the thyroid may no longer be able to synthesize sufficient amounts of thyroid hormone. The resulting low level of thyroid hormones in the blood (hypothyroidism) is the principal factor responsible for damage to the developing brain and other harmful effects known collectively as "iodine deficiency disorders" (*7*). The adoption of this term emphasizes that the problem extends far beyond simply goitre and cretinism (Table 1).

The most critical period is from the second trimester of pregnancy to the third year after birth (*8*,*9*). Normal levels of thyroid hormones are required for optimal development of the brain. In areas of iodine deficiency, where thyroid hormone levels are low, brain development is impaired. In its most extreme form, this results in cretinism, but of much greater public health importance are the more subtle degrees of brain damage and reduced cognitive capacity which affects the entire population. As a result, the mental ability of ostensibly normal children and

Table 1 The spectrum of iodine deficiency disorders (IDD)[a]

PHYSIOLOGICAL GROUPS	HEALTH CONSEQUENCES OF IODINE DEFICIENCY
All ages	Goitre Hypothyroidism Increased susceptibility to nuclear radiation
Fetus	Spontaneous abortion Stillbirth Congenital anomalies Perinatal mortality
Neonate	Endemic cretinism including mental deficiency with a mixture of mutism, spastic diplegia, squint, hypothyroidism and short stature Infant mortality
Child and adolescent	Impaired mental function Delayed physical development Iodine-induced hyperthyroidism (IIH)
Adults	Impaired mental function Iodine-induced hyperthyroidism (IIH)

[a] Adapted from BS Hetzel, 1983 (*7*).

adults living in areas of iodine deficiency is reduced compared to what it would be otherwise.

Thus, the potential of a whole community is reduced by iodine deficiency. Where the deficiency is severe, there is little chance of achievement and underdevelopment is perpetuated. Indeed, in an iodine-deficient population, everybody may seem to be slow and rather sleepy. The quality of life is poor, ambition is blunted, and the community becomes trapped in a self-perpetuating cycle. Even the domestic animals, such as village dogs, are affected. Livestock productivity is also dramatically reduced (*10*).

Identification of the occurrence of IDD

In the past, the likely occurrence of iodine deficiency in a given region was regarded as being signalled by certain geographical characteristics. These include mountain ranges and alluvial plains, particularly at high altitude and at considerable distance from the sea. This occurrence was confirmed by a high prevalence of goitre in the resident population.

However, the greater use of urinary iodine estimation and other methods for assessing iodine deficiency (see Chapter 4) has demonstrated that IDD can and does occur in many areas where none of these conditions are met. Indeed, significant iodine deficiency has been found:

- Where the prevalence of goitre is low and doesn't suggest a problem;

- In coastal areas;
- In large cities;
- In highly developed countries;
- Where iodine deficiency has been considered to have been eliminated.

In recognition of a much wider occurrence of IDD than previously thought, certain countries have come to regard the whole country as being at risk of iodine deficiency and therefore the entire population as a target for IDD control with iodized salt. The need for continued vigilance is underlined, as is the importance of all countries carrying out periodic urinary iodine surveys.

2.2 Correction of iodine deficiency

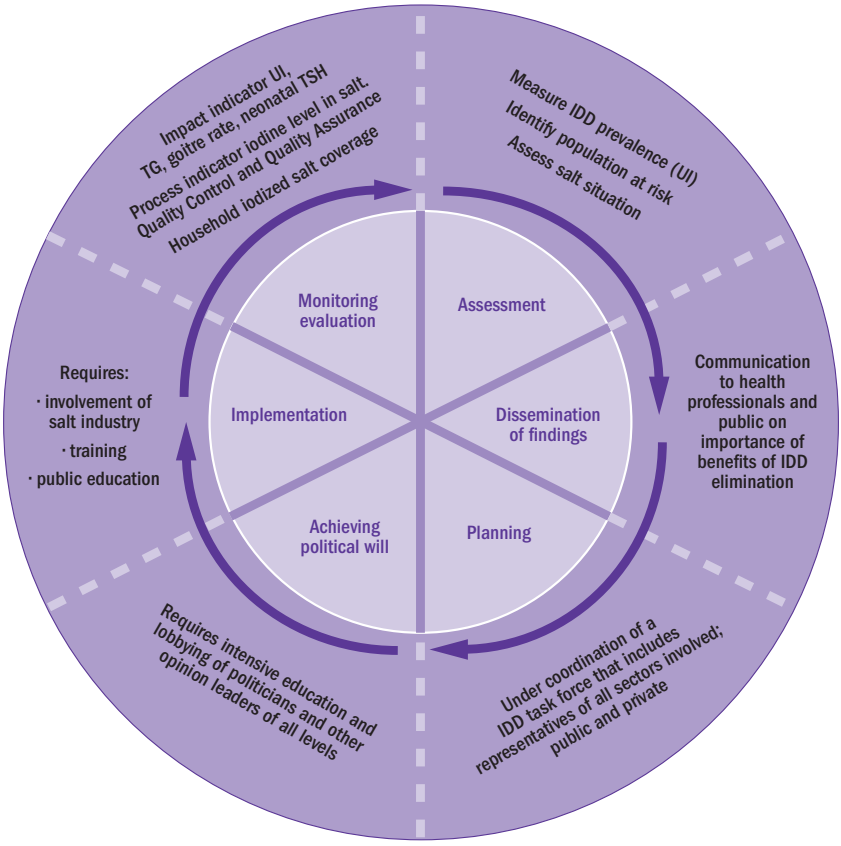
Administrative arrangements

The national body responsible for the management of the IDD control programme should operate with a process model. A useful example of such a process model is known as the "wheel" (Figure 1).

This cycle, which is described in details following, shows the different elements of national IDD control. The successful achievement of this overall process requires the establishment of a national IDD control commission, with the ability to influence the political and legislative process. Several elements included within this model reflect programmatic needs that will determine the sustainability of the programme into the future (see Chapter 6). The model involves six components, clockwise in the hub of the wheel.

1. **Assessment** and periodic evaluation of the situation requires prevalence surveys of iodine status, including measurement of urinary iodine levels and an analysis of the salt situation. Most countries have completed this step, and now need to do periodic reassessment.
2. **Dissemination of findings** implies **communication** to health professionals and the public, so that there is full understanding of the IDD problem, the importance of using iodized salt and the potential benefits of iodine deficiency elimination. This needs to be an ongoing activity.
3. **Planning:** Development of a plan of action includes the establishment of an intersectoral task force on IDD including the salt industry and the formulation of a strategy document on achieving the elimination of IDD. The task force will need to remain active to ensure programme sustainability.
4. **Achieving political will** requires intensive education and lobbying of politicians and other opinion leaders on an ongoing basis.

Figure 1 National IDD control programming cycle[a]



[a] Adapted from BS Hetzel, 1994 (*11*).

5. **Implementation** needs the full involvement of the salt industry. Special measures, such as negotiations for monitoring and quality control of imported iodized salt, are required. It is also necessary to ensure that iodized salt delivery systems reach all affected populations, including those in greatest need. In addition, the establishment of cooperatives for small producers, or restructuring to larger units of production, may be needed. Implementation requires training at all levels in management, salt technology, laboratory methods, and communication.
6. **Monitoring and evaluation** require the establishment of an efficient system for the ongoing and routine collection of relevant data, including measures of salt iodine quality assurance and household use, and measures of programme performance.

The multidisciplinary orientation required for a successful programme poses special difficulties in implementation. Experience indicates that particular problems often arise between health professionals and the salt industry – with their different professional orientations. There is need for mutual education about the health and development consequences of iodine deficiency, and about the problems encountered by the salt industry in the continued production of high quality iodized salt. Such teamwork is required in order to achieve sustainability.

2.3 Universal salt iodization (USI)

In 1994, a special session of the WHO and UNICEF Joint Committee on Health Policy recommended USI as a safe, cost-effective, and sustainable strategy to ensure sufficient intake of iodine by all individuals (*2*). In nearly all countries where iodine deficiency occurs, it is now well recognized that the most effective way to achieve the virtual elimination of IDD is through USI.

USI involves the iodization of all human and livestock salt, including salt used in the food industry. Adequate iodization of all salt will deliver iodine in the required quantities to the population on a continuous and self-sustaining basis.

The additional cost of iodine fortification in the process of salt production should eventually be borne by the consumer, but is negligible. This will greatly assist sustainability.

National salt iodization programmes are now implemented worldwide and have followed a common pattern of evolution, which includes the following phases:

- **Decision phase:** This phase involves making the decision for USI supported by industry, backed by standards and regulation, and supported by an implementation plan.
- **Implementation phase:** This phase ensures the infrastructure for iodization and packaging of all human and livestock salt, and supports that infrastructure with quality assurance measures, communication and demand creation, regulation, and enforcement.
- **Consolidation phase:** Once the goal of USI is achieved, it needs to be sustained and assessed through ongoing process and impact monitoring, as well as periodic evaluation; the latter may include international multidisciplinary teams.

A successful salt iodization programme depends upon the implementation of a set of activities at the national level by various sectors:

- Government ministries (legislative and justice, health, industry, agriculture, education, communication, and finance);
- Salt producers, salt importers and distributors, food manufacturers;
- Concerned civic groups, including consumer associations; and
- Nutrition, food, and medical scientists, and other key opinion makers.

Opening the channels of communication and maintaining commitment and cooperation across these various groups is perhaps the greatest challenge to reaching the IDD elimination goal and sustaining it for the long term.

Salt producers and distributors are critical in ensuring that IDD is eliminated. Protecting consumers requires that a framework be established to ensure quality control of the production of iodized salt, as well as the distribution of adequately packaged and labelled iodized salt. The establishment of this framework is the main responsibility of the government.

Ensuring a demand for the product and understanding the reason for insisting upon only iodized salt is a shared responsibility of the private sector and government. Establishment of iodization as the norm and ensuring customer demand will determine the success and sustainability of the programme.

USI, which ensures that all salt for human and animal consumption is adequately iodized, has been remarkably successful in many countries. Over 30 countries have achieved the goal of USI (>90% of households using iodized salt), and many others are on track. Most countries that have failed to achieve coverage over 20% have conflict situations that hinder all health efforts. In rare instances, it may happen that salt iodization efforts are unable to meet the requirement of women during pregnancy, exposing the progeny to potential developmental risks. In such situations, while efforts to improve the salt iodization programme continue, iodine supplementation may be considered for both pregnant women and children less than two years of age as a daily oral dose of iodine or a single oral dose of iodized oil every six to 12 months (*6*).

There is much evidence that correction of iodine deficiency has been followed by a "coming to life" of a community suffering from the effects on the brain of hypothyroidism due to iodine deficiency. Such an increase in vitality is responsible for improved learning by schoolchildren, improved work performance of adults, and a better quality of life. The economic significance of the prevention of iodine deficiency disorders needs to be clearly understood (*10*). Education about these

basic facts has to be repeated, with the inevitable changes over time in Ministries of Health and the public heath community and salt producers. Otherwise, a successful programme will lapse, as has occurred in a number of countries.

2.4 Iodine supplementation

In some countries and areas with insufficient access to iodized salt for vulnerable groups of the population, additional temporary strategies need to be considered to ensure optimal iodine nutrition for these groups while strengthening the salt iodization programmes to reach universal coverage (*12*). In particular, each country should assess the current situation of its salt iodization programme to identify national or subnational problems and to update its strategies and action plans. The most vulnerable groups, pregnant and lactating women, should be considered for supplementation with iodine until the salt iodization programme is scaled up. For children seven to 24 months of age, either supplementation or use of iodine-fortified complementary foods may be a possible temporary public health measure.

Table 2 Recommended dosages of daily and annual iodine supplementation (6)

POPULATION GROUP	DAILY DOSE OF IODINE SUPPLEMENT (µg/d)	SINGLE ANNUAL DOSE OF IODIZED OIL SUPPLEMENT (mg/y)
Pregnant women	250	400
Lactating women	250	400
Women of reproductive age (15–49 y)	150	400
Children < 2 y[a,b]	90	200

[a] For children 0–6 months of age, iodine supplementation should be given through breast milk. This implies that the child is exclusively breastfed and that the lactating mother received iodine supplementation as indicated above.

[b] These figures for iodine supplements are given in situations where complementary food fortified with iodine is not available, in which case iodine supplementation is required for children of 7–24 months of age.

2.5 Sustainability

The progress made with IDD programs in the past decade reflects program maturation, and raises the question of how well these programs will be sustained into the future. IDD cannot be eradicated in one great global effort like smallpox and, hopefully, poliomyelitis, since these are infectious diseases with only one host: man. Once eliminated, they cannot come back. By contrast, IDD is a nutritional deficiency that is primarily the result of deficiency of iodine in soil and water. IDD can therefore return at any time after their elimination if program success is not sustained. Indeed, there is evidence that iodine deficiency is returning to some countries where it had been eliminated in the past (*13*).

Ideally, salt iodization programs ensure that there is adequate iodine

intake for the entire population, and the cost of iodization is included as part of the cost of doing business within the salt industry. The IDD program in this case simply needs to monitor the situation.

In reality, even with mature salt iodization programs with high coverage, programs remain vulnerable to changes in the salt industry, changes in political will, and changes in awareness or consumer acceptance. Thus, it is important to monitor the overall programmatic indicators as well as measures of salt iodization and impact to ensure that achievements are sustained.

Chapter 6 describes indicators of programme sustainability, including programmatic indicators. These fall generally into two categories: 1) measures of achievement in salt iodization and iodine status; and 2) measures of ongoing political support and programme strength.

Monitoring achievement

Sustainable programmes must have a monitoring system that provides basic information about salt iodization, and about population iodine status. This includes monitoring the proportion of households using iodized salt adequate to meeting iodine intake needs, and assessing iodine status through population-based median urinary iodine levels. Monitoring needs to provide information on where problems may arise at different levels in the salt iodization production and distribution system that might contribute to less-than-optimal iodine status. This includes measures of quality assurance at production facilities, or measures of compliance with government requirements for imported salt.

When the monitoring system is robust, corrective measures are taken to ensure that iodized salt use provides adequate intake, and this is confirmed by periodic population assessment, including understanding the status of pregnant and lactating women.

Monitoring political support and program strength

Programmatic indicators have been used in the past to assess program strength and political commitment. These indicators have been revised, and are presented in Chapter 6. The indicators included reflect the degree to which political commitment is present and likely to continue, and different program elements critical to sustainability.

Sustainable programs should have mechanisms for oversight such as a multisectoral coalition. They should have political commitment reflected in budget allocation for program activities, and should have established the legislative and regulatory environment for salt iodization. There should be mechanisms for ongoing public education, and inclusion of information on IDD in education curricula. There should be

strong partnership with the salt industry, with evidence of their participation reflected in sound quality assurance measures and absorption of the cost of potassium iodate into the cost of doing business. And there should be, as noted above, mechanisms for adequate monitoring of salt and iodine status, periodic reporting, and establishment of an ongoing national database to track sustained progress.

With these elements in place, and with achievement of high iodized salt use, programs have reduced vulnerability, and are likely to be sustained.

2.6 Global progress in the elimination of IDD

Between 1994 and 2006, the number of countries that carried out a urinary iodine national survey increased to 94, and survey data on iodine deficiency now covers 91.1% of the world population. There is still no data for 63 countries, which together represent 8.9% of the world population. Out of the 130 countries with estimates based on surveys at both the national and subnational level, there are only 47 countries where IDD still remains as a public health problem, compared to 54 in 2004 and 126 in 1993. Iodine intake (reflected by the median urinary iodine concentration) in the other 83 countries is as follows: "adequate"[1] or "above recommended nutrient intakes"[2] in 76 countries; and "excessive"[3] in seven countries. About 31% (1 900.9 million) of the world population is estimated to have insufficient iodine intakes, with the most affected WHO regions being South-East Asia and Europe (Table 3).

It is currently estimated that 70% of households throughout the world have access to (and use) iodized salt (*14*).

2.7 Challenges for the future: consolidating the achievement

It is clear that, despite the great success in many countries, challenges remain for the future.

- As programmes mature, ensuring their sustainability is critical (see Chapter 6).
- Continued and strong government commitment and motivation, with appropriate annual budgetary allocations to maintain the process, are essential to eliminate IDD.
- The salt industry should have the capacity to implement effective iodization, in particular with regard to compliance with the regulations and monitoring of quality assurance.

[1] UI between 100 µg/l and 199 µg/l
[2] UI between 200 µg/l and 299 µg/l
[3] UI above 300 µg/l

Table 3 Proportion of population and number of individuals in the general population (all age groups) with insufficient iodine intake by WHO regions during the period between 1994 and 2006,[a,b] and proportion of households using iodized salt[c]

WHO REGIONS	INADEQUATE IODINE NUTRITION		% HOUSEHOLD WITH WITH ACCESS TO IODIZED SALT
	PROPORTION (%)	TOTAL NUMBER (MILLION)[d]	
Africa	41.5	312.9	66.6
Americas	11.0	98.6	86.8
South-East Asia	30.0	503.6	61.0
Europe	52.0	459.7	49.2
Eastern Mediterranean	47.2	259.3	47.3
Western Pacific	21.2	374.7	89.5
Total	30.6	1 900.9	70

[a] Source: WHO global database on IDD: http://www.who.int/vmnis

[b] Based on surveys from 130 countries made available to WHO and carried out between January 1994 and December 2006.

[c] Country data on proportion of households using iodized salt based on UNICEF global database: http://www.childinfo.org and the State of the World's Children (SOWC) nutrition table http://www.unicef.org/sowc07/statistics/statistics.php

[d] UN population division. World population prospects: the 2004 revision. New York, United Nations, 2005.

- Monitoring systems should be in place to ensure specified salt iodine content, and should be coordinated with effective regulation and enforcement.
- Small-scale producers need to be included in this process to ensure that their products are also brought up to standard and that they deliver the right amount of iodine to the population. This is often best achieved by the formation of cooperatives working with a common distributor or any other business models that reduce the need for many small iodization units.
- The contribution of iodine from salt used in the food industry should be considered and monitored in the IDD elimination effort.
- In some countries, salt for animal consumption has not been included in the iodization programme and is not covered by legislation. Animal productivity is also enhanced by elimination of IDD. Ensuring this salt is iodized also means eliminating leakage of non-iodized salt into the market and resultant use by the general population.
- There are still numerous places in the world where iodized salt is not available. Identifying these areas and developing in them a market for iodized salt is critical to successful IDD elimination. This process includes creating consumer awareness and demand.

Ensuring the required daily intake of iodine to maintain normal brain function is as important as the provision of clean water. There is adequate knowledge and expertise to ensure the sustained elimination of IDD from the entire world.

3 Indicators of the salt iodization process

3.1 Factors that determine salt iodine content

Appropriate legislation and supportive regulations constitute the point of departure, or cornerstone, of the salt iodization programme within a country, providing the framework within which the salt iodization programme functions. Regulations specify the iodine content that should be in salt at the point of production for both human and animal consumption. Ideally, they should also outline specific activities for internal and external monitoring of the iodine in salt at the production or iodization sites, and encourage the use of the titration method, or an equivalent method, in order to provide precise measurements of the iodine content in salt. Ultimately, the regulatory environment represents the primary factor determining the iodine content of salt in any country.

Iodization of salt may take place inside the country at the main production or packing sites, or outside the country for those countries importing salt which has already been iodized. Salt is iodized by the addition of fixed amounts of potassium iodate (KIO_3) or potassium iodide (KI), as either a dry solid in a powder form or an aqueous solution, at the point of production. The amount of iodine added to salt should be in accordance with the regulation of the specific country where it will be used.

Iodate is recommended as fortificant in preference to iodide because it is much more stable (*15*,*16*).[1] The stability of iodine in salt and levels of iodization are issues of crucial importance to national health authorities and salt producers, as they have implications for programme effectiveness, safety, and cost.

The actual availability of iodine from iodized salt at the consumer level can vary over a wide range as a result of:

[1] Potassium iodate and potassium iodide have a long-standing and widespread history of use for fortifying salt without apparent adverse health effects. Potassium iodate has been shown to be a more suitable substance for fortifying salt than potassium iodide because of its greater stability, particularly in warm, damp, or tropical climates. In addition, no data are available indicating toxicological hazard from the ingestion of these salts below the level of Provisional Maximum Tolerable Daily Intake or PMTDI (*15*).

- Variability in the amount of iodine added during the iodization process;
- Uneven distribution of iodine in the iodized salt, within batches and individual bags, due to insufficient mixing of salt after the salt iodization process and/or variation in particle size of salt crystals in a batch or bag;
- The extent of loss of iodine due to salt impurities, packaging, and environmental conditions during storage and distribution;
- Loss of iodine due to food processing, and washing and cooking processes in the household;
- The availability of non-iodized salt from unconventional marketing sources.

In order to determine appropriate levels of iodization, an accurate estimate within countries is required of the losses of iodine occurring under local conditions between the time of iodization and the time of consumption. Control of moisture content in iodized salt throughout manufacturing and distribution, by improved processing, packaging and storage, is critical to the stability of the added iodine. Earlier estimates of losses have proven to be too high. With adequate packaging, losses are minimal under most conditions.

Iodized salt is usually distributed from the producer to the repackager, wholesaler, or retailer either in 50 kg bulk bags, or in consumer packages usually in 500 g or 1 kg polyethylene bags, although smaller or bigger sized packaging may also be used in some countries. Considerable losses of iodine (30–80%) resulting from high humidity and porous 50 kg packaging can be significantly reduced by the use of woven high-density polyethylene bags, with a continuous film insert, or laminate of low-density polyethylene bags, which provides a good moisture barrier.

The loss of iodine in salt from 500 g or 1 kg good quality polyethylene packaging appears to be less than previously thought. There is some evidence that the loss of iodine from salt packaged in good quality small polyethylene bags of about 75 to 80 micron thickness and containing 500 g salt, is generally less than 10% over an 18-month period, regardless of climatic conditions, fine or coarse texture, or whether the packaging had been opened or not.[1]

Recommendations

WHO/UNICEF/ICCIDD (*19*) recommend that, in typical circumstances, where the iodine lost from salt is 20% from production site to

[1] P Joost, personal communication, December 2006.

household, another 20% is lost during cooking before consumption, and average salt intake is 10 g per person per day, *iodine concentration in salt at the point of production should be within the range of 20–40 mg of iodine per kg of salt* (i.e., 20–40 ppm of iodine) in order to provide 150 μg of iodine per person per day (*17*). In countries where iodized salt is used in processed foods, the iodine content in salt should be closer to the lower end of this range and *vice versa*. The iodine should preferably be added as potassium iodate. Under these circumstances, median urinary iodine levels are expected to vary from 100–199 μg/l.

However, in some instances the quality of iodized salt is poor, or the salt is incorrectly packaged, or the salt deteriorates due to excessive long-term exposure to moisture, heat, and contaminants. Iodine losses from point of production to consumption can then be well in excess of 50%. In addition, salt consumption is sometimes much less than 10 g per person per day. As a result, actual iodine consumption may fall well below recommended levels, leading to low urinary iodine values for the population.

Regular surveys of median iodine urinary iodine levels should therefore be carried out in a nationally representative sample, along with measurements of the iodine content in salt and other sources of iodine in the diet to ensure that those levels are within the recommended range (100–199 μg/l). If not, the level of iodization of salt, and factors affecting the utilization of iodized salt, should be reassessed focusing on:

- The percentage of households using adequately iodized salt, i.e. salt containing 15 to 40 ppm of iodine at the household level;
- Production-level quality assurance;
- Factors affecting the iodine content of salt such as packaging, transport, and storage;
- Food habits in relation to salt intake and cooking practices.

National authorities should establish initial levels for iodization in consultation with the salt industry, taking into account expected losses and local salt consumption. Once iodization has commenced, regular surveys of salt iodine content and urinary iodine levels should be carried out to determine if the programme is having the desired effect.

Discussions and regulations about iodine levels in salt must clearly specify whether they refer to total content of iodine alone or to content of iodine compound (KIO_3 or KI).

It is recommended that the level be expressed as content of iodine alone. This approach emphasizes the physiologically important component (iodine) and facilitates comparison of its different forms.

Managing the iodized salt program in a country

For optimal management and functioning of the salt iodization programme in a country, a governmental health official, a national multisectoral coalition including all the partners involved in IDD control should take responsibility for coordinating and driving IDD-related activities in a country. Ideally, salt producers should be integral members of such commissions to jointly manage the various components of the salt iodization programme along with other role players such as government officials, international health agencies, consumer representatives, researchers, academics, etc. (See Section 2.4 and Figure 1.)

3.2 Determining salt iodine levels

The iodine content of salt can be determined quantitatively with the titration method, and qualitatively using rapid test kits. In addition to the titration method, technology has advanced the possibilities of analysing the iodine content of salt quantitatively using potentiometry or spectrophotometry. A simple and portable single wavelength spectrophotometer has recently been developed. These methods should yield similar quantitative results and should therefore be seen as equivalent methods.

All of these methods have certain advantages and disadvantages which generally influence the choice of method in specific circumstances. However, the titration method, which is by far the most commonly used quantitative method, still remains the reference method for determining the iodine concentration in salt. When other methods are used, it should be standardized against the titration method.

Facilities for titration are usually available in public health or food standards laboratories. In addition, ideally it should be standard practice for salt producers to use the titration method to routinely check the accuracy of their salt iodization at the site where salt is iodized. Titration should preferably be carried out on-site.

Titration method

The titration method requires the use of a small laboratory equipped with some basic instruments, such as a precision scale, a burette, glassware, and pipettes. Additional equipment, such as a magnetic stirrer and dispensers, will save time and optimize the analytical procedure.

Basically, iodine analysis by titration involves the preparation of four solutions and a standard solution which will last for variable periods of time, and then determining the iodine concentration in a salt solution by adding the pre-made reagents/solutions followed by the titration step. The iodine content of salt is determined by liberating iodine from salt and titrating the iodine with sodium thiosulfate using starch as an external

indicator. The method of liberating iodine from salt varies depending on whether salt is iodized with iodate or iodide. Details of the method are given in Annex 1. The procedure requires some training and laboratory skills, which can be conveyed to salt producers during a training course.

Titration, or an equivalent method, is preferred for accurate testing of salt batches produced in factories or upon their arrival in a country, and in cases of doubt, contestation, etc. This method is recommended for determining the concentration of iodine in salt at various levels of the distribution system where such accurate testing is required, and for testing when there are legal enforcement issues. Once the method is established, it is necessary to adhere to proper internal and external quality control measures.

Rapid test kits (RTK)

These are small 10–50 ml bottles containing a stabilized starch-based solution. One drop of the solution dripped on a teaspoon of salt containing iodine produces a blue/purple colour change. Colouration indicates that iodine is present. Different test kits are used depending on whether the salt is iodized with potassium iodate or iodide. In cases where there is suspicion of alkalinity in the salt sample, a 'recheck solution' is used. A drop of this solution is applied first, followed by the test solution (see Annex 1 for further details).

Recent evaluations of these kits showed that the colour reaction cannot be used as a quantitative indication of the iodine content (*18*). These kits should therefore be regarded as qualitative rather than quantitative and are most appropriate to indicate the presence or absence of iodine, but not of the concentration.

An advantage of rapid test kits is that they can be used in the field to give an immediate result. They are therefore useful to health inspectors and others who are involved in carrying out spot checks on food quality or household surveys. They may also play a valuable educational role, in that they provide a visible indication that salt actually is iodized. Accordingly, they can be used for demonstration purposes in schools and other institutions. However, because rapid test kits do not give a reliable estimate of iodine content (*19*,*20*), results must be backed up by titration.

There are a large number of test kits available on the market and many countries are currently producing their own. These kits are of variable quality and accuracy. UNICEF, with CDC and WHO, evaluated available test kits, and confirmed that the quality of the kits is quite variable. The evaluation resulted in recommendations for basic qualifications for kits, including instructions in English, recommended sample weight or size, shelf life, and directions for use.

National surveys to estimate the household coverage of adequately iodized salt using rapid test kits alone will only be able to determine the percentage of households using salt containing any iodine. However, in order to make inferences about the household coverage of adequately iodized salt, it is necessary to employ the quantitative titration method for iodine analysis, either on all salt samples or on a sub-sample. For the latter, a sub-sample of salt which has been analysed by the rapid test kit should also be analysed using the titration method for quantification. In this way, more reliable information on the adequacy of salt iodine and its likelihood of providing adequate iodine intake is available for tracking progress.

3.3 Indicators for monitoring at different levels

Ideally, monitoring the iodine content of salt should be conducted internally by the salt producer at the site of iodization, as well as externally by the health authorities. Internal monitoring should be done routinely, and external monitoring intermittently, and where feasible, both these monitoring systems should use the titration method for determining the iodine content of salt. The different steps of the monitoring process are summarized in Figure 2.

Internal monitoring by producers and distributors

A critical indicator of adequate salt iodization is a measure of the quality of iodized salt leaving production facilities. This may be reflected in a proportion of samples meeting government standards, or samples plotted regularly in a control chart to demonstrate that samples fall within the acceptable range.

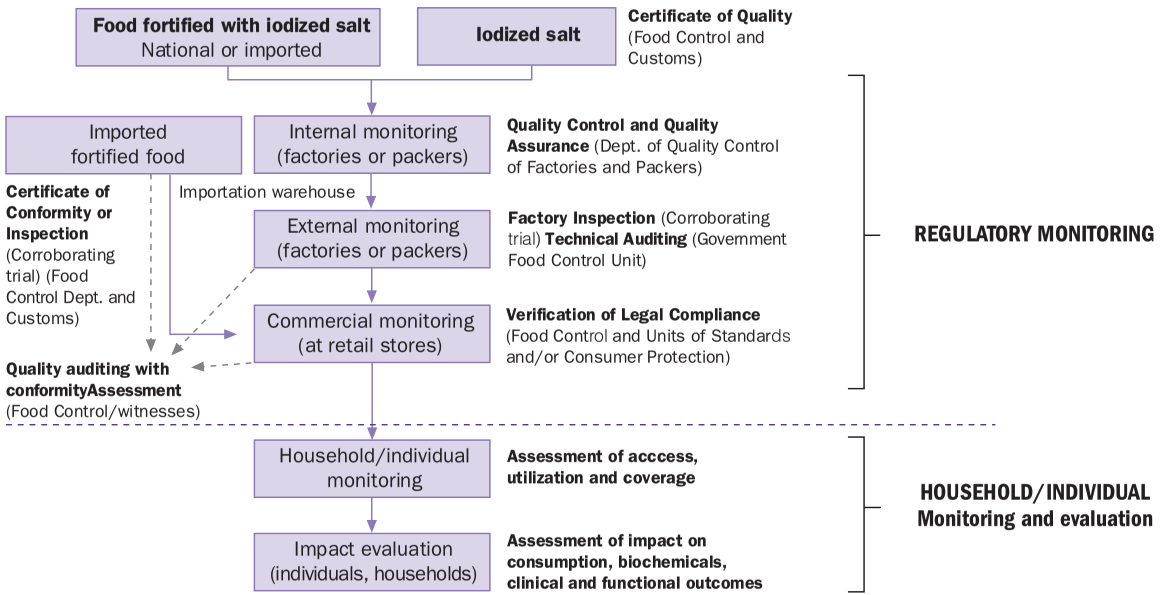
The Ministry of Industry, the Bureau of Standards, or Codex Alimentarius are useful reference sources for guiding producers in the process of iodizing salt. They can also establish the ultimate standards expected in the production of iodized salt.

Adherence to these manufacturing standards is perhaps the most important issue in the elimination of IDD. Therefore, the producer plays a pivotal role both in improving the accuracy of the iodization process and in reducing the considerable variations observed in iodine concentration in many countries.

Among the areas of greatest concern is the very important mixing or spraying step (*21*). This area not only includes the actual iodization method chosen by a production or packaging facility, but also the assurance that the producer closely adheres to the amount of time for mixing.

Salt samples taken from the production line should be regularly analysed by titration. The iodine concentration of each batch should be

Figure 2 A monitoring and evaluation system for salt iodization



Adapted from L. Allen (*17*).

checked at least once. Rapid test kits can be used more frequently to check that the addition of iodine has not been interrupted.

It is recommended that wherever possible adequate staff at a production plant should be trained and their skills standardized to determine the iodine concentration accurately using the titration method. Furthermore, key persons at each production site, including the managers, should be aware of the detrimental consequences of iodine deficiency and excess, as well as the health benefits of correctly iodized salt.

Results should be recorded and plotted in a quality assurance chart. When levels are not satisfactory, immediate corrective action should be taken and that action entered into the record book.

Because production methods and factory sizes vary so widely, it is beyond the scope of this manual to define this process in any greater detail. Whatever the method adopted, the process, combined with external quality assurance measures, should result in salt that has an iodine level within the upper and lower range established by regulations. In other words, internal and external quality control should ensure that the level of iodine is in the range stipulated by national regulations, that is both effective to control iodine deficiency and safe with regard to excessive iodine intake.

When importers and distributors procure salt, they have the responsibility to either ensure that it meets specifications as stipulated in the requirements, or to ensure that these are met before salt goes out to the wholesale or retail market. This implies that they should have a quality assurance system that includes salt iodine titration measurements.

If the salt they receive is not up to standard, they will need to have their own iodization facility. All salt should be distributed in polyethylene bags with appropriate labels.

External monitoring by governments

Legislation and regulations establish the authority of the government to ensure that iodized salt meets government standards, and external monitoring by the government is done under the guidance of relevant regulations.

Governments must have some method of periodically checking that salt producers are maintaining adequate quality assurance measures, and that salt leaving production facilities meets government standards. The main indicator for this level of monitoring is the proportion of samples taken that fall within the accepted range for iodine content. In addition, there may be a need for monitoring at the retail level to assess the presence of counterfeit salt or salt not meeting standards in the marketplace. Capacity for retail monitoring varies, and the purpose may be for checking the availability of different types of salt in the market or

for advocacy, rather than providing a robust proportion as is done with household sampling.

External monitoring is based upon the establishment of a law which mandates that all salt for human and – in many countries, animal – consumption is iodized. Details of implementation, inspection, and enforcement are usually set out in the regulations. Guidelines for developing regulations are available (*22*). It is crucial to state in the regulations the amount of iodine as potassium iodate or potassium iodide to be added at the point of production.

Other legal requirements covered in regulations should include packaging in polyethylene bags, labelling to identify the iodine level, and the name and address of the company packaging the salt. The regulation also needs to designate a government agency or department which will be responsible for a system of licensing producers, importers, and distributors, and inspecting their facilities.

That agency must also be responsible for periodically checking the quality assurance records that must be kept, and for spot-checking the salt for iodine content. Several monitoring and inspection systems have emerged in different countries.

Often this monitoring becomes a function of the Food and Drugs Bureau of the Health Ministry. In other countries, the Ministry of Industry, or Mines, or Agriculture has this responsibility. In the case of importation of salt, the Customs Authority is often in charge of checking the specifications in the importation document, and in some circumstances taking samples to check the iodine level in the salt.

As indicated above, the salt testing kits that are used by these government agencies should not be used in enforcement at the production level, as they often give both false positive and false negative results and the colour does not always accord well with titration. Government inspection systems need to have access to and use of salt titration in a standardized laboratory on a regular basis.

When countries first began to introduce salt iodization, inspection systems were used largely to guide salt iodization programme managers in identifying problems with salt iodization, and were rarely used for enforcement purposes. As countries increase the coverage to 50%, these systems should be strengthened and used for enforcement against those producers who fail to comply with the law.

It is often the less expensive non-iodized salt in the market that prevents the realization of the elimination of IDD. Indeed, as coverage of iodized salt increases, special efforts need to be made to identify the non-compliant importer, producer and distributor and systematically eliminate that problem. To this end, a national register of all salt pro-

ducers supplying iodized salt to the market and of distributors/traders of iodized salt will enhance the interaction with health authorities and will create the opportunity of efficient external monitoring and mutual exchange of relevant IDD information in an effort to strengthen the salt iodization programme. These measures provide a 'level playing field' for producers complying with the law.

Salt must be iodized indefinitely, or until it is demonstrated that an adequate iodine intake is available from other sources. The infrastructure, together with the annual budget to support the government inspection system, must be permanently established. In order to guarantee this, it is essential that inspection and collection of iodized salt samples be integrated into the existing food inspection system in the country. The contact between the health authority and the salt producers could be used to inform and educate the producer about IDD and the need for optimal iodization of salt. Feedback of salt iodine results are an important component of this interaction.

Monitoring at the household level

Just as knowing whether salt leaving production facilities is adequately iodized, knowing whether consumers are using that salt is critical to a programme's success. The main indicator for assessing household use is the proportion of households using salt with adequate iodine. This indicator must accurately reflect the situation for the population sampled, and the level of iodine in the salt sampled.

In the past, rapid test kits have been used to assess household coverage, whether used in surveys or in other data collection activities. Results were presented as the percentage of households using salt with no iodine and the percentage using 'adequately' iodized salt. However, the ability of the rapid test kits to distinguish 'adequately' iodized salt has since been recognized as limited, and titration is recommended for at least a sub-sample of salt samples used in monitoring at the household level.

Household level monitoring methods are described in Chapter 5. Household monitoring is usually done through surveys or other community-based methods.

For use with cross-sectional surveys, a household questionnaire concerning the use of iodized salt and qualitative testing of that salt using a rapid test kit has been employed successfully to determine overall coverage of iodized salt and to identify geographical gaps in the programme. However, it must be emphasized that where rapid test kits are used alone, it will only be possible to report on the proportion of households using salt with any iodine, and not the proportion using 'adequately' iodized salt, as has been done in the past.

Questions on iodized salt use and salt testing have been included in the UNICEF Multiple Indicator Cluster Surveys (MICS) and in the Demographic and Health Surveys. Some countries have successfully added household salt testing to other national surveys, e.g., to either nutrition surveys or surveys that collect key economic and census data. These surveys provide estimates of the proportion of the population with iodized salt coverage, and identify areas where there is low use of iodized salt and/or where all the salt is non-iodized.

National surveys can be costly, and a community-based method may be possible on a more regular basis. This approach may be organized in the community or through the schools, particularly in areas with high rates of school enrolment. Providing salt testing kits to environmental health officers, community midwives, nutrition officers, schoolteachers, mayors, and other government workers responsible for community health, has been helpful in this process. These approaches are very effective communication and awareness tools, particularly when this awareness is linked to action. This action could involve approaching the salt producers or distributors and directly requesting them to supply iodized salt.

Depending on the sampling methods and survey design adopted, it may be possible for monitoring at the household level to provide results that allow for visual representation of variations of coverage and provide a basis for targeting resources and focusing interventions in areas where they are most needed. Monitoring at this level should be followed by specific action to identify further reasons for low iodized salt usage, and should result in a range of actions to correct the problem.

Finally, the occurrence of parallel markets of non-iodized salt has frequently been a barrier to achieving USI. National cross-sectional household surveys and community monitoring have often been useful in identifying such salt and in developing strategies to address the problem.

4 Indicators of impact

4.1 Overview

Assessment of thyroid size by palpation is the time-honoured method of assessing IDD prevalence. However, because of the lack of sensitivity to acute changes in iodine intake, this method is of limited usefulness in assessing the impact of programmes once salt iodization has commenced. In this case, urinary iodine is the most useful indicator because it is reflective of the current intake of iodine in the diet (*23*).

Since most countries have now started to implement IDD control programmes, urinary iodine rather than thyroid size is emphasized in this manual as the principal indicator of impact. Thyroid size is more useful in baseline assessments of the severity of IDD, and also has a role in the assessment of the long-term impact of control programmes.

The introduction of ultrasonography for the assessment of thyroid size has been a significant development. In areas of mild to moderate IDD, measurement of thyroid volume using ultrasound is preferable to palpation for grading goitre. New international reference values for thyroid volume by ultrasound have recently become available and can be used for goitre screening in the context of IDD monitoring (*24*).

Two other indicators are included in this chapter: thyroid stimulating hormone (TSH), and thyroglobulin (Tg). While TSH levels in neonates are particularly sensitive to iodine deficiency, and although difficulties in interpretation remain, there is a potential future for the use of neonatal TSH in the identification of IDD and their control; although the cost of implementing a TSH screening programme is too high for most developing countries. Measurement of Tg in children is a sensitive indicator of iodine status and improving thyroid function after iodine repletion. A standardized dried blood spot Tg assay has been developed and can be used for assessing and monitoring iodine nutrition in the field (*25*).

4.2 Urinary iodine

Biological features

Most iodine absorbed in the body eventually appears in the urine. Therefore, urinary iodine excretion is a good marker of very recent dietary

iodine intake. In individuals, urinary iodine excretion can vary somewhat from day to day and even within a given day. However, this variation tends to even out among populations.

Studies have convincingly demonstrated that a profile of iodine concentrations in morning or other casual urine specimens (child or adult) provides an adequate assessment of a population's iodine nutrition, provided a sufficient number of specimens are collected. Round the clock urine samples are difficult to obtain and are not necessary.

Relating urinary iodine to creatinine, as has been done in the past, is cumbersome, expensive, and unnecessary. Indeed, urinary iodine/creatinine ratios are unreliable, particularly when protein intake – and consequently creatinine excretion – is low.

Feasibility

Acceptance of this indicator is very high, and casual urine specimens are easy to obtain. Urinary iodine assay methods are not difficult to learn or use, but meticulous attention is required to avoid contamination with iodine at all stages. Special laboratory areas, glassware, and reagents should be set aside solely for this determination.

In general, only small amounts (0.5–1.0 ml) of urine are required, although the exact volume depends on the method. Some urine should also be kept in reserve for replicate testing or for external quality control. Samples are collected in small cups and transferred to tubes, which should be tightly sealed with screw tops. They do not require refrigeration, addition of preservative, or immediate determination in most methods. They can be kept in the laboratory for months or more, preferably in a refrigerator to avoid unpleasant odour.

Evaporation should be avoided, because this process artificially increases the concentration. Samples may safely be frozen and refrozen, but must be completely defrosted before aliquots are taken for analysis.

Many analytical techniques exist, varying from very precise measurement with highly sophisticated instruments, to semi-quantitative 'low tech' methods that can be used in regional, country, or local laboratories. Most methods depend on iodine's role as a catalyst in the reduction of ceric ammonium sulfate (yellow colour) to the cerous form (colourless) in the presence of arsenious acid (the Sandell-Kolthoff reaction). A digestion or other purification step using ammonium persulfate or chloric acid is necessary before carrying out this reaction, to rid the urine of interfering contaminants.

A brief description of some of the methods introduced in this section is presented in the following pages.

Methods with ammonium persulfate (method A)

Small samples of urine (0.25–0.5 ml) are digested with ammonium persulfate at 90–110 °C; arsenious acid and ceric ammonium sulfate are then added. The decrease in yellow colour over a fixed time period is then measured by a spectrophotometer and plotted against a standard curve constructed with known amounts of iodine (*26*). This method requires a heating block and a spectrophotometer, which are both inexpensive instruments. About 100–150 subject samples can be run in a day by one experienced technician. Several versions of this method exist and details of one of these are given in Annex 3.

Methods with chloric acid (method B)

Chloric acid can be substituted for ammonium persulfate in the digestion step, and the colorimetric determination carried out as for method A (*27*). A disadvantage is the safety concern, because the chemical mixture can be explosive if residues dry in ventilating systems. Handling these chemicals in a fume cupboard and using a chloric acid trap when performing sample digestion is strongly recommended (see Annex 3).

Other methods

A modification of method B uses the redox indicator ferroin and a stopwatch instead of a spectrophotometer to measure colour change (*28*). Urine is digested with chloric acid and colour changes in batches of samples measured relative to standards of known iodine content. This places samples in categories (e.g., below 50 µg/l, 50–100 µg/l, 100–200 µg/l, etc.) that can be adjusted to desired levels. This method is currently being adapted to ammonium persulfate digestion.

Another, semi-quantitative method is based on the iodide-catalysed oxidation of 3,3',5,5'-tetramethylbenzidine by peracetic acid/H_2O_2 to yield coloured products that are recognized on a colour strip indicating three ranges: <100 µg/l, 100–300 µg/l, and >300 µg/l (*29*). Interfering substances are removed by pre-packed columns with activated charcoal. Analyses must be run within two hours, and the procedure requires the manufacturer's pre-packed columns.

In still another method, samples are digested with ammonium persulfate on microplates enclosed in specially designed sealed cassettes and heated to 110 °C (*30*). Samples are then transferred to another microplate and the ceric ammonium sulfate reduction reaction carried out and read on a microplate reader. Field tests are promising: up to 400 urine samples can be analysed in one day, depending on manufacturers' supplies.

Choice of method

Criteria for assessing urinary iodine methods are reliability, speed, technical demands, complexity of instrumentation, independence from sole-source suppliers, availability of high quality reagents, safety, and cost. The choice among the above and other methods depends on local needs and resources. Large central laboratories processing many samples may prefer 'high-tech' methods, while smaller operations closer to the field may find the simplest methods more practical.

Due to the potential hazards of chloric acid, method A (see Annex 3) using ammonium persulfate is currently recommended. It can adequately replace the chloric acid method, since the main difference is the substitution of ammonium persulfate for chloric acid in the digestion step. Results are comparable.

The other methods described above show promise but are not yet fully tested.

Quality control and reference laboratories

All laboratories should have clearly defined internal quality control procedures in place, and should be opened to external audit. In addition, all laboratories should participate in an external quality control programme in conjunction with a recognized reference laboratory. This is important because unrecognized iodine contamination has been a common occurrence in UI laboratories. An international network of resource laboratories (IRLI[1]) was established to fill this need. It closely collaborates with the Programme for Ensuring the Quality of Iodine Procedures (EQUIP) run by the Centers for Disease Control of the United States of America.[2]

Active efforts are now in progress, both to define performance criteria for laboratories and to develop a global system of reference laboratories. These reference laboratories will provide reliable measurements of urinary iodine, and will conduct technical training and supervision. This initiative is a major priority for ensuring sustainability of iodine sufficiency.

---

[1] IRLI Network was jointly established by CDC, WHO, UNICEF, ICCIDD and MI to identify laboratories to serve as effective resources for their regions, thus strengthening the capacity of laboratories throughout the world to accurately measure iodine in urine and salt. The network currently includes 12 laboratories (Australia, Belgium, Bulgaria, Cameroon, China, Guatemala, India, Indonesia, Kazakhstan, Peru, the Russian Federation, South Africa). http://iodinenetwork.net/Resources_Lab.htm

[2] EQUIP uses laboratory quality assurance as a tool for eliminating IDD worldwide. It is a CDC standardization program designed to provide urinary iodine laboratories with an independent assessment of their analytical performance. The program assists laboratories to monitor the degree of variability and bias in their urinary iodine assay. IRLI laboratories are invited to participate in the EQUIP program. http://www.cdc.gov/nceh/globalhealth/projects/labactivites.htm

Performance

Most of the above methods perform reliably, although some of the newer ones need further testing as of this date. With appropriate dilutions, they can be extended upward to examine whatever range is desired. The coefficient of variation is generally under 10% for all methods. Proper training is necessary but not complicated.

Since casual specimens are used, it is desirable to measure a sufficient number from a given population to allow for varying degrees of subject hydration and other biological variations among individuals, as well as to obtain a reasonably narrow confidence interval (see Annex 4). In general, 30 urine determinations from a defined sampling group are sufficient.

Interpretation

Simple modern methods make it feasible to process large numbers of samples at a low cost and to characterize the distribution according to different cut-off points and intervals. The cut-off points proposed for classifying iodine nutrition into different degrees of public health significance are shown in Table 4 and Table 5.

The median value for the sampled population is the most commonly assessed indicator. Urinary iodine values from populations are usually not normally distributed. Therefore, the median rather than the mean should be used as the measure of central tendency. Likewise, percentiles rather than standard deviations should be used as measures of spread. Frequency distribution curves can also be very useful for full interpretation, particularly if there is salt iodine level data available for the same population.

In children and non-pregnant women, median urinary iodine concentrations of between 100 µg/l and 299 µg/l define a population which has no iodine deficiency.[1] In addition, not more than 20% of samples should be below 50 µg/l. In non-pregnant, non-lactating women, a urinary iodine concentration of 100 µg/l corresponds roughly to a daily iodine intake of about 150 µg under steady-state conditions.

During pregnancy, median urinary iodine concentrations of between 150 µg/l and 249 µg/l define a population which has no iodine deficiency (*6*).

Establishing the ideal range of values for urinary iodine is difficult. Historically, schoolchildren were assessed by palpation, establishing a pre-intervention baseline for the prevalence of IDD. This population

[1] By definition, when the median is 100 µg/l, at least 50% of the samples will be lower than 100 µg/l.

Table 4 Epidemiological criteria for assessing iodine nutrition based on median urinary iodine concentrations of school-age children (≥6 years)[a]

MEDIAN URINARY IODINE (µg/l)	IODINE INTAKE	IODINE STATUS
< 20	Insufficient	Severe iodine deficiency
20–49	Insufficient	Moderate iodine deficiency
50–99	Insufficient	Mild iodine deficiency
100–199	Adequate	Adequate iodine nutrition
200–299	Above requirements	Likely to provide adequate intake for pregnant/lactating women, but may pose a slight risk of more than adequate intake in the overall population
≥300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)

[a] Applies to adults, but not to pregnant and lactating women.

Table 5 Epidemiological criteria for assessing iodine nutrition based on the median or range in urinary iodine concentrations of pregnant women[a]

POPULATION GROUP	MEDIAN URINARY IODINE CONCENTRATION (µg/l)	IODINE INTAKE
Pregnant women	< 150	Insufficient
	150–249	Adequate
	250–499	Above requirements
	≥ 500	Excessive[b]

[a] For lactating women and children <2 years of age a median urinary iodine concentration of 100 µg/l can be used to define adequate iodine intake, but no other categories of iodine intake are defined. Although lactating women have the same requirement as pregnant women, the median urinary iodine is lower because iodine is excreted in breast milk (*6*).

[b] The term "excessive" means in excess of the amount required to prevent and control iodine deficiency.

was also sampled for urinary iodine, thus establishing a normal range. This normal range has been extrapolated to the full population. It may be more logical to sample women of reproductive age, or adolescent girls – thus providing more information on populations that may include those with or on the verge of greater need. The upper limit of the recommended range for these populations reflects concern about the risk of hyperthyroidism when high levels are introduced to a previously endemic population.

Recent data have suggested that the normal range for pregnant and lactating women should reflect their additional need and the risk that these needs may not be met if population levels are too low. However, this leaves a relatively narrow range for a median UI level that will both meet the needs for pregnant/lactating women, and not be excessive for

the remainder of the population. This guide provides the best current estimates for the optimal values to meet the overall population needs.

Urinary iodine concentration is currently the most practical biochemical marker for iodine nutrition when carried out with appropriate technology and sampling. This approach assesses iodine nutrition only at the time of measurement, whereas thyroid size reflects iodine nutrition over months or years. Therefore, even though populations may have attained iodine sufficiency on the basis of median urinary iodine concentration, goitre may persist, even in children.

With rapid global progress in correcting iodine deficiency, examples of iodine excess are being recognized, particularly when salt iodization is excessive and poorly monitored (*20*). Tolerance to high doses of iodine is quite variable, and many individuals ingest amounts of several milligrams or more per day without apparent problems. The major epidemiological consequence of iodine excess is iodine-induced hyperthyroidism (IIH) (*24*,*31*). This occurs more commonly in older subjects with preexisting nodular goitres, and may occur even when iodine intake is within the normal range.

Iodine intakes above 300 μg/l per day should generally be discouraged, particularly in areas where iodine deficiency has previously existed. In these situations, more individuals may be vulnerable to adverse health consequences, including iodine-induced hyperthyroidism and autoimmune thyroid diseases.

In populations characterized by long-standing iodine deficiency and a rapid increase in iodine intake, median values for urinary iodine above 200 μg/l (and in pregnant women, above 250 μg/l) are not recommended because of the possible risk of iodine-induced hyperthyroidism. This adverse condition can occur during the 5 to 10 years following the introduction of iodized salt (*24*,*31*). Beyond this period of time, median values up to 300 μg/l have not demonstrated side-effects, at least not in populations with adequately iodized salt. In schoolchildren, urinary iodine concentrations >500 μg/l are associated with increasing thyroid volume, which reflects the adverse effects of chronic iodine excess (*32*).

4.3 Thyroid size

The traditional method for determining thyroid size is inspection and palpation. Ultrasonography provides a more precise and objective method.

Both methods are described below. Issues common to palpation and ultrasound are not repeated in the section on ultrasound.

4.3.1 Thyroid size by palpation

The size of the thyroid gland changes inversely in response to alterations in iodine intake, with a lag interval that varies from a few months to several years, depending on many factors. These include the severity and duration of iodine deficiency, the type and effectiveness of iodine supplementation, age, sex, and possible additional goitrogenic factors.

The term "goitre" refers to a thyroid gland that is enlarged. The statement that "a thyroid gland each of whose lobes have a volume greater than the terminal phalanges of the thumb of the person examined will be considered goitrous" is empiric, but has been used in most epidemiological studies of endemic goitre and is still recommended (see Table 6).

Feasibility

Palpation of the thyroid is particularly useful in assessing goitre prevalence before the introduction of any intervention to control IDD, but much less so in determining impact. Costs are associated with mounting a survey, which is relatively easy to conduct, and training of personnel. These costs will vary depending upon the availability of health care personnel, accessibility of the population, and sample size. Feasibility and performance vary according to target groups, as follows:

Neonates: It is neither feasible nor practical to assess goitre among neonates, whether by palpation or ultrasound. Performance is poor.

School-age children (6–12 years): This is the preferred group, as it is usually easily accessible. However, the highest prevalence of goitre occurs during puberty and childbearing age. Some studies have focused on children 8 to 10 years of age.

There is a practical reason for not measuring very young age groups. The smaller the child, the smaller the thyroid, and the more difficult it is to perform palpation.

If the proportion of children attending school is low, schoolchildren may not be representative (Annex 4). In these cases, spot surveys should be conducted among those who attend school and those who do not, to ascertain if there is any significant difference between the two.

Alternatively, children can be surveyed in households. For further discussion, see Chapter 5 on survey methods.

Adults: Pregnant and lactating women are of particular concern. Pregnant women are a prime target group for IDD control activities because they are especially sensitive to marginal iodine deficiency. Often they are relatively accessible given their participation in antenatal clinics. Women of childbearing age – 15 to 44 years – may be surveyed in households.

Technique

The subject to be examined stands in front of the examiner, who looks carefully at the neck for any sign of visible thyroid enlargement. The subject is then asked to look up and thereby to fully extend the neck. This pushes the thyroid forward and makes any enlargement more obvious.

Finally, the examiner palpates the thyroid by gently sliding their own thumb along the side of the trachea (wind-pipe) between the cricoid cartilage and the top of the sternum. Both sides of the trachea are checked. The size and consistency of the thyroid gland are carefully noted.

If necessary, the subject is asked to swallow (e.g. some water) when being examined – the thyroid moves up on swallowing. The size of each lobe of the thyroid is compared to the size of the tip (terminal phalanx) of the thumb of the subject being examined.[1] Goitre is graded according to the classification presented in Table 6.

Table 6 Simplified classification of goitre[a] by palpation

Grade 0	No palpable or visible goitre
Grade 1	A goitre that is palpable but not visible when the neck is in the normal position (i.e., the thyroid is not visibly enlarged) Thyroid nodules in a thyroid which is otherwise not enlarged fall into this category
Grade 2	A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated

[a] A thyroid gland will be considered goitrous when each lateral lobe has a volume greater than the terminal phalanx of the thumbs of the subject being examined.

The specificity and sensitivity of palpation are low in grades 0 and 1 due to a high inter-observer variation. As demonstrated by studies of experienced examiners, misclassification can be high.

Interpretation

Table 7 gives the epidemiological criteria for establishing IDD severity, based on goitre prevalence in school-age children. The terms mild, moderate, and severe are relative and should be interpreted in context with information from other indicators.

[1] Another method is to stand behind the subject with the neck in the neutral position and hold the fingers (not thumb) over the area of the gland. The person is asked to swallow and the gland is palpated by the fingers as it glides up. This is repeated on each side of the neck.

It is recommended that a total goitre rate or TGR (number with goitres of grades 1 and 2 divided by total examined) of 5% or more in school-children 6 to 12 years of age be used to signal the presence of a public health problem. This recommendation is based on the observation that in normal, iodine-replete populations, the prevalence of goitre should be quite low. The cut-off point of 5% allows both for some margin of error of goitre assessment, and for goitre that may occur in iodine-replete populations due to other causes such as goitrogens and autoimmune thyroid diseases.

Table 7 Epidemiological criteria for assessing the severity of IDD based on the prevalence of goitre in school-age children[a]

	DEGREES OF IDD, EXPRESSED AS PERCENTAGE OF THE TOTAL OF THE NUMBER OF CHILDREN SURVEYED			
Total goitre rate (TGR)	None	Mild	Moderate	Severe
	0.0–4.9%	5.0–19.9%	20.0–29.9%	≥ 30%

[a] Goitre prevalence responds slowly to changes in iodine intake.

Finally, in this context it is emphasized that thyroid size in the community may not return to normal for months or years after correction of iodine deficiency.

4.3.2 Thyroid size by ultrasonography

In areas of mild to moderate IDD, the sensitivity and specificity of palpation are poor and measurement of thyroid size using ultrasound is preferable. Ultrasonography is a safe, non-invasive, specialized technique that can be quickly done (2–3 minutes per subject) and is feasible even in remote areas using portable equipment. Ultrasonography provides a more precise measurement of thyroid volume compared with palpation. This becomes especially significant when the prevalence of visible goitres is small, and in monitoring iodine control programmes where thyroid volumes are expected to decrease over time. The technical aspects of thyroid ultrasonography are reported in Annex 2.

Feasibility

Portable (weight 12–15 kg) ultrasound equipment with a 7.5 MHz transducer currently costs about US $15 000. A source of electricity is needed, and the operator needs to be specially trained in the technique. Differences in technique (e.g. the pressure applied with the transducer) and estimation of thyroid anatomy (e.g. inclusion of the thyroid isthmus and/or capsule thickness) can result in high inter-observer variability.

Interpretation

Results of ultrasonography from a study population should be compared with reference data (*33*). Reference values for thyroid volume measured by ultrasonography in schoolchildren of iodine-sufficient populations are shown in Table 8. These are presented as a function of age, sex, and body surface area (BSA) in order to take into account the differences in body development among children of the same age in different countries. This approach is potentially useful in countries with a high prevalence of child growth retardation due to malnutrition with both stunting (low height-for-age) and underweight (low weight-for-age).

An advantage of the thyroid volume-for-BSA is that the age of the child is not required, which in some populations is not known with certainty. A limitation of the thyroid volume-for-BSA is that it requires the collection of weights and heights: in severely malnourished populations of schoolchildren, 10% or more may have a BSA below the lowest BSA cut-off of 0.7.

The thyroid volume references proposed here are applicable for goitre screening only if thyroid volume is determined by the standardized method described in Annex 2.

Table 8 Gender-specific 97th percentile (P97) of thyroid volume (ml) by age and body surface area (BSA) measured by ultrasound in iodine-sufficient 6–12 year-old children[a]

	BOYS	GIRLS
AGE (y)	P97	P97
6	2.91	2.84
7	3.29	3.26
8	3.71	3.76
9	4.19	4.32
10	4.73	4.98
11	5.34	5.73
12	6.03	6.59

	BOYS	GIRLS
BSA (m^2)	P97	P97
0.7	2.62	2.56
0.8	2.95	2.91
0.9	3.32	3.32
1.0	3.73	3.79
1.1	4.20	4.32
1.2	4.73	4.92
1.3	5.32	5.61
1.4	5.98	6.40
1.5	6.73	7.29
1.6	7.57	8.32

[a] MB Zimmermann, 2004 (*33*).

4.4 Blood constituents

Two blood constituents, TSH and Tg, can serve as surveillance indicators. In a population survey, blood spots on filter paper or serum samples can be used to measure TSH and/or Tg.

Determining serum concentrations of the thyroid hormones, thyroxin (T4) and triiodothyronine (T3), is usually not recommended for monitoring iodine nutrition, because these tests are more cumbersome, more expensive, and less sensitive indicators.

In iodine deficiency, the serum T4 is typically lower and the serum T3 higher than in normal populations. However, the overlap is large enough to make these tests impractical for ordinary epidemiological purposes.

4.4.1 Thyroid stimulating hormone (TSH)

Biological features

The pituitary secretes TSH in response to circulating levels of T4. Serum TSH rises when serum T4 concentrations are low, and falls when they are high. Iodine deficiency lowers circulating T4 and raises the serum TSH, so iodine-deficient populations generally have higher serum TSH concentrations than do iodine-sufficient groups.

However, the difference is not great and much overlap occurs between individual TSH values. Therefore, the blood TSH concentration in school-age children and adults is not a practical marker for iodine deficiency, and its routine use in school-based surveys is not recommended.

In contrast, TSH in neonates is a valuable indicator for iodine deficiency. The neonatal thyroid has a low iodine content compared to that of the adult, and hence iodine turnover is much higher. This high turnover, which is exaggerated in iodine deficiency, requires increased stimulation by TSH. Hence, TSH levels are increased in iodine-deficient populations for the first few weeks of life – this phenomenon is called transient hyperthyrotopinemia (*25*).

The prevalence of neonates with elevated TSH levels is therefore a valuable indicator of the severity of iodine deficiency in a given population. It has the additional advantage of highlighting the fact that iodine deficiency directly affects the developing brain.

In iodine-sufficient populations, about one in 4000 neonates has congenital hypothyroidism, usually because of thyroid dysplasia. Prompt correction with thyroid hormone is essential to avoid permanent mental retardation.

Thyroid hormone affects proper development of the central nervous system, particularly its myelination; a process that is very active in the perinatal period. To detect congenital hypothyroidism and initiate rapid treatment, most developed countries conduct universal screening of neonates with bloodspot TSH taken on filter papers, or occasionally with blood spot T4 followed by TSH.

While screening in developed countries is directed at detecting

neonates with TSH elevations which are 20 mIU/l whole blood or higher, the availability of TSH assays sensitive to 5 mlU/l permits detection of mild elevations above normal. This permits detection of transient hyperthyrotopinemia. To be broadly applicable in a population, the screening must be universal, and not omit children born in remote or impoverished areas. For countries and regions that already have a system of universal neonatal screening with a sensitive TSH assay in place, the data can be examined and transient iodine deficiency recognized, usually without further surveying.

Feasibility

Serum TSH is widely used in the field of thyroidology as a sensitive marker for both hypothyroidism and hyperthyroidism. Methods for determining TSH concentrations, from either dried whole blood spots on filter paper or from serum, are well established and widely available. Typically, a few drops of whole blood are collected on filter paper from the cord or by prick of the heel or other site.

It is essential that sterile equipment be used, either lancets for blood spot collection or needles and syringes for collecting whole blood from which the serum is separated. Standard procedures for handling blood products or objects contaminated with blood should be followed. The risk of contracting HIV or hepatitis infection from dried blood spots is extremely low.

Some experimental data suggest normal values for cord blood are higher than those for heel prick blood. Blood spots, once dried, are stable. They can be stored in a plastic bag and transported even through normal postal systems and are usually stable for up to six weeks.

It must be emphasized that the primary purpose of screening programmes is to detect congenital hypothyroidism, and its use as an indicator of iodine nutrition will be a spin-off. Hence, the only additional cost will be for data analysis. It is not recommended that a neonatal screening programme be set up solely to assess community iodine deficiency. Less expensive means for obtaining this information exist.

TSH screening is inappropriate for developing countries where health budgets are low. In such countries, mortality among children under five is high due to nutritional deficiencies and infectious diseases, and screening programmes for congenital hypothyroidism are not cost effective.

Performance

A variety of kits for measuring TSH are available commercially in developed countries. Most have been carefully standardized, and perform adequately. Assays that utilize monoclonal antibodies, which can detect

TSH as low as 5 mIU/l in whole blood spots, are more useful for recognizing iodine deficiency.

Interpretation

Permanent sporadic congenital hypothyroidism, with extremely elevated neonatal TSH, occurs in approximately one of 4000 births in iodine-sufficient countries. Other than infrequent cases of goitrogen exposure, iodine deficiency is the only significant factor to increase this incidence.

The increase in the number of neonates with moderately elevated TSH concentrations (above 5 mlU/l whole blood) is proportional to the degree of iodine deficiency during pregnancy. It may be higher than 40% in severe endemic areas. When a sensitive TSH assay is used on samples collected three to four days after birth, a <3% frequency of TSH values >5 mlU/l indicates iodine sufficiency in a population (*34*).

Interpretation is complicated when antiseptics containing beta-iodine, such as povidone iodine (Betadine™), are used for cleaning the perineum prior to delivery or even the umbilical area of the baby. Beta-iodine increases TSH levels in the neonate in both cord blood and heel prick specimens.

4.4.2 Thyroglobulin (Tg)

Biological features

Tg is a thyroid protein that is a precursor in the synthesis of thyroid hormone, and small amounts of Tg can be detected in the blood of all healthy individuals. The thyroid hyperplasia and goitre characteristic of iodine deficiency increases serum Tg levels, and in this setting serum Tg reflects iodine nutrition over a period of months or years. This contrasts to urinary iodine concentration, which assesses more immediate iodine intake. A serum Tg assay has recently been adapted for use on dried whole blood spots (DBS) (*35*,*36*). The assay makes sampling practical even in remote areas. Measurement of DBS Tg in school-age children is a sensitive indicator of iodine status in a population and can be used to monitor improving thyroid function after iodine repletion.

Interpretation

Standard reference material for the DBS Tg assay is now available from WHO. It is stable when stored for up to one year at temperatures ≤ -20 °C. An international reference range for DBS Tg has been established in iodine-sufficient five to 14 year-old children that can be used for monitoring iodine nutrition. The DBS Tg reference interval for iodine-sufficient school-age children is 4–40 μg/l.

Performance

DBS Tg correlates well with urinary iodine and thyroid size (*35*,*36*), the other recommended indicators for monitoring iodine status in populations. It complements these tests, and can be used in conjunction with urinary iodine to measure recent iodine intake, and thyroid volume to assess long-term anatomic response.

Feasibility

The method is simple and robust. A drop of whole blood from a finger stick (or a venipuncture sample) is spotted directly onto good-quality filter paper.[1] The spots are allowed to dry at room temperature (~20 °C), and then stored in sealed low-density polyethylene bags; preferably refrigerated at 4 °C, but they also can be stored for several weeks at cool, dry room temperatures before analysis.

[1] An example of the type of paper that can be used is Grade 903 Filter Paper produced by Schleicher & Schuell; Einbeck, Germany.

Table 9 Indicators of impact at population level: summary

MONITORING INDICATOR (UNITS)	AGE GROUP FOR ASSESSMENT	ADVANTAGES	DISADVANTAGES
Median urinary iodine concentration (µg/l)	School-age children and pregnant women	– Spot urine specimens are easy to obtain – The most practical biochemical marker for iodine nutrition, when carried out with appropriate technology and sampling – Feasible to process large numbers of samples at low cost – Cut-off points proposed for classifying iodine nutrition into different degrees of public health significance are well established – External quality control program in place	– Assesses iodine intake only over the past few days – Meticulous laboratory practice is required to avoid contamination with iodine – A sufficiently large number of samples must be collected to allow for varying degrees of subject hydration and other biological variations among individuals – Not valuable for individual assessment
Goitre rate assessed by palpation (%)	School-age children	– Simple and rapid screening test – Requires no specialized equipment	– Specificity and sensitivity of palpation are low in grades 0 and 1 due to a high inter-observer variation – Responds slowly to changes in iodine intake
Goitre rate assessed by ultrasound (%)	School-age children	– A more precise measurement of thyroid volume compared with palpation – Safe, non-invasive – International reference values for thyroid volume in schoolchildren are available as a function of age, sex, and body surface area	– Expensive equipment and a source of electricity is needed – operator needs to be specially trained in the technique – Responds slowly to changes in iodine intake
TSH (mIU/l)	Newborns	– Measures thyroid function at a vulnerable age when iodine deficiency directly affects the developing brain – If screening programs to detect congenital hypothyroidism is in place then only additional cost will be for data analysis – Collection by heel stick and storage on filter paper is simple – Blood spots can be stored for several weeks at cool, dry room temperatures	– Not recommended to be set up solely to assess community iodine deficiency due to expense – Cannot be used when antiseptics containing iodine are used during delivery – Requires use of a standardized, sensitive assay – Should be taken either from the cord at delivery or by heel prick at least 48 hours after birth to avoid physiological newborn surge
Tg (µg/l)	School-age children	– Collection by finger stick and storage on filter paper is simple – Can be stored for several weeks at cool, dry room temperatures, so sampling practical even in remote areas – Measures improving thyroid function within several months after iodine repletion – Standard reference material is now available, but needs to be validated – An international reference range has been established	– Expensive immunoassay – Requires laboratory infrastructure

5 Monitoring and evaluation methods

5.1 Overview

This book has so far dealt with *what* should be measured, i.e. the indicators of process and impact, and the technical details of their assessment. This chapter describes *how* to monitor and evaluate these indicators in the field.

This chapter includes methodologies for *monitoring the process* of salt iodization at the population level to complement the discussion in Chapter 3, and provides some details on monitoring methods for assessing the impact of programs on iodine status and thyroid function. For some monitoring activities such as performing surveys at schools or in households, both salt and impact indicators can be assessed at the same time, thus providing a more comprehensive picture of the situation.

Attention to proper survey methodology will result in representative results from the population. Careful attention to monitoring methods will assure the monitoring is carried out as efficiently as possible.

5.2 Monitoring and evaluation of salt iodization programs

An IDD control programme based on salt iodization clearly cannot succeed unless all salt for human consumption is being adequately iodized. Therefore the most important indicator to monitor is salt, and the most important place to monitor salt is at the site of production and importation. If all salt leaving production facilities and imported salt is properly iodized, packaged, and labelled, populations consuming this salt are likely to have their iodine requirements met.

Monitoring iodine content of salt at sites of production

Monitoring salt iodine at the production site provides an answer to the question: "Is the salt adequately iodized, i.e. according to the level required by the law of the country?" In view of the potential loss of iodine further down the supply chain, this is the appropriate place where law enforcement can take place.

Salt monitoring at the site of production is the responsibility of both

the salt producer (internal monitoring) as well as governmental food inspectors (external monitoring), as discussed in Chapter 3.

The methods at the production level reflect industrial quality assurance procedures. Production facilities should have a quality assurance system that documents that their machinery is functioning correctly, and that iodized salt leaving the facility meets government standard. Since rapid test kits (RTK) cannot accurately measure the iodine content, titration should be used for quality control. The exact number of samples to test and the frequency of testing will vary, but should be defined in an operation manual with results recorded on a daily basis. A modified Lot Quality Assurance Sampling (LQAS) scheme is recommended for implementation by producers (*37*).

Government food inspectors or health inspectors should carry out periodic visits to salt production facilities to check on the in-house quality control mechanisms through record review and review of quality assurance activities. They should also collect samples randomly from several production batches, and have these analysed by titration at a government laboratory. Depending on the capacity of the food inspection system, results should be reported monthly or quarterly.

Monitoring iodine content of salt at ports of entry

Large producers should certify that the salt they produce is iodized within a specified range. Such producers, particularly if exporting salt, should seek certification by the International Organization for Standardization (International Standard ISO 9000 series) as an added guarantee that their salt is adequately iodized.

Several factors affect the methods used for inspecting imported salt. First, the lines of authority, and thus the procedures used, differ between the food inspection system and customs control. Second, the practical realities of border check points prevent optimal checking of salt consignments entering the country.

At the actual point of entry, customs officers can realistically be expected to check documentation on large consignments of salt, and visibly inspect all imports to check that the salt is suitably packed and labelled. Documentation should distinguish between salt for human consumption and industrial salt, which is not covered by iodization regulations. Ideally, each consignment should be tested with a rapid test kit, accepting that this is not any kind of representative sampling, and that it cannot assess actual iodine levels. Suspect salt should be held at the border. Documentation should distinguish between salt for human consumption and industrial salt, which is not covered by iodization regulations.

Establishing titration laboratories at points of entry for salt would appear to be an attractive option, but is difficult to implement in practice. Unloading bags from a lorry or railway wagon to check a consignment thoroughly is difficult, and only a few easily accessible bags can be tested. Staff would have to be specially recruited and laboratories established at considerable expense.

Monitoring salt at the wholesale and retail levels

Monitoring the iodine in salt at the retailer level provides an answer to the question: "What is the availability of iodized salt to the consumer?" Monitoring at this level yields a quick and easy indication of whether or not iodized salt is available in the marketplace, and the degree to which non-iodized salt is competing for household use. Retail-level monitoring is not the appropriate place for law enforcement or compliance monitoring, since it is difficult to confirm the level of loss since production.

The methods used for wholesale and retail monitoring depend on the capacity of the food inspection system, which often covers a wide range of products entering the market. Thus, there is no prescribed sampling method at this level, and countries have widely variable capacity and have used many approaches. Ideally, for any given district, there are enough market samples tested on an annual basis to determine the degree to which non-iodized salt remains available in the marketplace, thus giving some perspective to household coverage figures.

Monitoring salt at the household level

Monitoring the iodine in salt at the household level answers the question: "What percentage of households uses salt iodized at any iodine concentration and what percentage uses salt that is within an acceptable range of iodine concentration?" This information indicates what is actually used in households on a national basis and provides important information about the successful delivery of iodized salt to the consumer as well as about use of non-iodized salt obtained from unconventional marketing sources.

Coverage, and the methods used to determine it, is critical for program monitoring. Most countries assess household use of iodized salt through school or household surveys. These may be done by district health staff or as part of periodic national surveys.

In order for school or household surveys to accurately represent the populations from which the sample is taken, attention must be given to the sampling methodology. The most common sampling methods, including the cluster survey method, are described below, and in the appendices.

Salt from each selected household should be tested. Testing using rou-

tine test kits will provide an estimate of the percent of households using salt with no iodine, but will not provide accurate information on the percent using adequately iodized salt, or information on salt with excessive iodine. Thus, titration or another quantitative method should be performed on at least a sub-sample of households for any coverage survey.

5.3 Iodine status assessment

Assessing iodine status provides information on whether there is adequate iodine intake in the population surveyed. Monitoring the iodine status of a population answers the questions: "Is the salt iodization program (or other interventions) improving iodine intake? Has iodine deficiency been eliminated in this population?" Iodine status is the most immediate measure of whether the thyroid gland has adequate iodine to function normally and protect the individual from the manifestations of iodine deficiency. The median urinary iodine concentration reflects population status and is the indicator most commonly assessed.

As iodized salt use is assessed through coverage surveys which frequently employ cluster sampling, assessment of iodine status usually involves the same sampling technique. Salt coverage surveys may be conducted more frequently, and are more easily 'attached' to other national surveys. Iodine status assessment may be less frequent since it involves the collection of urine, and therefore requires more financial and human resources. Follow-up urinary iodine assessments are generally performed after intervention programs achieve a certain level of success (*38*).

Urinary iodine is frequently assessed through school surveys (since this is an efficient way to estimate the household iodine nutrition situation) or through overall population assessments, as in DHS or MICS. While the median value in a representative sample of schoolchildren or the general population provides a reasonable population estimate, it may not reflect the situation in pregnant women, whose iodine requirements are greater. Sampling of pregnant women can be difficult because the number of pregnant women present in household-based surveys may be small. Assessing the median value in women of reproductive age or among adolescent girls is more feasible in a population-based survey, and may be helpful in interpreting the median population value.

Ideally, assessment of iodine status should include concurrent assessment of household use of iodized salt. This provides information on both the likely iodine intake and iodine status, making it easier to distinguish between difficulties with iodized salt quality, and iodized salt use. When adequately iodized salt is used, this should be reflected in adequate iodine status in the population sampled.

5.4 Thyroid function assessment

Assessing thyroid function provides information on whether the thyroid gland is responding to adequate iodine intake, and is the ultimate measure of whether a population is protected from iodine deficiency. Assessing the thyroid status of a population answers the question: "Is there evidence of thyroid dysfunction that may reflect inadequate iodine intake?" Thyroid function reflects the ability of the thyroid to produce thyroid hormone, which is essential for normal development. Thyroid size and various measures of status such as TSH and Tg are the most common measures of thyroid function.

The methods used for assessing thyroid function have changed with the changing role of goitre assessment as noted in Chapter 4. In some instances, where there is no information on whether IDD is present, or when there is concern that IDD may be re-emerging, goitre surveys may be useful. In such cases, the selection of schools or communities for surveying should be purposive, i.e. on the basis of IDD being suspected or predicted in that particular location. Goitre palpation of each subject takes very little time, and the examination of a relatively large number of children will provide a good picture of the overall IDD status in the area sampled. Ultrasound provides a more accurate estimate of thyroid size. Because this type of investigation is purposive, it will most likely not be representative of any population except those in the communities or schools assessed.

While urinary iodine is the most commonly used measure of iodine status, the newly tested dried blood spot Tg may provide a reasonable assessment of thyroid function in schoolchildren. Tg can be used in household or school surveys, or through purposive sampling as described above.

5.5 Common monitoring methods

Two approaches to monitoring iodized salt and IDD in populations are cross-sectional surveys and sentinel surveillance. **Cross-sectional surveys** are generally performed to provide representative estimates for a population. Cross-sectional surveys can be household-based, school-based, or clinic-based. In most cross-sectional surveys there are two stages of selection with units selected at the first stage referred to as "clusters". For household-based surveys, the first stage is the selection of communities or enumeration units, and the second stage is selection of households from which individuals are assessed. For school-based surveys, the first stage is the selection of schools and the second stage is the selection of students. For clinic-based surveys, the first stage is the selection of clinics and the second stage is the selection of patients.

At the first stage in cross-sectional surveys to select clusters, a frequently used approach is the probability proportion to size (PPS) method. This method requires an estimate of the size at the first stage of selection. For household-based surveys this is generally based on census data, for school-based surveys based on school enrolment, and for clinic-based surveys based on the number of enrolled patients. Using this method, the larger the size at the first stage of selection, the greater the likelihood of being selected as a cluster. There are a number of advantages to PPS including the issue of not having to "weight" the data at the analysis stage, i.e. it is a self-weighted design. The details of PPS sampling are provided in Annex 4.

If the size of the population is not known at the first stage, then either simple random sampling (SRS) or systematic sampling can be used to select clusters. However, if SRS or systematic sampling is used there will be a need to "weight" the data based on the size of the cluster at the analysis stage.

At the second stage of selection in cross-sectional surveys there is a need to assure a random or systematic selection process. For household-based surveys this entails a method for selecting households, for school-based surveys a method for selecting students, and for clinic-based surveys a method for selecting patients. For school-based and clinic-based surveys, the selection of individuals for the survey is relatively straightforward in that a listing of eligible individuals is used from which the desired number to assess are selected using SRS or systematic sampling. For household-based surveys, the selection of households from a cluster may be complicated if the cluster is large in terms of the number of households, spread out over a large geographical area, or very unorganized. The segmentation method is frequently used in these latter situations to narrow down the area to be assessed, and is described in more detail in Annex 4.

Cross-sectional surveys may be stratified by different geographical areas; usually provinces or regions. Stratified surveys allow the presentation of stratum-specific estimates as well as a national estimate, but dramatically increase the sample size of the survey. Ideally, a minimum of around 30 clusters are needed for each stratum. Depending on the goals of the survey and resources available, a single 30-cluster survey may or may not be sufficient for all countries. Some surveys may focus primarily on the coverage and quality of iodized salt whereas some others include measures of IDD status. Stratified surveys of iodized salt coverage can be useful to identify geographical areas where coverage is insufficient and lead to further enquiry concerning the causes of low coverage. In most countries the primary prevention of IDD is through iodized salt,

and therefore knowledge of variations in IDD status by strata would primarily identify variations in iodized salt coverage.

A common mistake in interpreting the results from a cluster survey is to assume that the result from a single cluster is representative of that area. While it is possible to look at the geographic patterns among the clusters surveyed, it is only the overall coverage figure that is representative of the full area surveyed.

A major concern arising in school-based surveys is that children not attending school are not represented, which may possibly lead to biased estimates. Also, if there are feeding or vitamin-mineral supplement programmes in the schools, schoolchildren may not be a good target group in terms of assessing IDD for the entire population. Details of school sampling are also provided in Annex 4.

A second approach to monitoring is to collect data through **sentinel surveillance**. Because cross-sectional surveys tend to be performed infrequently and can be costly, countries should consider using this method, particularly if there is concern about the status of pregnant women. Sentinel surveillance involves selection of a number of sites from which routinely collected data provide results on trends. The number and location of sites, number of individuals or samples per site, and frequency of data collection depends on the primary purpose of the sentinel surveillance and resources available. Some countries may have sentinel surveillance for other conditions for which iodized salt or IDD monitoring could be added. Sentinel sites might be based on prenatal care clinics or schools where urinary iodine specimens are collected on a sample of pregnant women or students. Sites may be selected in areas where IDD is known to be prevalent or in areas with low iodized salt coverage, or they may be selected to be reasonably representative of the country. There are three target groups for surveillance of IDD control programmes:

1. **School-age children:** School-age children are a useful target group for IDD surveillance because of their combined high vulnerability, easy access, and applicability to a variety of surveillance activities. Affected children can be readily examined in large numbers in school settings, and can be assessed for urinary iodine, thyroid size, and Tg. At the same time, other health concerns in this age group, including helminth infections, anaemia, and behavioural factors affecting health, can be assessed. Appropriate educational interventions can then be implemented.

2. **Women of childbearing age and pregnant women:** Assessing urinary iodine in women 15 to 44 years of age provides an opportu-

nity to establish the iodine status of a group that is particularly crucial because of the susceptibility of the developing fetus to iodine deficiency. Antenatal clinics may have high use rates, and thus a sentinel sampling may provide a reasonable sample of pregnant women.

3. **Neonates:** Neonatal screening to identify congenital defects is well established in many developed countries and is being introduced in some relatively prosperous developing countries. Regular collection of blood-spot specimens, where this is practiced, can be an important source of information for IDD surveillance given their use in assessing TSH status. This approach is recommended for monitoring IDD control *only* when a screening programme is already established.

5.6 Combined micronutrient deficiency surveys

IDD prevalence surveys may be efficiently combined with those aimed at assessing the prevalence of other micronutrient deficiencies, such as vitamin A and iron, or other cluster surveys designed for other purposes. The simplest way of including an IDD component is to collect urine in order to assess urinary iodine concentration in the target group and to ask for a household salt sample.

Benchmark national surveys such as DHS and MICS often include information on micronutrient programs, and in some instances can be modified to meet specific micronutrient program needs. These large national surveys help provide periodic information, but may not be adequate for routine monitoring of program progress.

6 Indicators of the sustainable elimination of IDD

As programs mature, it is important to understand their vulnerability and whether they are likely to be sustained. A number of criteria have been established to determine whether elimination goals have been met, and a series of programmatic indicators have been developed to help understand the likelihood that a program will be sustained. This chapter outlines these factors.

In considering whether the sustainable elimination of iodine deficiency as a public health problem has been achieved, the following criteria should be met (see also Table 10):

6.1 With regard to salt iodization:

- Availability and use of adequately iodized salt (>20 ppm iodine and <40 ppm) must be guaranteed. This is demonstrated by its use by more than 90% of households.
- Conditions demonstrating successful use of salt as vehicle for eliminating IDD are:
  - 95% of salt for human consumption must be iodized according to government standards for iodine content as determined by titration, at the production or importation levels;
  - The percentage of food-grade salt with iodine content of between 20 and 40 ppm in a representative sample of households must be equal to or greater than 90% as determined by RTK and by titration in a sub-sample.

6.2 With regard to the population's iodine status:

- The median urinary iodine concentration in the general population should be within the range 100–199 μg/l.
- The median urinary iodine concentration in the pregnant women population should be within the range 150–249 μg/l.
- The most recent monitoring data (national or regional) should have been collected within the last five years.

6.3 With regard to the programmes:

1. Presence of a national multi-sector coalition responsible to the government for the national programme for the elimination of IDD with the following characteristics:
   - National stature;
   - All concerned sectors, including the salt industry, represented, with defined roles and responsibilities;
   - Convenes at least twice yearly.
2. Demonstration of political commitment as reflected by:
   - Inclusion of IDD in the national budget (either as specific programme funds or through inclusion in existing programme funds) particularly with regard to procurement and distribution of potassium iodate (KIO_3).
3. Enactment of legislation and supportive regulations on universal salt iodization, which establishes a routine mechanism for external quality assurance.
4. Establishment of methods for assessment of progress in the elimination of IDD as reflected by:
   - Reporting on national programme progress every three years.
5. Access to laboratories as defined by:
   - Laboratories able to provide accurate data on salt and urinary iodine levels and thyroid function.
6. Establishment of a programme of education and social mobilization as defined by:
   - Inclusion of information on the importance of iodine and the use of iodized salt, within educational curricula.
7. Routine availability of data on salt iodine content as defined by:
   - Availability at the factory level at least monthly, and at the household level at least every five years.
8. Routine availability of population-based data on urinary iodine every five years.
9. Demonstration of ongoing cooperation from the salt industry as reflected by:
   - Maintenance of quality control measures and absorption of the cost of iodate/iodide.
10. Presence of a national database for recording of results of regular monitoring procedures which include population-based household coverage and urinary iodine (with other indicators of iodine status and thyroid function included as available).

Table 10 Summary of criteria for monitoring progress towards sustainable elimination of IDD as a public health problem

INDICATORS	GOALS
Salt iodization	
Proportion of households using adequately iodized salt	>90%
Urinary iodine	
Median in the general population	100–199 µg/l
Median in pregnant women	150–249 µg/l
Programmatic indicators	Attainment of eight out of 10 indicators specified in Section 6.3

6.4 Programme evaluation

There is a need for periodic review of the entire programme, with the help of WHO, UNICEF, ICCIDD, and other appropriate organizations involved in IDD elimination. Such external evaluation provides independent assessment, which is extremely helpful to a country programme. It can also provide programmes with reassurance of their performance and effectiveness.

For acknowledgement of attainment of the sustainable elimination of IDD, countries may request an evaluation through UNICEF, WHO, or ICCIDD country offices. Details for this process are provided in Annex 6.

Annexes

ANNEX 1

Titration method for determining salt iodate and salt iodide content

A1.1 Titration method for determining salt iodate content

The iodine content of iodated salt samples is measured using the iodometric titration method (*16*,*23*,*37*). The method consists of preparing the reagent solutions, which may last for variable periods of time, and then using these reagents in the titration procedure.

Usually, salt samples of 10 g each are dissolved in a measured amount of water for the titration analysis. However, in the case of coarse salt and in salt containing impurities, a bigger sample weight of 50 g salt will yield more accurate results. A chemical analyst will be able to advise on the appropriate glassware, preparation of reagents (including adjustments to the concentrations of some of the reagents), and the necessary calculations to obtain the correct results.

For community or population surveys, 10 g salt samples are sufficient; however, for monitoring the iodine content at the production level, 50 g salt samples are preferred for the titration procedure.

A1.1.1 Description of the reaction

The reaction mechanism includes two steps:

- **Liberation of free iodine from salt:** The addition of H_2SO_4 liberates free iodine from the iodate in the salt sample. Excess potassium iodide (KI) is added to help solubilise the free iodine, which is quite insoluble in pure water under normal conditions.
- **Titration of free iodine with thiosulfate:** free iodine is consumed by sodium thiosulfate in the titration step. The amount of thiosulfate used is proportional to the amount of free iodine liberated from the salt. Starch is added as an external (indirect) indicator of this reaction and reacts with free iodine to produce a blue colour. When added towards the end of titration (i.e. when only a trace amount of free iodine is left) the loss of blue colour, or end-point, which occurs with further titration, indicates that all remaining free iodine has been consumed by thiosulfate.

Reaction steps for iodometric titration of iodate

1.	IO_3 (from salt)	+	$5I^-$ (from KI)	+	$6H^+$ (from H_2SO_4)	→	$3I_2$	+	$3H_2O$
2.	$2Na_2S_2O_3$ Sodium thiosulfate	+	I_2 Iodine	→	2NaI Sodium iodide	+	$Na_2S_4O_6$ Sodium tetrathionate		

A1.1.2 Reagent preparation

The preferred water for this method should be double-distilled or deionized water, which requires provision of a distillation unit. As a simpler alternative, regular tap water treated with a mixed bed deionizing resin can be used, thus avoiding the need for an expensive distillation unit. Many reputable chemical and pharmaceutical companies supply deionized, double-distilled, and purified water which is iodine-free.

- **0.005 N Sodium thiosulfate ($Na_2S_2O_3$):** Dissolve 1.24 g $Na_2S_2O_35H_2O$ in 1000 ml water. Store in a cool, dark place. This volume is sufficient for 100 to 200 samples, depending on their iodine content. The solution is stable for at least one month, if stored properly. Standardization of sodium thiosulfate with a volumetric solution of potassium iodate is recommended. The concentration of the sodium thiosulfate could be adjusted to accommodate the analysis of larger sample weights (e.g. 50 g or 100 g salt samples).
- **2 N Sulfuric acid (H_2SO_4):** Slowly add 6 ml concentrated H_2SO_4 to 90 ml water. Make to 100 ml with water. This volume is sufficient for 100 samples. The solution is stable indefinitely. Always add acid to water, not water to acid, to avoid excess heat formation and spitting of acid. Stir solution while adding acid.
- **10% Potassium iodide (KI):** Dissolve 100 g KI in 1000 ml water. Protect reagent from direct light. Store in a brown bottle in a cool, dark place. Properly stored, the solution is stable for six months, provided no change occurs in the colour of the solution. This volume is sufficient for 200 samples.
- **Starch indicator solution:** Dissolve approximately 15-30 g of reagent-grade sodium chloride (NaCl) in 100 ml water. While stirring, add NaCl until no more dissolves. Heat the contents of the beaker until excess salt dissolves. While cooling, the NaCl crystals will form on the sides of the beaker. When it is completely cooled, decant the supernatant into a clean bottle. This solution is stable for six to 12 months. Suspend 1 g chemical starch in 10 ml water at room temperature, then continue to boil until it completely dissolves. Add the saturated NaCl

solution to make 100 ml starch solution. This volume is sufficient for testing 20 to 45 samples. Preferably, prepare fresh starch solution every day since this solution deteriorates easily, although it is stable for up to one month.

A1.1.3 Procedure

Sampling of salt

Prior to taking a 10 g or 50 g salt sample for analysis, salt should be thoroughly mixed, preferably in zip-lock bags or appropriate containers to ensure that the iodine is homogeneously distributed in the salt. Usually 10 g iodated salt is dissolved in 50 ml distilled water. Optional: 50 g iodated salt could be thoroughly dissolved in 250 ml distilled water, from which an aliquot of 50 ml could be analysed as mentioned in the titration step below, without adjusting the concentrations of the reagents or calculation.

Titration step

Once the salt is dissolved in the measured amount of water, sulfuric acid (1–2 ml) and potassium iodide (5 ml) is added to the salt solution, which in the presence of iodine will turn yellow. The reaction mixture is then kept in a dark place (with no exposure to light) for five to 10 minutes to reach the optimal reaction time, before titrated with sodium thiosulfate using starch (2 ml) as the indirect indicator. The concentration of iodine in salt is calculated based on the titrated volume (burette reading) of sodium thiosulfate according to the formula mentioned below, or alternatively it could be read off a pre-calculated table for the specific method (e.g. method: 10 g salt titrated with 0.005N sodium thiosulfate).

Calculation

mg/kg (ppm) iodine = titration volume in ml x 21.15 x normality of sodium thiosulfate x 1000 / salt sample weight in g

Special note: 0.005 N sodium thiosulfate consumes 0.1058 mg iodine/ml.

Precaution

The 10% potassium iodide reagent stock needs to be protected from direct light, and the reaction mixture (after the addition of sulfuric acid and potassium iodide) should be kept in the dark before titration to prevent a side reaction which may occur when these solutions are exposed to light, causing iodide ions to be oxidized to iodine.

A1.2 Titration method for determining salt iodide content

While the use of potassium iodide (KI) is not common for salt fortification in many developing countries, basic details of a titration method (*23*) suitable for analysing salt iodized with KI are provided here.

A1.2.1 Description of the reactions

In the iodometric titration for salt fortified with potassium iodide:

- **Liberation of iodine:** Bromine water oxidizes iodide ions to free iodine. Sodium sulfite and phenol are added to destroy excess bromine so that no further oxidation of iodine can occur before KI solution is added.
- **Titration:** The titration reaction with thiosulfate is the same as that described in the iodometric titration method for iodated salt mentioned earlier.

A1.2.2 Reagent preparation

Reagents for oxidization of iodide to free iodine:

- **Methyl orange indicator ($C_{14}H_{14}N_3NaO_3S$):** Dissolve 0.01 g methyl orange in 100 ml water.
- **Bromine water (Br_2ag):** Place required volume (e.g. 5–50 ml) in a small flask (keep in fume hood due to dangerous fumes and wear appropriate personal protective clothing, e.g. masks, gloves and goggles). Safety precaution in case of spills: neutralize bromine water of its halogen component by sprinkling sodium metabisulfite, sodium sulfite or even domestic baking soda (bicarbonate of soda).
  Preparation of bromine water from liquid bromine (Br_2): Decant the vapours from the liquid bromine in 50 ml distilled water into a 100 ml wide mouth glass bottle with a screw cap or stopper. Cap the bottle when the airspace above water is filled with red vapours. Swirl the bottle containing the water in order to mix the contents. As the bromine dissolves, the solution will become yellow in colour. The process above should be repeated at least once more. Typically bromine water should be orange in colour.
- **Sodium sulfite solution (Na_2SO_3):** Dissolve 1 g sodium sulfite in l00 ml water. Prepare fresh sodium sulfite solution regularly, since the solution deteriorates easily.
- **Phenol solution (C_6H_6O):** Dissolve 5 g phenol in 100 ml water.

All reagents prepared and used in the iodate method are also applicable to the iodide method for the titration step.

A1.2.3 Procedure

Sampling

As described in the iodate method.

Oxidation step (iodide method)

Once the salt (10 g) is dissolved in the measured amount of water (50 ml), a few drops of methyl orange indicator are added, followed by a few drops of sulfuric acid until the orange colour turns to pink, resulting in the neutralization of the reaction mixture. With the addition of bromine water (0.5 ml-5.0 ml, depending on the level of salt iodization), the reaction mixture changes to yellow. To consume the excess bromine, the reaction mixture is titrated with sodium sulfite until the solution turns to pale yellow, followed by the washing down of the sides of the flask with small amounts of water, and the addition of three drops of phenol, resulting in a clear reaction mixture.

Titration step (iodide & iodate method)

Follow the same titration steps and calculations as described in the iodate method.

ANNEX 2

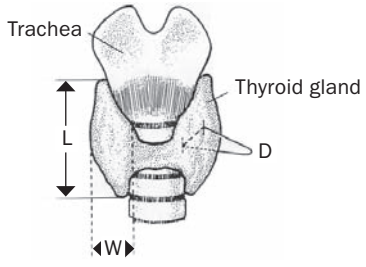
Method for determining thyroid size by ultrasonography

Thyroid gland size can be measured in the field by ultrasonography. In choosing an echocamera for this purpose, durability, reliability, good screen quality, sharp focus, and an easy-to-use marking system should be emphasized. The machine should be equipped with a high resolution, real-time, 4 to 6 cm linear, 7.5–10 MHz transducer.

A2.1 Location and anatomy of the thyroid gland (Figure 3)

- Superficial, butterfly-shaped gland in lower, anterior portion of neck.
- Right and left lobes are connected at midline by isthmus.
- Lateral borders: common carotid artery and internal jugular vein.
- Medial border: trachea.
- Anterior borders: sternocleidomastoid, sternothyroid, and sternohyoid muscles.
- The normal thyroid is variable in size. At age 6 to 12 years, its approximate weight is 15–25 g.

Figure 3 Anatomic description of the thyroid gland



Width (W): medial – lateral dimension
Depth (D): anterior – posterior dimension
Length (L): cranial – caudal dimension

A2.2 Sonographic appearance

- The normal thyroid is mid-gray with medium-level echoes and an even, homogeneous texture.
- Lobes appear more echogenic or hyperechoic to adjacent muscles.
- Branches of intrathyroid arteries and veins may appear as 0.5–1.0 mm anechoic tubular, linear structures, but they are rarely delineated.
- The capsule of the thyroid surrounds the gland and appears as a thin line hyperechoic to the gland parenchyma.
- In diffuse goitre, the gland is enlarged and its echogenicity is slightly enhanced.

A2.3 Scanning protocol

A2.3.1 Subject position

- Children can be measured supine with a pillow or rolled towel under the shoulders to maintain neck extension. Alternatively, they can be seated upright in a hard-backed chair with their back and shoulders straight, neck mildly hyperextended, and head turned slightly away from side of interest.
- The standing position is generally not recommended because of instability.

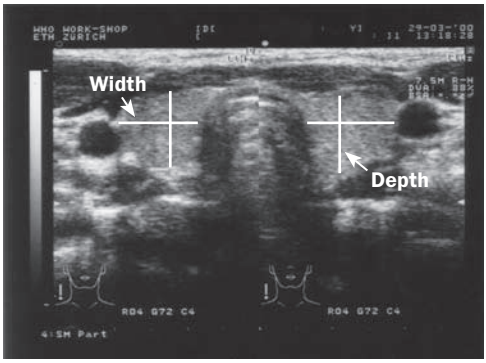
A2.3.2 Transducer

- Water-soluble gel is used.
- Transducer held at a 90-degree angle to skin, using only minimal pressure so as not to distort the gland anatomy.

A2.3.3 Transverse Study (Figure 4)

- Best done on a split screen, visualizing both lobes per screen.
- The trachea with its echogenic cartilage rings and air shadows appears in the midline; the echo-free lumina of the carotid arteries (pulsation) and jugular veins (distension on Valsalva) delineate the lateral aspect.
- Begin with the transducer perpendicular in the transverse plane above the sternal notch; move the transducer superiorly to view the entire gland from inferior to superior aspect; return to image which shows the lobe at its greatest depth and width; and freeze the image.
- Change to other side of the screen, repeat scan on opposite lobe, and freeze.
- Measure the maximal width (mediolateral) and depth (anteroposterior) of the transverse section of each lobe, with the depth measurement at a 90-degree angle to the skin surface and the width measurement at 90 degrees to the depth measurement.

Figure 4 Transverse scan



- The measurement should not include the thyroid capsule (hyperechoic to the gland tissue) or the thyroid isthmus.
- Note that the carotid, particularly in a subject with an enlarged thyroid, may indent the posterolateral aspect of the gland.

A2.4 Longitudinal Study (Figure 5)

- One thyroid lobe is measured per screen. The strap muscles appear anteriorly as hypoechoic structures relative to the thyroid. Posterior to the medial portion of the thyroid, the trachea with its echogenic cartilage and air shadows is often seen. Posterior to the lateral portion of the thyroid, venous structures and the common carotid appear as echo-free tubular structures.
- Begin with the transducer perpendicular in the sagittal plane above the sternal notch, move the transducer superiorly to view the entire gland from inferior to superior and medial to lateral aspect, return to

Figure 5 Longitudinal scan

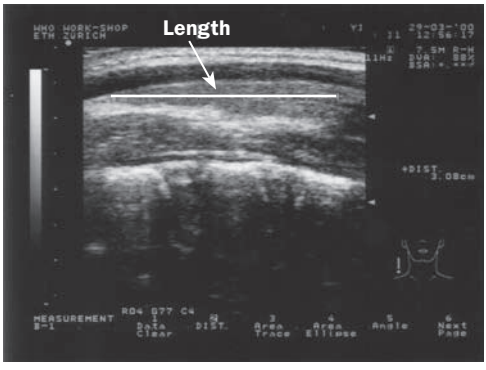


image which shows the lobe at its greatest length (craniocaudal), and freeze.

- To obtain the greatest length, because of the inferior convergence of the lobes, the transducer is often oriented with its superior end slightly diverging from the midline. Measure the maximal length of the longitudinal section of the lobe.
- Repeat scan on opposite lobe and again measure the maximal length of the longitudinal section.
- If the length of the gland exceeds the length of the transducer, the longitudinal measurement is done by splitting the lobe length in two scans, measuring to an internal (preferable) or external landmark, and summing the measurements to obtain the length.

A2.5 Calculation of thyroid volume and body surface area

The volume of the lobe is calculated from the measurements of the depth (d), the width (w), and the length (l) of each lobe by the formula:

$$\mathbf{V\ (ml) = 0.479 \times d \times w \times 1\ (cm)}$$

The thyroid volume is the sum of the volumes of both lobes. The volume of the isthmus is not included.

Thyroid volume can be easily calculated using a calculator or personal computer during data entry. Portable ultrasound equipment is relatively rugged, but requires electricity. However, it can be operated from a car battery with the aid of a transformer. Trained operators can perform up to 100 or more examinations per day.

The body surface area is calculated using the formula of Dubois and Dubois (*39*):

$$\mathbf{BSA\ (m^2) = W^{0.425} \times H^{0.725} \times 71.84 \times 10^{-4}}$$

It should be emphasized that by using the ultrasonography criteria, a thyroid gland will be called goitrous when its values will be above the 97th percentile of the volume found in an iodine-replete population used as control. Reference values for the 97th percentile for thyroid volume, as a function of both age and body surface area (BSA), are available (*33*). In areas with a high prevalence of protein-energy malnutrition, the BSA reference is recommended.

ANNEX 3

Method for measuring urinary iodine using ammonium persulfate (method A)

A3.1 Principle

Urine is digested with ammonium persulfate. Iodide is the catalyst in the reduction of ceric ammonium sulfate (yellow) to the cerous form (colourless), and is detected by the rate of colour disappearance (Sandell-Kolthoff reaction).

A3.2 Equipment

Heating block with a temperature range up to 110°C or above (vented fume hood recommended, but not essential); spectrophotometer; thermometer, test tubes (13 x 100 mm); assorted glassware and storage bottles; pipettes; vortex; magnetic hotplate; magnetic stirrer; analytical balance or top loader scales with a readability of at least 0.001 g and a capacity of approximately 250 g.

A3.3 Reagents

1. Ammonium persulfate ($H_8N_2O_8S_2$)
2. Arsenic trioxide (As_2O_3)
3. Sodium chloride (NaCl)
4. Sulfuric acid (H_2SO_4)
5. Sodium hydroxide (NaOH)
6. Cerric ammonium sulfate [$Ce(NH_4)_4(SO_4)_4 \cdot 2H_2O$]
7. Deionized water (H_2O)
8. Potassium iodate (KIO_3)

Use analytical grade chemicals for the preparation of all solutions

A3.4 Solutions

Ammonium persulfate (1.0 mol/l): Dissolve 114.1 g ammonium persulfate in 500 ml deionized water. Store in darkness; stable for one month. Keep refrigerated to prevent decomposition.

5 N Sulfuric acid: Slowly add 140 ml concentrated (36 N) sulfuric acid to about 700 ml deionized water (careful – this generates heat!). When cool, adjust with deionized water to a final volume of 1 litre.

3.5 N Sulfuric acid: Slowly add 97 ml concentrated (36 N) sulfuric acid to about 700 ml deionized water (careful – this generates heat!). When cool, adjust with deionized water to a final volume of 1 litre.

Sodium hydroxide (0.875 mol/l): Dissolve 17.5 g sodium hydroxide pellets in 500 ml deionized water.

Arsenious acid solution (0.025 mol/l): Place 5 g arsenic trioxide and 25 g sodium chloride in a 1-L Erlenmeyer flask, then slowly add 200 ml of 5 N sulfuric acid, heat gently while stirring to dissolve, and then cool to room temperature. Dilute with deionized water to 1 litre. Store in darkness; stable for months.

Alternative Arsenious acid solution (0.05 mol/l): Dissolve 10 g arsenic trioxide in 200 ml of 0.875 mol/l sodium hydroxide solution. Slowly add 32 ml of concentrated (36 N) sulfuric acid to the solution in an ice bath while stirring. After cooling, add 25 g of sodium chloride and then adjust to 1 litre with cold deionized water with stirring to dissolve. Store in darkness, stable for months. This solution is recommended for the microtiter plate application as well as for manual spectrophotometric analysis.

Ceric ammonium sulfate solution (0.038 mol/l): Dissolve 24 g ceric ammonium sulfate in 1 litre 3.5 N H_2SO_4. Make up at least 24 h before use, and store in darkness; stable for months.

Standard iodine solution (KIO_3):
Stock standard A: Dissolve 0.840 g potassium iodate in deionized water to a final volume of 500 ml in a volumetric flask. This solution is equivalent to 1000 µg/ml.
Stock standard B: Dilute 5 ml of standard A in deionized water to a final volume of 500 ml in a volumetric flask. This solution is equivalent to 10 µg/ml. Store all stock standards in white or brown plastic bottles, in a refrigerator away from light. The solution is stable for 6-12 months.
Working standards: Prepare by adding aliquots of 200, 400, 800, 1200, 2000, and 3000 µl of standard B, each diluted with water to a final volume of 100 ml in volumetric flasks. These standards are equivalent to iodine concentrations of 20, 40, 80, 120, 200, and 300 µg/l. Include a zero standard (deionized water). Store in plastic bottles in a refrigerator away from light. Stable for 1-3 months.
Note: 1.68 mg KIO_3 contains 1.0 mg iodine. 1000 µg iodine/l is equivalent to 7.9 µmol/l.

A3.5 Procedure

1. Allow urine to reach room temperature, then mix urine to suspend sediment.

2. Pipette 250 µl of each urine sample, working standards ranging from 0 to 300 µg/l and internal urine controls, into 13 x 100 mm test tubes. Duplicate iodine standards and a set of internal urine controls should be included in batch.
3. Add 1 ml ammonium persulfate to each tube.
4. Heat all tubes for 60 minutes at 91-95 °C.
5. Cool tubes to room temperature.
6. Add 2.5 ml arsenious acid solution. Mix by inversion or vortex. Let stand for 15 minutes.
7. Add 300 µl of ceric ammonium sulfate solution to each tube at 15 to 30-second intervals between successive tubes, mixing each with a vortex after addition. A stopwatch should be used for this. With practice, a 15-second interval is convenient.
8. Allow to sit at room temperature. Exactly 30 minutes after the addition of ceric ammonium sulfate to the first tube, read its absorbance at 405 or 420 nm. Read successive tubes at the same time intervals as when adding the ceric ammonium sulfate.

A3.6 Calculation of results

Construct a standard curve on graph paper by plotting the iodine concentration of each standard on the abscissa against its optical density at 405 nm (OD_{405}) on the ordinate. Alternatively, a standard curve can be constructed by plotting the **log** of the absorbance at 405 nm on the X-axis versus the standard iodine concentration in µg/l on the Y-axis with a scatter plot, using Exel on a desktop computer. The iodine concentration in µg/l of each specimen is calculated by using the equation of the linear trendline of this chart. As this is an inverse endpoint colour reaction, all specimens that have absorbance values lower than the acceptable standard curve (or calculate concentration >300 µg/l) should be diluted, preferably 1:3 or 1:5 dilutions, or as required, with water and re-essayed. The most common absorbancies observed using this method range between 0.300 and 1.800 for standards with concentrations between 300 µg/l and 0 µg/l.

A3.7 Notes

1. This is modified from the former method (method B, see page 30), substituting ammonium persulfate for chloric acid (more toxic) as the digestant (26, 27, 40).
2. Since the digestion procedure has no specific end-point, it is essential to run blanks and standards with each assay to allow for variations in heating time, etc.

3. The exact temperature, heating time, and cooling time may vary. However, within each assay, the interval between the time of addition of ceric ammonium sulfate and the time of the reading must be the same for all samples, standards, and blanks.
4. With the longer ceric ammonium sulfate incubation and with 15-second interval additions of ceric ammonium sulfate, up to 120 tubes can be read in a single assay.
5. The volumes and proportions of samples and reagents can be varied to achieve different concentrations or a different curve shape, if conditions warrant. If different tube sizes are used, corresponding sized holes in the heating block are also needed.
6. If necessary, this method could probably be applied without a heating block, using a water, oil, or sand bath, but this is not recommended. It is essential that all tubes be uniformly heated and that the temperature be constant within the range described above.
7. Test tubes can be reused if they are carefully washed to eliminate any iodine contamination. Durable 13 x 100 mm or 16 x 100 mm culture tubes with screw caps are recommended (e.g., Corning or KIMAX tubes).
8. This method can be slighty modified to be suitable for automation, which allows for colorimetric readings to be done in microtiter plates and subsequently with a scanner. For example, with the same digestion step, only the ceric ammonium sulfate concentration could be adjusted to approximately 0.016 or 0.019 mol/l to accomodate the microtiter plate applications (*30*).
9. The Centers for Disease Control and Prevention (CDC), Atlanta, USA provides urinary iodine laboratories the opportunity to participate in an external quality control program (EQUIP).

ANNEX 4

Methodology for selection of survey sites by PPS sampling[1]

Since it is usually not possible to randomly select households, a stratified method for household selection is used for population-based surveys. Such "cluster" surveys require identification of a sampling unit such as a village or ward as the "cluster" or site from which households are selected. In the selection of survey sites (or clusters), the basic goal is to select sites that will be representative of the area to be surveyed. Methods used for performing household-based and school-based surveys are described in this annex.

A4.1 Household-based surveys

For a standard, population-based "cluster" survey, the first step is to obtain the "best available" census data for all of the communities in the area of interest. This information is usually available from the central statistical office within the ministry that performs the census for the country.

From the census data, select the data for the area chosen for the survey. Make a list with four columns (see Table 11). The first column lists the name of each community. The second column contains the total population of each community. The third column contains the cumulative population – this is obtained by adding the population of each community to the combined population of all of the communities preceding it on the list. The list can be in any order: alphabetical; from smallest to largest population; or geographical.

The sampling interval (k) for the survey is obtained by dividing the total population size by the number of clusters to be surveyed. A random number (x) between 1 and the sampling interval (k) is chosen as the starting point using random number tables, and the sampling interval is added cumulatively. The communities to be surveyed are those with the (x+n)th person, the (x+2n)th, (x+3n)th, person and so on up to the (x+30n)th person.

The 30 clusters should be plotted on a map. Next, a logical sequence for the fieldwork should be developed for each of the survey teams.

[1] Adapted from: Sullivan KM et al. (*40*)

A4.1.1 An example of selecting communities in a cluster survey

In the fictitious area of El Saba, there are 50 communities (Table 11). In practice there would usually be many more than 50 communities, but this number is used for illustrative purposes to describe the method.

In Table 11 on the opposite page, the first column contains the names of the communities, the second column the population of each community, and the third column the cumulative population. A fourth column is used for identifying which communities will have one or more clusters selected.

Follow four steps to select communities to be included in the survey:

1. Calculate the sampling interval by dividing the total population by the number of clusters. In this example, 24 940 / 30 = 831.
2. Choose a random starting point (x) between 1 and the sampling interval (k, in this example, 831) by using the random number table. For this example, the number 710 is randomly selected.
3. The first cluster will be where the 710th individual is found, based on the cumulative population column, in this example, Mina.
4. Continue to assign clusters by adding 831 cumulatively. For example, the second cluster will be in the village where the value 1541 is located (710 + 831 = 1541), which is Bolama. The third cluster is where the value 2372 is located (1541 + 831 = 2372), and so on. In communities with large populations, more than one cluster will probably be selected.

If two clusters are selected in one community, when the survey is performed the survey team would divide the city into two sections of approximately equal population size and perform a survey in each section. Similarly, if three or more clusters are in a community, the community would be divided into three or more sections of approximately equal population size.

A4.1.2 Selecting households within clusters

Within each cluster there is a need to select households for the assessment. As a general rule, we recommend that, through appropriate sample size calculations, the same number of households be visited in each cluster. In most instances, a sample size between 600 and 900 is sufficient to have a reasonable confidence interval around the coverage estimate. Thus, for example, a 30-cluster survey is desired, and based on sample size calculations, it is found that 20 households are to be visited in each cluster. There are several methods for selecting households within a cluster. In some settings the national census organization may have maps of the areas and census personnel can randomly select the households to

Table 11 Selection of communities in El Saba using the PPS method

NAME	POPULATION	CUMULATIVE POPULATION	CLUSTER	NAME	POPULATION	CUMULATIVE POPULATION	CLUSTER
Utural	600	600		Ban Vinai	400	10 800	13
Mina	700	1 300	1	Puratna	220	11 100	
Bolama	350	1 650	2	Kegalni	140	11 240	
Taluma	680	2 380	3	Hamali-Ura	80	11 320	
War-Yali	430	2 810		Kameni	410	11 730	14
Galey	220	3 030		Kiroya	280	12 010	
Tarum	40	3 70		Yanwela	330	12 340	
Hamtato	150	3 220	4	Bagvi	440	12 780	15
Nayjaff	90	3 310		Atota	320	13 100	
Nuviya	300	3 610		Kogouva	120	13 220	16
Cattical	430	4 040	5	Ahekpa	60	13 280	
Paralai	150	4 190		Yondot	320	13 600	
Egala-Kuru	380	4 570		Nozop	1 780	15 380	17
						18	
Uwarnapol	310	4 880	6	Mapazko	390	15 770	19
Hilandia	2 000	6 880	7				
			8	Lotohah	1 500	17 270	20
Assosa	750	7 630	9	Voattigan	960	18 230	21
						22	
Dimma	250	7 880		Plitok	420	18 650	
Aisha	420	8 300	10	Dopoltan	270	18 900	
Nam Yao	180	8 480		Cococopa	3 500	22 400	23
						24	
						25	
						26	
						27	
Mai Jarim	300	8 780		Famegzi	400	22 820	
Pua	100	8 880		Jigpelay	210	22 840	
Gambela	710	9 590	11	Mewoah	50	22 890	
Fugnido	190	9 880	12	Odigla	350	23 240	28
Degeh Bur	150	10 030		Sanbati	1 440	24 680	29
Mezan	450	10 480		Andidwa	260	24 940	30

be sampled, and provide detailed maps to enumeration teams. In other situations, detailed maps may not be available at the national level and the teams may need to initially spend time at each cluster to perform the household selection themselves. One approach to household selection is to carefully map all households within the cluster and then either randomly or systematically select households to survey. While this approach is ideal, it often requires an additional visit to the cluster, and this can add significantly to the survey cost. Another approach, frequently used in EPI surveys in the past, is to randomly select one household within the cluster and then select subsequent households using the "next nearest household" approach, or selecting households in a specified direction. We do not recommend these approaches, as they may allow some bias in household selection. An alternative recommended method is a segment method. On arrival in the cluster, if the cluster is large, visually divide the cluster into segments. With segmentation, there is an attempt to divide the cluster into approximately equal sample size segments based on roads, rivers, or other geographic demarcations. Each segment should have approximately the same number of households. Once divided, one segment is randomly selected, and a random or systematic selection of households is sampled within that segment.

A4.1.3 Selecting individuals within households

Once households are selected, the response can be taken from the head of the household since the type of salt used in the household likely affects all household members. It is useful to consider collection of urine specimens for urinary iodine assessment in school-age children and pregnant and lactating women, as this will help understand overall iodine intake in these vulnerable groups.

The considerations noted above apply to estimating the proportion of households using iodized salt. Further sample size calculations are needed if additional information is collected, such as urinary iodine or vitamin A supplementation, and this may affect both the number of households to be sampled, and the selection of individuals within the household.

A4.2 School-based surveys

If a school-based survey is to be performed, the Ministry of Education should be contacted to obtain a listing of all schools with children of the appropriate age for the survey. Because the age range for the survey is 6 to 12 years, the grades in which these children are likely to be enrolled should be determined. Ideally, the Ministry of Education will have such a listing.

If one nationwide survey is performed, a listing of schools for the entire nation is needed. If subnational estimates are required, then a listing of the schools for each subnational area is needed. If enrolment information for each school is available, the PPS method should be used for selection. If enrolment information is not available, then systematic sampling can be performed.

A4.2.1 Selecting schools

When performing school-based surveys in a geographical area, the first questions are:

- Is there a list of all schools in the geographic area with the appropriate age range?
- If there is a list of schools, is the number of pupils in each school known?

In most areas, a list of schools and their respective enrolments is available. Ensure that there is the same number of grades/levels in the schools. If a list of schools and enrolments is available, the selection of schools should be performed using the PPS method described for selecting communities. If there is a list of schools but the enrolments are not known, schools can be selected using systematic selection.

Using systematic selection, rather than PPS, complicates analysis somewhat. However, if enrolment information cannot be obtained easily there may be no alternative. If there is an extremely large number of schools in an area, or if a listing of all schools does not exist, another method can be used. This alternative method is described later in these guidelines.

Method 1 – schools when their enrolments are known

In this situation the PPS method for selecting communities, as described earlier in this chapter, should be used. First, generate a list of schools similar to that shown in Table 12. Second, determine the cumulative enrolment. Finally, select schools using the same PPS method as described for selecting communities (see Table 11).

Table 12 Selection of schools using the PPS method

SCHOOL	ENROLMENT	CUMULATIVE ENROLMENT
Utural	600	600
Mina	700	1300
Bolama	350	1650
Etc.		

Method 2 – a list of schools is available, but enrolments are not known

When a list of schools is available but the enrolment of each school is not known, the systematic selection method should be employed as follows.

- Obtain a list of the schools and number them from 1 to N (the total number of schools).
- Determine the number of schools to sample (n), usually 30.
- Calculate the "sampling interval" (k) by N/n (always round down to the nearest whole integer).
- Using a random number table, select a number between 1 and k. Use the randomly selected number to refer to the school list, and include that school in the survey.
- Select every kth school after the first selected school.

Example of systematic selection of schools

For illustrative purposes, Table 13 lists 50 schools. The following method would be used to select eight schools:

Step one: There are 50 schools, therefore N = 50.

Step two: The number of schools to sample is eight; therefore n = 8.

Step three: The sampling interval is 50 / 8 = 6.25; round down to the nearest whole integer, which is 6; therefore, k = 6.

Step four: Using a random number table, select a number from 1 to (and including) 6. In this example, suppose the number selected had been 3. Accordingly, the first school to be selected would be the third school on the list, which in this example is Bolama.

Step five: Select every sixth school thereafter; in this example, the selected schools would be the 3rd, 9th, 15th, 21st, 27th, 33rd, 39th, and 45th schools on the list.

In some circumstances, this method might result in the selection of more than the number needed. In the above example, for instance, had the random number chosen in step four been 1 or 2, then nine schools would have been selected rather than eight. This is because the value for k was rounded down from 6.25 to 6.

In this situation, to remove one school so that only eight are selected, again go to the random number table to pick a number. The school that corresponds to that random number is removed from the survey.

To analyse properly the data collected using systematic sampling, additional information needed would include the number of eligible pupils in each school. Note that usually 30 clusters are selected; the eight indicated in Table 13 have been selected in this example for illustrative purposes only.

Table 13 Selection of schools using the systematic selection method

SCHOOL	SELECTED	SCHOOL	SELECTED
1 Utural		26 Ban Vinai	
2 Mina		27 Puratna	Y
3 Bolama	Y	28 Kegalni	
4 Taluma		29 Hamali-Ura	
5 War-Yali		30 Kameni	
6 Galey		31 Kiroya	
7 Tarum		32 Yanwela	
8 Hamtato		33 Bagvi	Y
9 Nayjaff	Y	34 Atota	
10 Nuviya		35 Kogouva	
11 Cattical		36 Ahekpa	
12 Paralai		37 Yondot	
13 Egala-Kuru		38 Nozop	
14 Uwarnapol		39 Mapazko	Y
15 Hilandia	Y	40 Lotohah	
16 Assosa		41 Voattigan	
17 Dimma		42 Plitok	
18 Aisha		43 Dopoltan	
19 Nam Yao		44 Cococopa	
20 Mai Jarim		45 Famegzi	Y
21 Pua	Y	46 Jigpelay	
22 Gambela		47 Mewoah	
23 Fungido		48 Odigla	
24 Degeh Bur		49 Sanbati	
25 Mezan		50 Andidwa	

Method 3 – an extremely large number of schools

In very large populations, it may not be possible or efficient to select schools using either the PPS or the systematic selection method. For example, Szechwan Province in China has a population of approximately 100 million. Even if a list of schools were available at the provincial level, it would take much time and effort to select schools using either of these methods.

Accordingly, another approach may be more appropriate. First, select districts using the PPS method. Develop a listing of the districts, their populations, and cumulative populations similar to the PPS selection

described earlier. Next, determine the number of schools to survey, based on the cumulative population using PPS.

For districts with one or more clusters to be selected, select schools in each district using a random number table. For example, if a district has 200 schools, number them from 1 to 200. Then, randomly select a number from 1 to 200 using the table. If two schools are to be selected, then randomly select two numbers. Finally, and while not technically correct, it would be acceptable to analyse the school-based data as though the schools were selected using PPS methodology.

Selecting students within each selected school

Once the school has been selected, it is usual to select one class or grade, and to sample all students in that class – both male and female. If the schools are large, it may be necessary to divide the class, and pick one of the divisions randomly, sampling all children in the selected portion. If schools are small, it may be necessary to include more than one class.

Other possibilities

In situations where male and female children attend the same school, the selection of schools and pupils would be the same as discussed above. In situations where males and females attend separate schools, when a school of one sex is selected the nearest school of the opposite sex should also be surveyed.

For example, a survey is to be performed in an area where males and females attend separate schools. Thirty schools are to be selected, and 20 pupils sampled in each. When an all-male school is visited, information should be collected on 10 male pupils. Then, the nearest female school is visited, and information collected on 10 female pupils.

ANNEX 5

Summarizing urinary iodine data: a worked example

Some actual urinary iodine data from schoolchildren in Cameroon, following the implementation of USI, are presented in the first (left) column of Table 14. The data have been entered into a spreadsheet on a personal computer for ease of calculation. However, with small numbers such as these, the calculations are relatively easily performed by hand.

A5.1 Steps in processing the data

1. Before proceeding, carefully check the data entered against the original. Ensure that the same number of data points (n) is present, and look for any anomalous results.
2. Next, sort the data from highest to lowest, or vice-versa. The spreadsheet will do this automatically.[1] The sorted data are shown under "Value" in Table 14, starting with the highest value, and a summary is shown in Table 15. The next columns show the rank and percentile for each data point.
3. The median is the middle value of the ranked data. In other words, it is the value of the (n+1) / 2th value. In this case, there are 98 data points, so the median is the value of (98+1) divided by 2 = 49.5th data point. Accordingly, use the middle point between the 49th and 50th values: 122 and 121 µg/l, respectively. The mid-point is 121.5 µg/l, so the median is 121.5 µg/l.
4. Next, calculate the number of values below 100, 50, and 20 µg/l, respectively. The ranking will allow this to be done very easily. In this case, there are 33 values below 100 µg/l, 6 below 50 µg/l, and one below 20 µg/l. These should be calculated as percentages: 33 of 98 is 33.7%, 5 of 98 is 5.1% and 1 of 98 is 1.0%.
5. Check if any values are above 500 µg/l. There is one (1.0%).
6. The 20th and 80th percentiles may be readily observed, or automatically displayed using the PERCENTILE function [=PERCENTILE

[1] In Microsoft Excel, use the Data Analysis function on the Tools menu, and select "Rank and Percentile".

(range of cells, 0.2)]. The 20th percentile (P20) is 82.4 μg/l and P80 is 191.8 μg/l.

7. The "Descriptive Statistics" function of Data Analysis in Excel provides all statistics shown: select "Summary Statistics" in the dialogue box. Note that the mean is much higher than the median, indicating that the distribution is heavily skewed to the right. This is also shown by the much greater distance between P80 and the median, compared to that between P20 and the median.
8. In addition, the data can be shown as a histogram using the "Histogram" function of Data Analysis in Excel. Convenient ranges need to be chosen for making the frequency distribution, which will be reflected in the height of each bar of the histogram. 50 μg/l is suggested (i.e., the first bar is 0–49 μg/l, the second 50–99 μg/l, the third 100–149 μg/l, etc.). Appropriate modifications can be made using "Chart Options" and related functions. The histogram is shown in Figure 6. A fully detailed description for constructing that histogram is not given here.

In presenting this distribution, it is important not to misinterpret the different percentages. A common mistake is to assume that there is deficiency because 33.7% have a UI value <100 μg/l. This is not the correct interpretation of the median value and distribution statistics. Instead, this calculation shows the distribution of values around the median value, and helps determine if there is a large proportion with either very low or very high values.

These results indicate that there is no iodine deficiency, and that salt iodization is therefore having the required impact. There is no evidence of significant over-iodization. No changes are needed on the basis of these results, but further follow-up is always essential.

Table 14 Urinary iodine data in Cameroon schoolchildren following salt iodization

UI(µg/l)	VALUE	RANK	PERCENT	DESCRIPTIVE STATISTICS	
141	535	1	100.00%		
138	480	2	98.90%	Mean	142.7449
138	395	3	97.90%	Standard error	8.877338
154	340	4	96.90%	Median	121.5
162	320	5	95.80%	Mode	138
26	295	6	94.80%	Standard deviation	87.88117
63	273	7	92.70%	Sample variance	7723.099
111	273	7	92.70%	Kurtosis	5.463542
120	264	9	91.70%	Skewness	1.970291
65	261	10	90.70%	Range	525
190	240	11	89.60%	Minimum	10
142	232	12	87.60%	Maximum	535
138	232	12	87.60%	Sum	13989
95	224	14	86.50%	Count	98
273	208	15	85.50%	Confidence level (95.0%)	17.61905
132	200	16	83.50%		
164	200	16	83.50%		
66	198	18	82.40%		
158	193	19	80.40%		
114	193	19	80.40%		
118	190	21	79.30%		
232	188	22	78.30%		
145	180	23	77.30%		
94	174	24	76.20%		
90	164	25	75.20%		
122	162	26	74.20%		
114	160	27	73.10%		
340	158	28	72.10%		
193	154	29	71.10%		
135	150	30	70.10%		
261	146	31	68.00%		
75	146	31	68.00%		
63	145	33	67.00%		
264	144	34	65.90%		
142	142	35	63.90%		
174	142	35	63.90%		
121	141	37	62.80%		
395	140	38	60.80%		
320	140	38	60.80%		
240	138	40	57.70%		
140	138	40	57.70%		
66	138	40	57.70%		
146	135	43	56.70%		
115	133	44	55.60%		
82	132	45	54.60%		
82	128	46	53.60%		
535	124	47	52.50%		
74	122	48	50.50%		
35	122	48	50.50%	The median lies halfway between	
83	121	50	49.40%	these two values	

Table 14 continued

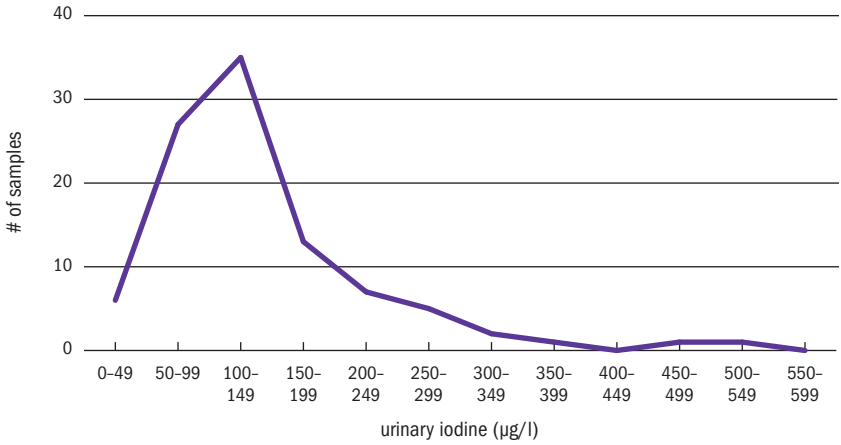
UI(µg/l)	VALUE	RANK	PERCENT	DESCRIPTIVE STATISTICS
104	120	51	46.30%	
64	120	51	46.30%	
208	120	51	46.30%	
49	118	54	45.30%	
89	117	55	44.30%	
109	115	56	42.20%	
106	115	56	42.20%	
32	114	58	40.20%	
128	114	58	40.20%	
232	111	60	39.10%	
88	110	61	38.10%	
115	109	62	37.10%	
144	108	63	36.00%	
86	106	64	35.00%	
150	104	65	34.00%	
224	96	66	32.90%	<100 µg/l
92	95	67	30.90%	
180	95	67	30.90%	
193	94	69	29.80%	
133	92	70	28.80%	
80	90	71	26.80%	
87	90	71	26.80%	
96	89	73	25.70%	
120	88	74	24.70%	
146	87	75	22.60%	
160	87	75	22.60%	
124	86	77	21.60%	
90	83	78	20.60%	
10	82	79	18.50%	
55	82	79	18.50%	
108	80	81	16.40%	
480	80	81	16.40%	
80	75	83	15.40%	
122	74	84	14.40%	
198	66	85	12.30%	
200	66	85	12.30%	
87	65	87	11.30%	
200	64	88	10.30%	
188	63	89	8.20%	
54	63	89	8.20%	
273	55	91	7.20%	
120	54	92	6.10%	
140	49	93	5.10%	<50 µg/l
110	42	94	4.10%	
42	35	95	3.00%	
95	32	96	2.00%	
117	26	97	1.00%	
295	10	98	.00%	<20 µg/l

Table 15 Summary of results

Number	98
Median	121.5 µg/l
20th percentile	82.4 µg/l
80th percentile	191.8 µg/l
Distribution	
<100 µg/l	33.7%
<50 µg/l	5.1%
<20 µg/l	1.0%
>500 µg/	1.0%

Figure 6 Frequency table and histogram to show distribution of urinary iodine values after iodization in Cameroon

URINARY IODINE (µg/l)	FREQUENCY
0–49	6
50–99	27
100–149	35
150–199	13
200–249	7
250–299	5
300–349	2
350–399	1
400–449	0
450–499	1
500–549	1
550–599	0



ANNEX 6

Guidelines to assess IDD national programmes[1]

A6.1 Background

The iodine deficiency elimination goal was set at the World Summit for Children in 1990, and subsequently in 1993 when WHO and UNICEF agreed to recommend USI to each nation where IDD is a public health problem. The IDD elimination goal was reaffirmed by multi-sector and national delegations during the UN Special Session for Children (UNGASS) in New York, May 2002, and a timetable was set for global elimination by 2005. At the same time, the Network for Sustained Elimination of Iodine Deficiency (the Network) was launched at a side event during UNGASS by the Director General of WHO which included contributions of high-level global leaders.

Many countries are now seeking acknowledgement of their USI accomplishments and asking for external reviews to assist them in achieving USI. The Network will provide USI/IDD review through simplified guidelines and in a cost-effective manner. Countries that have achieved USI can request a desk assessment by providing relevant data and information (see Annex 1) to the Network. For countries whose progress is stalled and with substantial gains towards USI yet to be made, external review missions might still be needed.

A6.2 Objectives

The following guidelines provide a framework for conducting the USI/IDD country assessment. The main objectives of the review are:

- To help governments and program managers assess and verify the country achievement towards their goals to sustain elimination of iodine deficiency;
- To identify lessons learned and best practices of the country programs;
- To facilitate progress comparisons across regions by means of standardized tools/guidelines;

[1] Adapted from: Country review guidelines. Network for sustained elimination of iodine deficiency. New York, 2006 (*41*).

- To identify ways to address bottlenecks to ensure USI;
- To recommend steps to sustain USI.

A6.3 Proposed mechanism

The process needs to be initiated by the government requesting an external USI review/assessment through the UNICEF or WHO country office. This step is important as it indicates national ownership and commitment to the process.

Once the request is received by the UNICEF/WHO country office, they would facilitate the preparation of country report as outlined in Annex 1. The report should be jointly prepared with all USI/IDD partners (National Coalition) in the country.

The Network Secretary will communicate with the Board members (UNICEF, WHO, WFP, Kiwanis International, Salt Institute, EuSalt, China National Salt Industry, ICCIDD, Micronutrient Initiative, Emory University, US CDC, and GAIN), obtain their inputs, and involve them as appropriate.

A6.3.1 Desk Review

Proposed criteria:

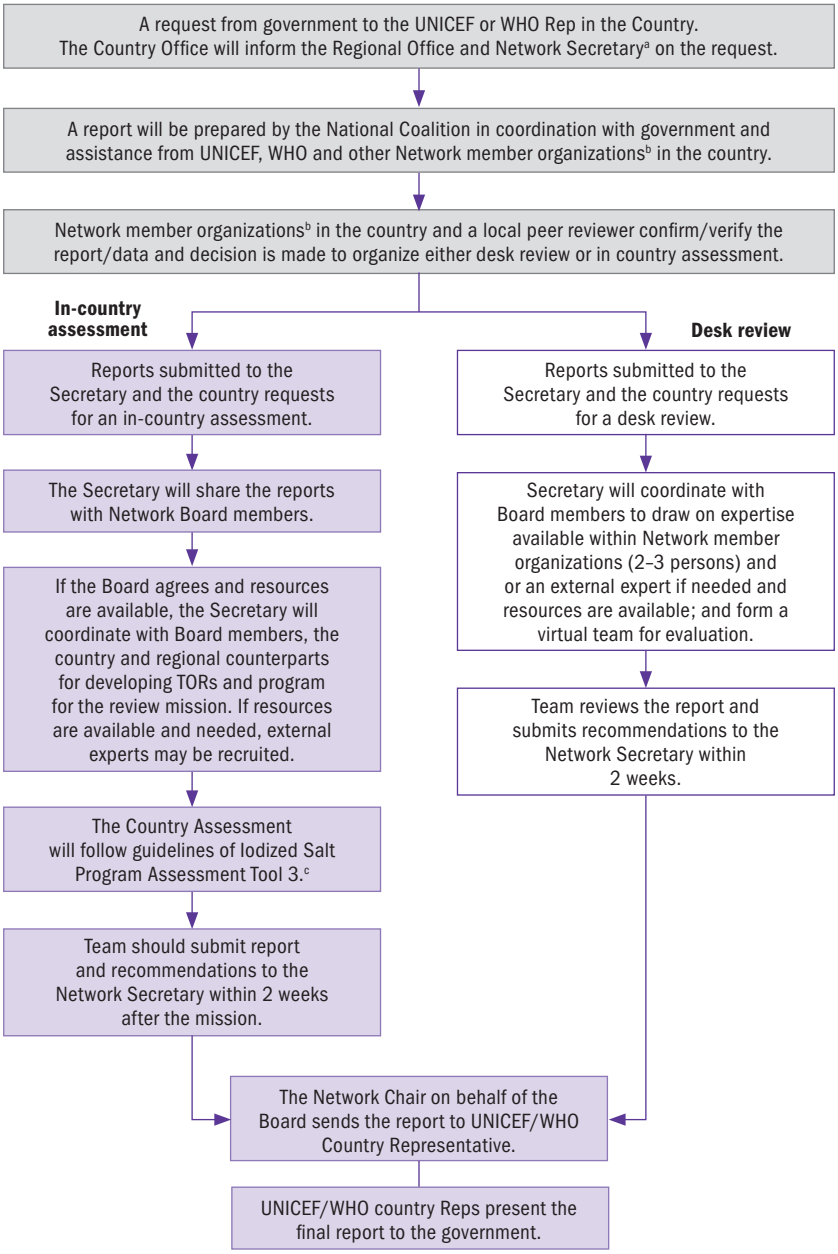
- The country report indicates that USI has been achieved as per:
  - The iodine status of the population and proportion of households with access to adequately iodized salt;
  - The WHO/UNICEF/ICCIDD programmatic indicators.
- There is a need for strategic guidance and sufficient information is available for a desk review.

Country report:

- The country report will be an important means of communicating the country situation. It should include a short executive summary and clear, concise summary on how the country plans to sustain the USI achievements.
- It will be important to have the report (or at least the executive summary and country plans) available to distribute at the 'stakeholder'/partners consultation prior to submission to the Network.
- Please see Annex 1 for a suggested outline for the country report.

Representatives of Network member organizations could be involved in the desk review, and if needed and resources are available, the Network might have an external expert.

Figure 7 Flow chart for Network Country Review



[a] Network Secretary can be contacted at Info@iodinenetwork.net.

[b] Network member organizations in the country include UNICEF, WHO, WFP, Kiwanis International, Salt Institute, EuSalt, China National Salt Industry Corporation, ICCIDD, MI, Emory U, US CDC, and GAIN.

[c] UNICEF, PAMM, MI, ICCIDD and WHO. 1995. Assessing Country Progress in Universal Salt Iodization Programs: Iodized Salt Program Assessment Tool (ISPAT). The Micronutrient Initiative, Ottawa, Canada.

A6.3.2 External Review Mission

Proposed criteria for conducting an external review:

- National progress has been stalled;
- Early and significant gains towards USI can be predicted and alternative or different strategies are considered worthwhile;
- Evidence of senior political commitment to goal achievement and national commitment to success is apparent;
- There is a need for an external mission.

Assessment team composition:

- Senior officers from selected central ministries and governmental departments;
- National coalition/committee;
- Salt producers, technicians, and traders;
- Civil, scientific, and communications elements of society;
- Representatives from the border inspection systems, importers and exporters, law enforcement personnel, agriculture and education;
- Senior officers from resident development agencies in the country, and representatives of other network member organizations, where possible;
- One or two regional/international consultants.

Country assessment and mission report will follow the procedure and format suggested in ISPAT (1999).

A6.3.3 Proposed outline for reporting country USI achievement

The country report should include:

- **Executive summary:** A summary of country USI/IDD status, analyses, and recommendations.
- **Summary of country action plans:** Key action plans for strengthening and sustaining the achievements.
- **Country profile:** In this section, a brief summary of information on the country is collected and recorded. It should provide a summary of the geographical and administrative description of the country, including demographics, vital health statistics, and basic government organization. A description of the health care system in the country should be provided, including an estimated health budget, and the budget for iodine deficiency elimination program activities – including the budget for the USI component. It would be useful to plot an historic time-line marking significant program activities for the past 10 to 20 years.

Country assessment

a. The product

This section should include information on all aspects of salt production or imports. It should focus on those aspects that pertain to the entire salt industry and should provide details on those areas of industry responsibility that can be improved and sustained. The discussion includes:

- Achievement of change in practices by food processing industries;
- Analysis of relationships between regulatory authorities and practices and salt producers and practices;
- Analysis of utility and impact of product advertising on public demand, use and understanding;
- Analysis of quality assurance at iodized salt production;
- Analysis on data of salt importation, production and iodization process, distribution, major companies, small scale producers/salt farmers, association of salt producers, prices of products and the market situation;
- Analysis on availability and procurement of KIO_3;
- A summary of salt situation (see Table 16);
- A summary of lessons learned;
- Key action plans related to the product might be elaborated.

Table 16 Summary of salt situation

SALT		IODIZED	NOT IODIZED	TOTAL
Total produced/imported	Total			
(total salt available in country)	Local Production			
	Import			
Industrial (non-food grade)	Total			
Food grade (including animal salt)	Total			

b. The process

This section should include all elements necessary for the long-term continuation of the program. The focus should be on elements that are the roles and responsibility of the national IDD program, or of other branches of the government. This should include assessments of each element's strengths and weaknesses, with specific suggestions for improvement. The discussion includes:

- Analysis of the political process and how that has been nurtured and sustained, and with what measurable results;
- Analysis of the history of formation of a National Coalition to assure achievement of USI and Sustained Iodine Nutrition and the current practices and issues;

- Analysis on laws and regulations, inspection, and enforcement processes in the country for USI and some indication of practice and results;
- Analysis of government oversight practices and procedures;
- Achievement of penetration into learning systems;
- Achievement of insertion of essential knowledge on iodine nutrition in the training of medical practitioners and other health personnel;
- Achievement of insertion in animal husbandry and some indication of impact and increase of iodized salt use for animals;
- Analysis of the communications tactics and strategies and the potential of their permanency;
- Analysis of national management capacities including appointment of a responsible officer for IDD elimination program;
- Analysis of financial commitments of state authorities, central budgets, and expenditure patterns, including private sector and civic sector commitments; and degree to which the nation is positioned with national resources to sustain iodine nutrition forever;
- Analysis of impact of international aid and collaboration;
- Analysis of potential for success absent international aid;
- A summary of lessons learned;
- Key action plans related to the process.

c. Households access to iodized salt and iodine nutrition status

This section should provide a summary of the most current data in the last two years on household and retail iodized salt coverage/access, and on the iodine nutrition status (urinary iodine concentration: median, percentage of population below 20 μg/l) of a population. If an independent, population-based survey (preferably nationally representative) is included, data methods should be described, and a summary presented. The discussion should include data collection methods and an assessment of the coverage and prevalence figures presented. The discussion includes:

- Achievement of government practices and procedures for obtaining, analyzing, publishing and utilizing data and information.
- Analysis of commitments to assess and reassess the progress towards elimination with access to laboratories able to provide accurate data on salt and urinary iodine. This should include:
  - — Regular data on salt iodine at the factory, retail, and household levels, and regular laboratory data on UIE in school-age children with appropriate sampling for higher risk areas;
  - — A database for recording of results of regular monitoring proce-

dures particularly for salt iodine, UIE, and if available neonatal TSH monitoring with mandatory public reporting.

- Analysis on trends/changes in iodized salt coverage and iodine status over time (last 10 years if possible).
- Achievement of public health laboratories related to iodine nutrition, their management, quality control practices and procedures.
- Program infrastructure, oversight committee, staff, budget, type and number of laboratories and annual number of samples processed.
- A summary of lessons learned.
- Key action plans to sustain regular USI monitoring and evaluation.

d. A summary of Country Program assessments by WHO, UNICEF, and IC CIDD

Table 17 Summary of Country Program assessments

PROGRAMMATIC INDICATORS	COUNTRY PROGRAM SITUATIONS	ACTION PLANS TO SUSTAIN USI
1. Presence of a national multi-sector coalition responsible to the government for the national programme for the elimination of IDD with the following characteristics: – National stature; – All concerned sectors, including the salt industry, represented, with defined roles and responsibilities; – Convenes at least twice yearly.		
2. Demonstration of political commitment as reflected by: – Inclusion of IDD in the national budget (either as specific programme funds or through inclusion in existing programme funds) particularly with regard to procurement and distribution of KIO_3.		
3. Enactment of legislation and supportive regulations on universal salt iodization, which establishes a routine mechanism for external quality assurance.		
4. Establishment of methods for assessment of progress in the elimination of IDD as reflected by: – Reporting on national programme progress every three years.		

Table 17 Continued

PROGRAMMATIC INDICATORS	COUNTRY PROGRAM SITUATIONS	ACTION PLANS TO SUSTAIN USI
5. Access to laboratories as defined by: – Laboratories able to provide accurate data on salt and urinary iodine levels and thyroid function.		
6. Establishment of a programme of education and social mobilization as defined by: – Inclusion of information on the importance of iodine and the use of iodized salt, within educational curricula.		
7. Routine availability of data on salt iodine content as defined by: – Availability at the factory level at least monthly, and at the household level at least every five years.		
8. Routine availability of population-based data on urinary iodine every five years.		
9. Demonstration of ongoing cooperation from the salt industry as reflected by: – Maintenance of quality control measures and absorption of the cost of iodate/iodide.		
10. Presence of a national database for recording of results of regular monitoring procedures which include population-based household coverage and urinary iodine (with other indicators of iodine status and thyroid function included as available).		

Conclusions

Conclusion on the country situation analysis and summary of agreed key action plans to sustain ID elimination in the country.

ANNEX 7

List of Contributors

Bruno de Benoist
Micronutrient Malnutrition Unit (MNM)
Department of Nutrition for Health and Development
World Health Organization
20 Avenue Appia
CH-1211, Geneva 27
Switzerland
Tel: +41 22 791 3412
Fax: +41 22 791 4156
E-mail: debenoistb@who.int

Gerard N. Burrow
Chairman
International Council for Control of Iodine Deficiency Disorders
110 Deepwood Drive
Hamden, CT 06517
USA
E-mail: gburrow55@comcast.net

François Delange[1]
ICCIDD
Hyde Park Residence
Chaussée de Waterloo 965 D.O.3
B 1180 Brussels
Belgium
Tel: +32 (2) 660 04 08
Fax: +32 (2) 660 0408
E-mail: fdelange@ulb.ac.be

[1] Deceased

Jonathan Gorstein
University of Washington
School of Public Health and Community Medicine
H-688 Health Sciences Building
Box 357660
1959 NE Pacific St.
Seattle, WA 98195
United States of America
Tel: 206–616–8530
Fax: 206–543–3964
Email: gorstein@u.washington.edu

Robin Houston
Monitoring and evaluation for vitamin A
MOST Project
9455 Big Gulch Road
Bozeman, MT 59715
United States of America
Tel: +1 (406) 582 7959
Fax: +1 (406) 582 7959
E-mail: houstonrmh@yahoo.com

Pieter Jooste
Nutritional Intervention Research Unit
PO Box 19070
Tygerberg 7505
Cape Town
South Africa
Tel: +27 (0) 21 938-0370
Fax: +27 (0) 21 938-0321
E-mail: pieter.jooste@mrc.ac.za

Nuné Mangasaryan
Nutrition and Child Growth & Development
Programme Division
United Nations Children's Fund (UNICEF)
3 United Nations Plaza, New York
NY 10017, USA
Tel: + 1 212 326 71 59
Fax: + 1 212 326 71 29
E-mail: nmangasaryan@unicef.org

Erin McLean
Micronutrient Malnutrition Unit (MNM)
Department of Nutrition for Health and Development
World Health Organization
20 Avenue Appia
CH-1211, Geneva 27
Switzerland
Tel: +41 22 791 3348
Fax: +41 22 791 4156
E-mail: mcleane@who.int

Eduardo Pretell
ICCIDD
Av. Paseo de la República 3691, Of. 401-A
San Isidro, Lima 27, Perú
E-mail: epretell@terra.com.pe
Tel: +(51-1) 421-0882
Fax: +(51-1) 421-3065
E-mail: epretell@terra.com.pe

Lisa Rogers
Micronutrient Malnutrition Unit (MNM)
Department of Nutrition for Health and Development
World Health Organization
20 Avenue Appia
CH-1211, Geneva 27
Switzerland
Tel: +41 22 791 1957
Fax: +41 22 791 4156
E-mail: rogersl@who.int

Kevin Sullivan
Department of Pediatrics, Epidemiology and International Health
Emory University
1518 Clifton Road, N.E.
Atlanta, GA 30322
United States of America
Tel.: +1 (404) 727 8714
Fax: +1 (404) 727 5369
E-mail: cdckms@sph.emory.edu

Juliawati Untoro
Nutrition and Child Growth & Development
Programme Division
United Nations Children's Fund (UNICEF)
3 United Nations Plaza, New York
NY 10017, USA
Tel: + 1 212 326 73 68
Fax: + 1 212 326 71 29
E-mail: juntoro@unicef.org

Michael Zimmermann
Laboratory of Human Nutrition
Swiss Federal Institute of Technology (ETH) Zürich
ETH Zentrum, Schmelzbergstrasse 7, LFV E19
CH-8092 Zürich
Switzerland
Tel: +41 44 632 8657
Fax: +41 44 632 1470
E-mail: michael.zimmermann@ilw.agrl.ethz.ch

References

1. Bleichrodt N, Born MA. A meta-analysis of research on iodine and its relationship to cognitive development. In: Stanbury J, ed. *The damaged brain of iodine deficiency: cognitive, behavioral, neuromotor, and educative aspects*. New York, Cognizant Communication Corporation, 1994: 195–200.
2. World Summit for Children – Mid Decade Goal: Iodine Deficiency Disorders. UNICEF–WHO Joint Committee on Health Policy. Geneva, United Nations Children's Fund, World Health Organization, 1994 (JCHPSS/94/2.7).
3. *Indicators for assessing iodine deficiency disorders and their control through salt iodization*. Geneva, World Health Organization, 1994 (WHO/NUT/94.6).
4. Last JM, ed. *A Dictionary of Epidemiology*. 4th ed. New York, Oxford University Press, 2001.
5. *Recommended iodine levels in salt and guidelines for monitoring their adequacy and effectiveness*. Geneva, World Health Organization, 1996 (WHO/NUT/96.13).
6. *Technical consultation for the prevention and control of iodine deficiency in pregnant and lactating women and in children less than two years old*. Geneva, World Health Organization, 2007. (To be published).
7. Hetzel BS. Iodine deficiency disorders (IDD) and their eradication. *Lancet*, 1983, 2:1126–1129.
8. Delong GR. Observations on the neurology of endemic cretinism. In: Delong GR, Robbins J, Condliffe PG, eds. *Iodine and the brain*. New York, Plenum Press, 1989: 231ff.
9. Delange F. Endemic cretinism. In: Braverman LE, Utiger RD, eds. *The thyroid. A fundamental and clinical text*. Philadelphia, Lippincott, 2000: 743–754.
10. Pandav CS and Rao AR. *Iodine deficiency disorders in livestock. Ecology and economics*. New Delhi, Oxford University Press, 1997.
11. Hetzel BS, Pandav CS. *S.O.S. for a Billion. The conquest of iodine deficiency disorders*. Oxford, Oxford University Press, 1994.

12. *Approaches to reach optimal iodine nutrition in pregnant and lactating women and young children: joint statement by the World Health Organization and the United Nations Children's Fund*. 2007. (To be published)
13. Delange F et al., eds. *Elimination of iodine deficiency disorders in Central and Eastern Europe, the Commonwealth of Independent States, and the Baltic States. Proceeding of a Conference held in Munich, Germany, 3–6 September 1997.* Geneva, World Health Organization, 1998.
14. UNICEF. *The State of the World's Children 2007: Women and Children – The double dividend of gender equality.* New York, United Nations Children's Fund, 2006.
15. *Evaluation of certain food additives and contaminants. Thirty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives.* Geneva, World Health Organization,1991 (WHO Technical Series No. 806).
16. Mannar V and Dunn JT. *Salt iodization for the elimination of iodine deficiency.* The Netherlands, International Council for Control of Iodine Deficiency Disorders, 1995.
17. Allen L et al., eds. *Guidelines on food fortification with micronutrients.* Geneva, World Health Organization and Food and Agricultural Organization of the United Nations, 2006.
18. WHO and UNICEF. *Report of the Technical Consultation to assess rapid test kits designed to monitor salt iodine content. New York, 28–29 September.* World Health Organization and The United Nations Children's Fund, 2004.
19. Pandav CS et al. Field validation of salt iodine spot testing kit using multiple observers to assess the availability of iodized salt: experience from India. In: Geertman RM, ed. *Salt 2000. Volume 2. 8th World Salt Symposium. The Hague, 8–11 May 2000.* Amsterdam, Elsevier, 2000: 1039–1043.
20. Delange F, de Benoist B, Alnwick D. Risks of iodine-induced hyperthyroidism after correction of iodine deficiency by iodized salt. *Thyroid*, 1999, 9:545–556.
21. *Quality assurance, monitoring and enforcement of salt iodization programs. Report of a Training Workshop. Blantyre, Malawi 9–13 March 1998.* Atlanta, Program Against Micronutrient Malnutrition, 1998.
22. Nathan R. *Food fortification legislation and regulation manual, 2nd ed.* Atlanta, GA, Program Against Micronutrient Malnutrition, 1995.
23. DeMaeyer EM, Lowenstein FW, Thilly CH. *The control of endemic goiter.* Geneva, World Health Organization, 1979.

24. Todd CH et al. Increase in thyrotoxicosis associated with iodine supplements in Zimbabwe. *Lancet*, 1995, 346:1563–1564.
25. Delange F, Bourdoux P, Ermans AM. Transient disorders of thyroid function and regulation in preterm infants. In: Delange F, Fisher D, Malvaux P, eds. *Pediatric Thyroidology*. Basel, S. Karger, 1985: 369–393.
26. Pino S, Fang SL, Braverman LE. Ammonium persulfate: a new and safe method for measuring urinary iodine by ammonium persulfate oxidation. *Experimental and Clinical Endocrinology & Diabetes*, 1998, 106 Suppl 3:S22–S27.
27. Dunn JT et al. *Methods for measuring iodine in urine*. The Netherlands, International Council for Control of Iodine Deficiency Disorders, 1993.
28. Dunn JT, Myers HE, Dunn AD. Simple methods for assessing urinary iodine, including preliminary description of a new rapid technique ("Fast B"). *Experimental and Clinical Endocrinology & Diabetes*, 1998, 106 Suppl 3:S10–S12.
29. Rendl J et al. Rapid urinary iodide test. *Journal of Clinical Endocrinology and Metabolism*, 1998, 83:1007–1012.
30. Ohashi T et al. Simple microplate method for determination of urinary iodine. *Clinical Chemistry*, 2000, 46:529–536.
31. Stanbury JB et al. Iodine-induced hyperthyroidism: occurrence and epidemiology. *Thyroid*, 1998, 8:83–100.
32. Zimmermann MB et al. High thyroid volume in children with excess dietary iodine intakes. *American Journal of Clinical Nutrition*, 2005, 81:840–844.
33. Zimmermann MB et al. New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. *American Journal of Clinical Nutrition*, 2004, 79:231–237.
34. Zimmermann MB et al. Increasing the iodine concentration in the Swiss iodized salt program markedly improved iodine status in pregnant women and children: a 5-y prospective national study. *American Journal of Clinical Nutrition*, 2005, 82:388–392.
35. Zimmermann MB et al. Development of a dried whole-blood spot thyroglobulin assay and its evaluation as an indicator of thyroid status in goitrous children receiving iodized salt. *American Journal of Clinical Nutrition*, 2003, 77:1453–1458.
36. Zimmermann MB et al. Assessment of iodine status using dried blood spot thyroglobulin: development of reference material and establishment of an international reference range in iodine-sufficient

children. *Journal of Clinical Endocrinology and Metabolism*, 2006, 91:4881–4887.

37. Sullivan KM et al., eds. *Monitoring universal salt iodization programs*. Atlanta, GA, Program Against Micronutrient Malnutrition, 1995.
38. Gorstein J et al. *Indicators and Methods for Cross-Sectional Surveys of Vitamin and Mineral Status of Populations*. Micronutrient Initiative and the Centers for Disease Control and Prevention, 2006.
39. Dubois D, Dubois EF. A formula to estimate the approximate surface area if height and weight be known. *Archives of Internal Medicine*, Chicago, 1916, 17:863–871.
40. Sullivan KM, May S, Maberly G. *Urinary iodine assessment: a manual on survey and laboratory methods*. 2nd ed. Atlanta, GA, Program Against Micronutrient Malnutrition, 2000.
41. *Network for Sustained Elimination of Iodine Deficiency Country Review Guidelines*. New York, United Nations Children's Fund, 2006.

This document is intended primarily for managers of national programmes for the prevention and control of micronutrient malnutrition.

It sets out principles governing the use of surveillance indicators in implementing interventions to prevent, control, and monitor iodine deficiency disorders (IDD). It presents methods for monitoring iodine status and determining urinary iodine and provides guidelines on the procedures for monitoring salt iodine content, whether at the factory, importation site, or household level. It also gives guidance on conducting surveys to assess iodine status in populations.

Finally, indicators are presented for monitoring progress towards achieving the goal of sustainable elimination of IDD as a significant public health problem.

ISBN 978 92 4 159582 7