Assessing iodine intake, iodine status, and the effects of maternal iodine supplementation: introduction to articles arising from 3 workshops held by the NIH Office of Dietary Supplements[1,2]

Abby G Ershow,[3] Gay Goodman,[4] Paul M Coates,[3] and Christine A Swanson[3]*

[3]Office of Dietary Supplements, NIH, Bethesda, MD; and [4]Human Health Risk Research, Seattle, WA

ABSTRACT

The NIH Office of Dietary Supplements (ODS) convened 3 workshops on iodine nutrition in 2014, each held in Rockville, Maryland. These workshops were part of the ongoing ODS Iodine Initiative, begun in 2011 in response to concerns that US pregnant women may be at risk of iodine deficiency and that a high fraction of prenatal dietary supplements do not contain the recommended amounts of iodine. The primary purpose of the workshops was to consider the data and resources necessary to evaluate the clinical and public health benefits and risks of maternal iodine supplementation in the United States. The first workshop focused on the assessment of iodine intake, the second focused on the assessment of iodine status, and the third focused on the design and interpretation of clinical trials of maternal iodine supplementation. Here we provide the background of the ODS Iodine Initiative, summarize the 3 workshops held in 2014, and introduce the articles that arose from the workshops and are published in this supplement issue. *Am J Clin Nutr* 2016;104(Suppl):859S–63S.

Keywords: biomarkers, clinical studies, iodine nutrition, neurodevelopment, supplementation

INTRODUCTION

The NIH Office of Dietary Supplements (ODS)[5] convened 3 workshops on iodine nutrition in Rockville, Maryland, in 2014. The workshops were held as part of an effort to consider issues related to iodine nutrition in the US population, including the data and resources necessary to evaluate the clinical and public health benefits and risks of maternal iodine supplementation. Participants were tasked with developing a research agenda to improve knowledge about the iodine status of subpopulations at risk for deficiency or excess and to address methodologic challenges and data gaps that hinder the design and evaluation of clinical trials of maternal iodine supplementation. The speakers and other participants contributed expertise in multiple knowledge areas, including the assessment of iodine intake, the development of biomarkers for assessing iodine status and thyroid function, and the evaluation of infant neurodevelopment. In addition, they brought broad training and experience in nutrition, food science, analytic chemistry, public health, epidemiology, biostatistics, clinical trial design, survey methodology, behavioral sciences, infant neurobehavioral development, and pertinent medical disciplines, including thyroidology, pediatrics, and obstetrics. In the following sections, we provide the background of the ODS Iodine Initiative, summarize the 3 workshops held in 2014, and introduce the articles that arose from the workshops and are published in this supplement issue.

BACKGROUND OF THE ODS IODINE INITIATIVE

Iodine, an essential nutrient, is an intrinsic component of thyroid hormone (1). Thyroid hormone regulates metabolism at all ages and is critical for fetal, infant, and child development, including neurodevelopment (2, 3). The primary circulating form of thyroid hormone is thyroxine (T4). Multiple homeostatic mechanisms, including those mediated by increased secretion of thyroid-stimulating hormone (TSH), act to increase the uptake of iodide ion by the thyroid when needed to maintain adequate circulating concentrations of T4; these mechanisms can fail if iodine intake is chronically too low or too high (4). For populations in which moderate iodine deficiency is common, prevalences of hypothyroidism, hyperthyroidism, and multinodular toxic goiter may be elevated (4, 5). For populations in which excessive iodine intake is common, prevalences of hypothyroidism and autoimmune thyroid diseases (including Graves disease) may be elevated (4, 6, 7).

A considerable reduction in the prevalence of severe iodine deficiency worldwide has been achieved through the fortification of salt and other foods and the use of dietary supplements. However, mild to moderate iodine deficiency is still of concern in many countries, more than half of which are in the industrialized world (8). On the basis of current surveys of urinary iodine

[1] Supported by the Office of Dietary Supplements, NIH.

[2] The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the NIH or the US Department of Health and Human Services.

*To whom correspondence should be addressed. E-mail:abby.ershow@nih.gov.

[5] Abbreviations used: FDA, US Food and Drug Administration; FT4, free thyroxine; NDL, Nutrient Data Laboratory; ODS, Office of Dietary Supplements; TDS, Total Diet Study; TSH, thyroid-stimulating hormone; T3, triiodothyronine; T4, thyroxine; UIC, urinary iodine concentration.

First published online August 17, 2016; doi: 10.3945/ajcn.115.111161.

concentration (UIC) performed in 152 countries, 29 are affected by iodine deficiency (5). At the same time, excessive iodine intake is also of concern (8), especially in areas where seaweed is common in the diet (7). Following upon the success of efforts to prevent severe iodine deficiency in countries where previously it was prevalent, the focus of iodine-related global public health efforts has shifted toward prevention of mild to moderate iodine deficiency—particularly in pregnant women—without causing iodine excess in any population subgroup (8).

The maternal requirement for iodine is elevated during pregnancy for several reasons, including the mother's need for increased T4 synthesis to maintain normal metabolism, the transfer of T4 and iodide ion from mother to fetus, and the mother's increased renal excretion of iodide ion (3). It has been suggested that mild to moderate maternal iodine deficiency is the most common cause of maternal hypothyroxinemia (i.e., subnormal concentrations of serum T4) (9); this may be particularly true in geographic regions where the iodine intake of the population as a whole is expected to be sufficient (10). The human fetus is entirely dependent on maternal T4 before the development of the fetal thyroid in the second trimester of pregnancy (9). For this reason, the possibility of maternal hypothyroxinemia during pregnancy, even in regions of mild to moderate iodine deficiency, is of particular concern with respect to the potential for adverse effects on fetal neurodevelopment (9, 11, 12). The placenta has the ability to concentrate iodine (13), but it is not known whether placental stores can provide the fetus with sufficient iodine if the mother is mildly or moderately deficient. Thus, there is concern that mild to moderate maternal iodine deficiency may lead to some degree of fetal dependence on maternal T4 even after the fetal thyroid is fully functional.

There is strong evidence that when started before or during pregnancy, an increase in maternal iodine intake improves infant and child neurodevelopmental outcomes in regions of severe iodine deficiency and that such benefits far outweigh the risks (12, 14). However, less is known about the benefits and risks of maternal iodine supplementation in regions of mild to moderate iodine deficiency (12).

A population's median UIC is considered to be a useful indicator of its iodine status. The WHO has established that in pregnant women, population median UIC values $\geq$150 μg/L are indicative of iodine sufficiency (15). The median UIC for US pregnant women sampled in NHANES, which was >150 μg/L for decades, has trended below that value in recent years. In the years 2005–2010, the median UIC for pregnant women was 129 μg/L (16), a decrease from 153 μg/L in 2001–2006 (17).

The ODS Iodine Initiative was started in 2011 in response to concerns that US pregnant women may be at risk of iodine deficiency (18) and that a high fraction of prenatal dietary supplements contain either no iodine or not enough to provide pregnant women with recommended amounts of dietary iodine (19). Since then, an analysis of NHANES 1999–2006 data found that, although 78% of the pregnant women sampled took dietary supplements during this period, only 22% used a supplement containing iodine (20). Some lactating women in the US population may also be at risk for mild to moderate iodine deficiency (21).

Iodine nutrition activities conducted by the ODS are summarized in the Strategic Plan 2010–2014 Progress Report (22). Federal partners include the National Institute of Standards and Technology, the Nutrient Data Laboratory (NDL) of the USDA Agricultural Research Service (23), the US Food and Drug Administration (FDA), and multiple institutes, centers, and offices of the NIH, including the National Library of Medicine (24) and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development. Additional information about the ODS Iodine Initiative and the 2014 iodine workshops is available online (25).

THE 2014 IODINE WORKSHOPS

The first iodine workshop, "Assessment of Iodine Intake: Foods and Supplements," was held 22–23 April 2014. Speaker presentations and group discussions considered the iodine content of foods, the assessment of iodine intake from foods and supplements, iodine fortification of foods, and the use of iodine-containing supplements by pregnant women in the United States. Workshop discussions highlighted the importance and unique potential of existing data systems and resources of the USDA, the FDA, and the CDC, particularly the USDA's nutrient databases, the FDA's Total Diet Study (TDS), and the CDC's NHANES. The participants noted that a person's iodine status (i.e., degree of deficiency or excess) depends to a large extent on variables that may differ across geographic regions. Such variables include the availability of nonlocal foods, the natural and adventitious iodine content of the local and nonlocal food supply, and the use of iodine-fortified foods or dietary supplements. Note that in the United States, most of the iodine in cow milk (26, 27) and chicken eggs (28) appears to be contributed by feed supplements. The postmilking disinfection of bovine teats by spraying with a 1% iodine solution may also contribute materially to the iodine content of cow milk (27). Currently, these adventitious sources of dietary iodine are not addressed by any public health policy.

The second iodine workshop, "Assessment of Iodine Status: Analytical Methods and Quality Control," was held 22–23 July 2014. Speaker presentations and group discussions focused primarily on improving the usefulness and reliability of several serum biomarkers of thyroid function. Workshop participants also discussed the development and use of Standard Reference Materials and the standardization and harmonization of clinical laboratory tests—topics of potential relevance to the conduct of iodine supplementation trials.

The third iodine workshop, "Maternal Iodine Supplementation: Clinical Trials and Assessment of Outcomes," was held 22–23 September 2014. Speaker presentations and group discussions considered current obstacles to establishing the iodine status of individuals and assessing the potential impact of mild to moderate maternal iodine deficiency on pregnancy outcomes and child neurodevelopment. The participants were asked to consider what types of studies (including multisite clinical trials, cohort and case-control studies, secondary sample and data analyses, and ancillary studies appended to existing trials) would be most useful for evaluating the benefits and risks of iodine supplementation in women who are pregnant or might become pregnant.

INTRODUCTION TO THE ARTICLES IN THIS SUPPLEMENT ISSUE

This supplement issue contains 14 articles—the present introduction, 4 articles from each of the 3 workshops, and a final

article that summarizes research and resource needs for iodine nutrition. In the following, each of the workshop articles is introduced and briefly discussed.

First workshop

Information on the iodine content of foods, infant formulas, and supplements

Trumbo (29) summarizes FDA regulations with regard to the addition of iodine to foods and infant formulas and the labeling of conventional foods, dietary supplements, and infant formulas that contain added iodine. The author indicates that iodide compounds may be added to table salt as a source of dietary iodine at a maximum concentration of 0.01% and, if added, the label must indicate that the salt contains an iodide compound. She reports that the FDA does not mandate the addition of iodine to over-the-counter dietary supplements or prescription prenatal vitamins; consequently, some include iodine and others do not. As indicated by the author, if a dietary supplement contains added iodine, then the label must list iodine as a nutrient ingredient.

Pehrsson et al. (30) describe how the FDA is working with the NDL of the USDA Agricultural Research Service to combine their data in an online database that can be used for estimating iodine intake from foods in the US population. The article also details how the NDL continues to analyze dietary supplements for iodine and, in collaboration with ODS, to publish the data online in the Dietary Supplement Ingredient Database. The goal of these efforts is to provide improved tools for estimating iodine intake in populations and individuals. As shown by the authors, dairy products and eggs are important sources of dietary iodine in the United States, especially for those who consume little or no seafood.

Every year, the TDS collects 286 foods quarterly from 4 US regions and measures their concentrations of iodine and other nutrients. Carriquiry et al. (31) analyzed the variability of the iodine concentrations of 8 common foods collected by the TDS in 2004–2011; these 8 were selected on the basis of a preliminary analysis that showed them to have higher iodine concentrations and greater iodine-concentration variability than most TDS foods. Over this period, nominally 32 measurements (4/y $\times$ 8 y) were available for each food. Some of the concentration distributions were highly right-skewed, such that the mean greatly exceeded the median. For these high-iodine foods, the authors found that the distribution of iodine concentrations cannot be adequately described by the mean or any other single summary statistic.

Methodologies for assessing iodine intake and iodine status

Carriquiry et al. (31) also investigated how variation in the iodine content of foods (and failure to account for this variation) affects estimates of iodine intake. They used food intake data reported by NHANES 2009–2010, iodine concentrations of the 286 TDS foods collected from 4 US regions in 2004–2011, and an electronic file in which each of the $\sim$6200 NHANES foods is mapped to a TDS food with similar ingredients. The authors estimated the iodine concentration of each NHANES food as the iodine concentration (described by a given summary statistic) of its map-linked TDS food. They find that the selection of the mean as the summary statistic for the iodine concentration of each consumed food generally fails to characterize the distribution of iodine intakes. They find also that estimates of iodine inadequacy are lower when iodine intakes are based on the mean concentration of each consumed food than when they are based on the median.

Juan et al. (32) evaluated the prevalences of iodine inadequacy and excess in sex- and life stage–specific subgroups of the US population (including pregnant women) using 2 methods: one based on UIC cutoffs, the other based on iodine intake cutoffs. The first method used UIC data from NHANES 2003–2010; the second method used dietary intake data from NHANES 2003–2010 and an electronic file (described above) in which NHANES foods are mapped to TDS foods. Each NHANES participant's estimated iodine intake from each NHANES food was based on the mean value of the iodine concentration of its mapped TDS food measured in the same 2-y period. UIC and iodine intake data obtained from the same NHANES participants were used to compare prevalences of iodine inadequacy and excess across the 2 methods.

Second workshop: biomarkers of iodine status and thyroid function

As summarized by Pearce and Caldwell (33), UIC is well validated as a biomarker for the iodine status of populations, but is not very useful as an individual biomarker for research, patient care, or public health applications. The authors note that UIC measured in a single untimed ("spot") urine sample is unreliable for assessing the iodine status of individuals because it reflects recent iodine intake, which may not be typical and can vary widely from day to day. They also summarize the evidence with regard to the potential usefulness of serum thyroglobulin as a biomarker for both maternal and neonatal iodine status.

Long et al. (34) describe how the National Institute of Standards and Technology has been working with the ODS to develop higher-order reference methods and Standard Reference Materials to support the validation of new routine analytical methods for iodine in foods and dietary supplements, for urinary iodine, and for serum biomarkers of iodine status and thyroid function. The latter consist of TSH, thyroglobulin, total T4, free T4 (FT4), total triiodothyronine (T3), and free T3.

Vesper et al. (35) provide an overview of standardization and harmonization—with emphasis on the commutability of reference materials as an important variable affecting testing accuracy. As explained by the authors, standardization ensures traceability to the International System of Units, whereas harmonization ensures traceability to a reference system that is agreed upon by convention. They describe recent progress: efforts to standardize clinical procedures for testing serum T4 and T3 are well underway, and approaches to the harmonization of measurement procedures for testing serum TSH are being developed.

Faix and Miller (36) discuss the observation that reference intervals for several common serum tests of thyroid function, including TSH, FT4, and thyroglobulin, vary widely because of variability in the commercially available immunoassays for these tests. They indicate that the Committee for Standardization of Thyroid Function Tests, an international advisory group, has established a conventional reference measurement procedure for serum FT4 and an approach to harmonization for serum TSH. According to the authors, recalibration of manufacturers'

methods has shown that the variability among immunoassays for serum FT4 and serum TSH can be successfully reduced for euthyroid individuals as well as for patients with thyroid disease.

Third workshop

Tests of neurocognitive function for use in maternal iodine supplementation studies

Bell et al. (37) identified 6 standardized global tests of infant neurodevelopment frequently used in psychological research and searched for journal articles that reported studies of prenatal iodine supplementation in which any of these tests were used. Their search identified 7 such studies: 6 that used the Bayley Scales of Infant Development, Second Edition (BSID-II), and 1 that used the Brunet-Lézine scale. The BSID-II assesses both psychomotor and mental development, whereas the Brunet-Lézine scale assesses only psychomotor development; neither test assesses the development of cognitive functions. As discussed by the authors, the 7 prenatal iodine supplementation studies yielded inconsistent findings with regard to psychomotor development, negative findings with regard to mental development, and no information with regard to the development of cognitive functions. To identify specific cognitive processes that might be affected by mild to moderate maternal iodine deficiency, the authors examine the timing of thyroid hormone action on discrete brain systems. This leads them to consider whether infant visual attention has the potential to be a sensitive measure of infant outcomes in prenatal iodine supplementation studies.

Cognitive functions that are identified with a particular brain system or structure are often referred to as "neurocognitive." Bauer and Dugan (38) point out that it is not known which neurocognitive functions are the most sensitive to maternal hypothyroxinemia secondary to iodine deficiency, and thus which may benefit most from prenatal iodine supplementation. Citing evidence in rats that maternal iodine deficiency during gestation and lactation causes abnormal hippocampal development in rat fetuses and pups, the authors consider whether the neurocognitive domain of memory in infants and young children has the potential to be sensitive to maternal iodine deficiency and prenatal iodine supplementation. They discuss several measures of memory function that have proven to be sensitive to the gestational deficiency of iron; these measures include habituation and dishabituation, imitation-based tasks, and event-related potentials.

Data gaps in supplementation outcomes and design considerations for clinical trials

Pearce et al. (39) examine the effects of iodine excess and varying degrees of iodine deficiency in pregnant women. The authors note that some observational studies have found that mild to moderate maternal iodine deficiency is associated with decreased child cognition, but there are insufficient data from controlled clinical trials on neurobehavioral development outcomes in the offspring of mildly to moderately iodine-deficient pregnant women supplemented with iodine.

Finally, Troendle (40) discusses statistical approaches and related considerations for the design of a large, randomized, placebo-controlled trial of iodine supplementation in pregnant women in a region of mild iodine deficiency, in which cognitive assessment of the offspring at $\geq$2 y of age is the primary outcome measure. Assuming the use of a standardized assessment tool scaled to a mean of 100 and with an SD of 15, $\geq$500 participants/group would be needed to have sufficient power to detect a reasonably modest difference in cognitive scores. Depending on the effect size, the noncompliance rate, and the proportion of the supplemented group that fails to yield primary outcome measurement data, the minimum adequate number of participants might be considerably larger (40).

RESEARCH AND RESOURCE NEEDS

We refer the reader to the closing article of this supplement issue for a list of research and resource needs that were brought to light by the workshops (41).

The ODS gratefully acknowledges Michael Bykowski for his excellent assistance with preparing the meeting notes, Megan Lyons for providing meeting management and logistics support, and Theodora Radcliffe for her careful presubmission style editing of all manuscripts. CAS, who played a key role in developing the ODS Iodine Initiative, developed the initial scientific programs for all 3 workshops and presided over the first workshop. AGE was responsible for final development of the scientific programs of the second and third workshops and for fostering publication of the articles in this supplement issue. PMC provided oversight of the organization and scientific development of the workshops. GG, the Iodine Initiative Consultant to the ODS, performed presubmission review, technical and scientific editing, and revision review for all articles and also provided scientific background information and technical guidance to the authors.

The authors' responsibilities were as follows—AGE and GG: wrote the manuscript; PMC and CAS: contributed to the content; AGE: had primary responsibility for the final content; and all authors: read and approved the final manuscript. The authors reported no conflicts of interest related to the study.

REFERENCES

1. Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Use of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes: vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington (DC): National Academies Press; 2001.
2. WHO/UNICEF/International Council for Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers. 3rd ed. Geneva (Switzerland): World Health Organization; 2007. [cited 2015 Mar 11]. Available from: http://apps.who.int/iris/bitstream/10665/43781/1/9789241595827_eng.pdf.
3. Delange F. Iodine requirements during pregnancy, lactation and the neonatal period and indicators of optimal iodine nutrition. Public Health Nutr 2007;10:1571–80.
4. Laurberg P, Cerqueira C, Ovesen L, Rasmussen LB, Perrild H, Andersen S, Pedersen IB, Carlé A. Iodine intake as a determinant of thyroid disorders in populations. Best Pract Res Clin Endocrinol Metab 2010;24:13–27.
5. Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. Lancet Diabetes Endocrinol 2015;3:286–95.
6. Bürgi H. Iodine excess. Best Pract Res Clin Endocrinol Metab 2010;24:107–15.
7. Luo Y, Kawashima A, Ishido Y, Yoshihara A, Oda K, Hiroi N, Ito T, Ishii N, Suzuki K. Iodine excess as an environmental risk factor for autoimmune thyroid disease. Int J Mol Sci 2014;15:12895–912.
8. Zimmermann MB, Andersson M. Update on iodine status worldwide. Curr Opin Endocrinol Diabetes Obes 2012;19:382–7.

9. de Escobar GM, Obregón MJ, del Rey FE. Iodine deficiency and brain development in the first half of pregnancy. Public Health Nutr 2007;10: 1554–70.
10. Moleti M, Trimarchi F, Vermiglio F. Doubts and concerns about isolated maternal hypothyroxinemia. J Thyroid Res 2011;2011:463029.
11. Berbel P, Mestre JL, Santamaría A, Palazón I, Franco A, Graells M, González-Torga A, de Escobar GM. Delayed neurobehavioral development in children born to pregnant women with mild hypothyroxinemia during the first month of gestation: the importance of early iodine supplementation. Thyroid 2009;19:511–9.
12. Zimmermann MB. The effects of iodine deficiency in pregnancy and infants. Paediatr Perinat Epidemiol 2012;26(Suppl 1):108–17.
13. Burns R, Azizi F, Hedayati M, Mirmiran P, O'Herlihy C, Smyth PP. Is placental iodine content related to dietary iodine intake? Clin Endocrinol (Oxf) 2011;75:261–4.
14. Puig-Domingo M, Vila L. The implications of iodine and its supplementation during pregnancy in fetal brain development. Curr Clin Pharmacol 2013;8:97–109.
15. WHO Vitamin and Mineral Nutrition Information System. Urinary iodine concentrations for determining iodine status in populations. Geneva (Switzerland): WHO; 2013. [cited 2015 Mar 11]. Available from: http://apps.who.int/iris/bitstream/10665/85972/1/WHO_NMH_NHD_EPG_13.1_eng.pdf.
16. Caldwell KL, Pan Y, Mortensen ME, Makhmudov A, Merrill L, Moye J. Iodine status in pregnant women in the National Children's Study and in U.S. women (15–44 years), National Health and Nutrition Examination Survey 2005–2010. Thyroid 2013;23:927–37.
17. Perrine CG, Herrick K, Serdula MK, Sullivan KM. Some subgroups of reproductive age women in the United States may be at risk for iodine deficiency. J Nutr 2010;140:1489–94.
18. Caldwell KL, Makhmudov A, Ely E, Jones RL, Wang RY. Iodine status of the U.S. population, National Health and Nutrition Examination Survey, 2005–2006 and 2007–2008. Thyroid 2011;21:419–27.
19. Leung AM, Pearce EN, Braverman LE. Iodine content of prenatal multivitamins in the United States [letter]. N Engl J Med 2009;360: 939–40.
20. Gahche JJ, Bailey RL, Mirel LB, Dwyer JT. The prevalence of using iodine-containing supplements is low among reproductive-age women, NHANES 1999–2006. J Nutr 2013;143:872–7.
21. Leung AM, Pearce EN, Braverman LE. Iodine nutrition in pregnancy and lactation. Endocrinol Metab Clin North Am 2011;40:765–77.
22. NIH Office of Dietary Supplements. About ODS: Strategic Plan 2010–2014 [cited 2015 Feb 1]. Available from: http://ods.od.nih.gov/About/Strategic_Plan_2010-2014.aspx.
23. Nutrient Data Laboratory, USDA Agricultural Research Service; NIH Office of Dietary Supplements. Dietary Supplement Ingredient Database (DSID). Version current 27 August 2014 [cited 2015 Feb 1]. Available from: http://dietarysupplementdatabase.usda.nih.gov.
24. NIH Office of Dietary Supplements. Research and funding: Dietary Supplement Label Database (DSLD) [cited 2015 Feb 1]. Available from: http://ods.od.nih.gov/Research/Dietary_Supplement_Label_Database.aspx.
25. NIH Office of Dietary Supplements. Research & funding: Iodine Initiative [cited 2015 Mar 6]. Available from: http://ods.od.nih.gov/Research/Iodine.aspx.
26. Flachowsky G, Franke K, Meyer U, Leiterer M, Schöne F. Influencing factors on iodine content of cow milk. Eur J Nutr 2014;53: 351–65.
27. Castro SI, Berthiaume R, Robichaud A, Lacasse P. Effects of iodine intake and teat-dipping practices on milk iodine concentrations in dairy cows. J Dairy Sci 2012;95:213–20.
28. Röttger AS, Halle I, Wagner H, Breves G, Dänicke S, Flachowsky G. The effects of iodine level and source on iodine carry-over in eggs and body tissues of laying hens. Arch Anim Nutr 2012;66:385–401.
29. Trumbo PR. FDA regulations regarding iodine addition to foods and labeling of foods containing added iodine. Am J Clin Nutr 2016; 104(Suppl):864S–7S.
30. Pehrsson PR, Patterson KY, Spungen JH, Wirtz MS, Andrews KW, Dwyer JT, Swanson CA. Iodine in food- and dietary supplement–composition databases. Am J Clin Nutr 2016;104(Suppl):868S–76S.
31. Carriquiry AL, Spungen JH, Murphy SP, Pehrsson PR, Dwyer JT, Juan WY, Wirtz MS. Variation in the iodine concentrations of foods: considerations for dietary assessment. Am J Clin Nutr 2016;104(Suppl): 877S–87S.
32. Juan WY, Trumbo PR, Spungen JH, Dwyer JT, Carriquiry AL, Zimmerman TP, Swanson CA, Murphy SP. Comparison of 2 methods for estimating the prevalences of inadequate and excessive iodine intakes. Am J Clin Nutr 2016;104(Suppl):888S–97S.
33. Pearce EN, Caldwell KL. Urinary iodine, thyroid function, and thyroglobulin as biomarkers of iodine status. Am J Clin Nutr 2016; 104(Suppl):898S–901S.
34. Long SE, Catron BL, Boggs ASP, Tai SSC, Wise SA. Development of Standard Reference Materials to support assessment of iodine status for nutritional and public health purposes. Am J Clin Nutr 2016;104 (Suppl):902S–6S.
35. Vesper HW, Myers GL, Miller WG. Current practices and challenges in the standardization and harmonization of clinical laboratory tests. Am J Clin Nutr 2016;104(Suppl):907S–12S.
36. Faix JD, Miller WG. Progress in standardizing and harmonizing thyroid function tests. Am J Clin Nutr 2016;104(Suppl):913S–7S.
37. Bell MA, Ross AP, Goodman G. Assessing infant cognitive development after prenatal iodine supplementation. Am J Clin Nutr 2016; 104(Suppl):928S–34S.
38. Bauer PJ, Dugan JA. Suggested use of sensitive measures of memory to detect functional effects of maternal iodine supplementation on hippocampal development. Am J Clin Nutr 2016;104(Suppl):935S–40S.
39. Pearce EN, Lazarus JH, Moreno-Reyes R, Zimmermann MB. Consequences of iodine deficiency and excess in pregnant women: an overview of current knowns and unknowns. Am J Clin Nutr 2016;104(Suppl): 918S–23S.
40. Troendle JF. Statistical design considerations applicable to clinical trials of iodine supplementation in pregnant women who may be mildly iodine deficient. Am J Clin Nutr 2016;104(Suppl):924S–7S.
41. Ershow AG, Goodman G, Coates PM, Swanson CA. Research needs for assessing iodine intake, iodine status, and the effects of maternal iodine supplementation. Am J Clin Nutr 2016;104(Suppl): 941S–9S.