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DOCUMENTS:

Uses and Challenges Related to Use of the DRIs

Developed by:

**Document 1
US Federal DRI Steering Committee**

**Document 2
Health Canada**

**Document 3
American Dietetic Association**

**Document 4
Dietitians of Canada**

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Uses and Challenges Related to Use of the DRIs

DOCUMENT 2:

Use of the DRIs by Health Canada: Case Studies, Challenges Encountered, and Ideas for Enhancing the DRI Development Process

Developed by:

Health Canada

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Use of the DRIs by Health Canada: Case Studies, Challenges Encountered, and Ideas for Enhancing the DRI Development Process

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1. Introduction

The Dietary Reference Intakes (DRIs) are a set of scientifically based nutrient reference values for healthy populations. They have been established using an expanded concept that includes indicators of good health and the prevention of chronic disease, as well as possible adverse effects of excess intakes of nutrients. There are four categories of reference values: the Estimated Average Requirement (EAR), the Recommended Dietary Allowance (RDA), the Adequate Intake (AI), and the Tolerable Upper Intake Level (UL).

In Canada, the DRIs have replaced the 1990 Recommended Nutrient Intakes (RNIs) as the nutrient reference values for the healthy Canadian population. Health Canada uses the DRIs in risk assessment, standard setting and planning, policy and program development and research programs aimed at protecting and promoting the health and safety of Canadians.

Although the DRI paradigm has brought with it many improvements to the usefulness of nutrient reference values, challenges have been encountered in using the DRI values. This paper presents two case studies of the application of the DRI values by Health Canada, along with the challenges encountered in using the DRIs for these purposes. The first case study examines the use of the DRIs in developing Health Canada's proposed revised policy on the discretionary addition of vitamin and minerals to foods. The second case study looks at the use of the DRIs in the development of the food intake pattern for the revised Canada's Food Guide. Following both case studies is a section proposing ideas for modifications to the DRI development process that could help reduce the number and extent of challenges to using the DRIs.

2. Case Study 1: Use of the DRIs in the development of the proposed revised policy on food fortification

2.1 Introduction

Canada has a long history of fortification that is based on previously identified nutrient deficiencies in the population. The Canadian government has used mandatory fortification to address documented deficiencies. For example, the iodization of salt has been mandatory in Canada since 1948, and the addition of vitamin D to all milks sold in Canada has been mandatory since 1975. As well, the addition of vitamin and mineral nutrients to foods to maintain and improve the nutritional quality of the food supply through restoration of processing losses and to provide for the nutritional equivalence of substitute foods has been set out in specific regulations through a policy first set out in 1971.

Health Canada undertook a review of its policy on the addition of vitamin and mineral nutrients to foods between 1998 and 2005. The proposed policy document (Health Canada, 2005) is available on the Health Canada website at http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/fortification_final_doc_1_e.html.

One of the guiding principles established early in the review process was to ensure that the decisions were based on the best available evidence. During this period the series of Dietary Reference Intakes reports evaluating the scientific basis for nutrient requirements for the healthy population in Canada and the United States were published. Health Canada was committed to applying the new DRIs to the policy review process.

This case study deals with three major applications of the new DRIs in the development of proposals for discretionary fortification, i.e., the voluntary addition of vitamins and minerals to foods at the discretion of the manufacturers. The first was a novel application in setting out risk categories of vitamins and minerals. The second application was in conducting exposure assessments under a range of fortification scenarios to identify low risk options for discretionary fortification. Linked to this was the third application, determining the permitted level of addition for each vitamin and mineral in the revised policy on discretionary fortification.

2.2 Risk Categories of Nutrients

It has long been recognized that certain vitamins have no demonstrated adverse effects even when consumed at very high levels, whereas other vitamins and minerals have demonstrated adverse effects at relatively modest increases above or even within usual intakes. The DRI process developed the UL using a risk assessment model that was created specifically for nutrients. The DRI reports identified the hazards (critical and other adverse effects) for most vitamin and minerals, quantified the levels based on either the No Observed Adverse Effect Level (NOAEL) or the Lowest Observed Adverse Effect Level (LOAEL), and applied an uncertainty factor (UF) in setting the ULs.

This new information was applied in developing a risk classification of the nutrients. The risk classification was originally developed to help simplify the statistical simulations of nutrient addition such that sample nutrients from a group with similar risk profile could be tested, rather than each vitamin and mineral individually. Subsequently the risk classification was used to help identify which nutrients would be eligible for discretionary fortification, based on risk to health. It was also related to the final proposed levels of discretionary fortification.

The risk classification was based on the margin of safety between the highest Recommended Dietary Allowance (RDA) or Adequate Intake (AI) for each nutrient and the lowest UL (the UL for children or the most vulnerable group), and considered the seriousness of the adverse effects. The margin was considered for these two population subgroups because of current practices related to labelling in Canada and labelling and fortification in the U.S. The Daily Value (DV) used in mandatory nutrition labelling of prepackaged foods sold in Canada is based on the highest adult male RNI of 1983 (except for iron); in the U.S. the DV is based on the highest adult male RDA of 1968 (except for iron, calcium, phosphorus, zinc, biotin and pantothenic acid). Health Canada looked to the U.S. for lessons that could be learned with regard to discretionary fortification. It was noted that foods have tended to be fortified in the U.S. to some fraction of the DV, 100% DV, 50% DV, and so on. A food fortified at 100% of the U.S. DV for folic acid (400 μg) would exceed the UL for children aged 1-3 (300 μg). Similarly a food fortified to 100% DV for zinc (13 mg) would exceed the UL for children aged 1 to 8 years. Thus in developing the risk categories, the margin of safety was estimated for each nutrient where an RDA or AI and UL were determined.

An example of the approach taken for vitamin A as retinol follows: the RDA for adult men is 900 :g and the UL for children 1-3 years is 600 :g. There is an overlap in these values, and hence the assigned margin of safety was zero. Further, the seriousness of the critical adverse effect was considered: for children, the critical adverse effect used in setting the LOAEL was hypervitaminosis A, including symptoms of occipital edema, bulging fontanels, and increased intracranial pressure. The symptoms occurred after doses of 5500 to 6750 :g per day for 1 to 3 months. The LOAEL was rounded to 6000 :g and an uncertainty factor of 10 was applied by the DRI expert panel to account for uncertainty of extrapolating a LOAEL to a NOAEL for a non-severe and reversible effect (bulging fontanels). Given the lack of margin of safety and the serious albeit non-severe reversible adverse effect, vitamin A as retinol was considered a nutrient with a high degree of risk with regard to discretionary fortification in Canada.

The risk categorization originally proposed for consultation in 2002 included three risk categories:

- **Risk A:** Those nutrients with lowest risk, i.e. *those nutrients with no reported adverse effects associated with excess intake and no UL set*: thiamin, riboflavin, vitamin B$_{12}$, pantothenic acid, biotin.
- **Risk B:** Those with a known low degree of risk, i.e. *those with a UL, but with a wide margin of safety (>10 fold), or those with a narrow margin of safety (0-5*

fold), including some overlap between children's UL and adult RDA/AI, and a non-serious critical adverse effect: vitamin B$_6$, Vitamin E, vitamin C, niacin*.

- **Risk C:** Those with a high degree of risk, *i.e. those with a UL, and with serious adverse effects, and either a narrow margin of safety or an overlap between children's UL and adult RDA/AI*: calcium, folic acid*, vitamin A*, zinc*, vitamin D, iodine, iron, copper*, selenium, manganese, magnesium**.

* Nutrients for which there is an overlap between a children's UL and the adult RDA;
** Overlap a concern only for supplements.

Other nutrients for which an RDA or AI has been established but for which a risk category was not assigned include choline, chromium, fluoride, molybdenum, phosphorus and vitamin K. For a variety of reasons, these were proposed to be excluded from discretionary fortification (choline: very limited evidence available to set an AI and a UL and 2-fold range of safety; chromium: data are too limited to set a UL; molybdenum: limited animal data used to set a UL; phosphorus: narrow range of safety and increasing use as additive; vitamin K: insufficient data to set a UL.

In response to Health Canada's proposals for risk categorization of the nutrients, Canadian stakeholder groups generally agreed with the approach taken to establish the risk categories. On the other hand some questioned the validity of the ULs themselves, and hence the use of the ULs for risk categorization. Some also commented on the subjectivity in deciding on the seriousness of the adverse effects. Other comments related to the placement of nutrients in the categories: the placement should be based on benefit as well as risk; the placement should be done by scientific consensus among experts; the placement had consequences with regard to discretionary fortification.

In response to these comments and to stakeholders' concerns with lack of potential access to certain nutrients of consumer interest for discretionary fortification, and with consideration of the levels that could be safely added to the food supply under discretionary fortification, the placement of nutrients in the risk categories was modified to the current listing as follows:

Risk Category A nutrients: Those nutrients for which no UL was set because of no reports of adverse effects, and no concern expressed; and those nutrients for which a UL was set but with a wide margin of safe intake; and those nutrients with a narrow margin of safety, but non-serious critical adverse effects: thiamin, riboflavin, pantothenic acid, biotin, vitamin B$_{12}$, ∃-carotene, vitamin C, vitamin B$_6$, vitamin E, niacin.

Risk Category B nutrients: Those nutrients with serious adverse effects, but with low risk of excessive intake at the proposed level of addition for discretionary fortification: calcium, folic acid, magnesium, vitamin D, potassium.

Risk Category C nutrients (to be excluded from discretionary fortification): Those nutrients with a narrow margin of safety, and with serious adverse effects, and/or with current levels of exposure to intakes above the UL by vulnerable subgroups: vitamin A as

retinol, zinc, iron, copper, selenium, manganese, iodine, fluoride. Nutrients in this category are currently permitted or required to be added to a range of foods sold in Canada for purposes of restoration, mandatory fortification, nutritional equivalence of substitute foods or to make a special purpose food such as a meal replacement. New or further additions for these purposes would continue to be subject to regulatory requirements.

Other vitamin and mineral nutrients for which a risk category has not been assigned include choline, chromium, molybdenum, phosphorus, vitamin K. These nutrients are proposed to be excluded from discretionary fortification for a variety of reasons, as indicated above.

2.3   Application of the ULs in Exposure Assessment

In developing the revised policy on the addition of vitamins and minerals to foods, and in responding to requests for fortification of certain food product categories, Health Canada has used the ULs as a benchmark for risk of excessive intake. Statistical modelling of a wide range of fortification scenarios was undertaken, and the UL was used to assess exposure to excessive intakes. The results were used to inform decisions about safe levels of discretionary addition.

The safety of various options for discretionary fortification was assessed through the use of modelling scenarios of exposure of the Canadian population to nutrients in each of the risk categories. The databases used for modelling included the pooled data from 24 hour recalls with repeats on a subsample from three Federal/Provincial surveys to provide a sample of 4489 adults and from the Quebec survey of children and youth to provide a sample of 1932 children aged 6 to 16 years.

Modelling was limited to selected nutrients representing each risk category. Nutrient addition simulations were conducted under several options for discretionary addition such as: no foods excluded except for a defined list of staple foods, natural or minimally processed foods; exclusions on the basis of saturated and trans fat and sodium content. Tested levels of the added nutrient in the food ranged from 5-100% of the RDA or AI. The impact on the % of the population with simulated intakes over the UL as well as the entire intake distribution was assessed.

There was no fixed exposure or cut-off for the proportion of the population with intake over the UL that was used to assess risk. The risk associated with excessive intake depends on the nutrient, the dose-response information that was used in determining the LOAEL and NOAEL, the degree of uncertainty, the critical adverse effect and other adverse effects, and the particular population groups affected. In the final scenarios tested for discretionary fortification, less than 10% of the most exposed age/sex group had intakes over the UL for nutrients tested in Risk Category B.

2.4 Application of the DRIs in Setting Limits on Nutrient Addition

The RDA/AI values for nutrients were used as benchmarks upon which different levels of nutrient addition were based. A variety of modelling scenarios were conducted.

The statistical modelling was conducted such that all eligible foods had simulated additions to bring the nutrient content to the defined level of the vitamin or mineral nutrient of interest. This was applied to the actual food intakes of the sample of Canadians as described above based on 24-hour recalls, with repeats in a subsample. The simulated intakes were adjusted to reflect usual intake.

In early simulations, in which all foods except a defined list of fresh whole foods were fortified, the nutrients with a UL but a low degree of risk (e.g. vitamin C, vitamin B_6) were demonstrated to present no exposure to excessive intake from foods, even with simulated addition to 100% of the RDA. However, those nutrients with a UL and which we originally classified as having a high degree of risk (e.g. calcium, folic acid, zinc) were demonstrated to present a high percentage of the population with exposure to intakes over the UL, even at levels of addition of 5-10% RDA/AI, i.e., there was no apparent safe level of addition if all foods were to be fortified.

The modelling was subsequently refined based on information to simulate conditions similar to those seen in the U.S. where a mature market of discretionarily fortified food prevails. This was done to explore the potential impact of discretionary addition of certain high risk nutrients under mature market conditions. The main commodities that appear to be voluntarily fortified under a mature market include breakfast cereals, instant breakfast powders, "bars" (cereal bars, power bars, including confectionary), beverages including fruit and vegetable juices and drinks, carbonated beverages and water, processed meats and spreads, and snack foods.

Under the simulation of 'mature market' conditions only certain foods were fortified, even though in principle others would not be prohibited from discretionary fortification. Under this scenario, it was demonstrated that certain higher risk nutrients (e.g., calcium, folic acid, vitamin D) could be added with low exposure to excessive intakes, while others (e.g., zinc) could not.

The proposed levels in the revised policy are based on the safe amounts identified during the modelling which used the RDA/AI as benchmark values. However, the final proposed levels are expressed in terms of the Canadian % DV in consideration of labelling provisions. The proposed levels permitted for discretionary fortification would result in a total vitamin or mineral nutrient content that would meet either the "good" or "excellent" source claims for the relevant nutrients according to their risk classification, and the IOM advice articulated in the 2003 report on Guiding Principles for Nutrition Labeling and Fortification.

2.5 Challenges encountered in using the DRIs

There were several challenges encountered in developing the proposed discretionary fortification policy. Many of these challenges were associated with the UL values and their derivation.

One problem encountered in the modelling process was that the UL was based only on certain forms of the vitamin (e.g retinol for vitamin A) but the food composition database did not distinguish between vitamin A from retinol and vitamin A from ∃-carotene. To overcome this deficiency, estimated retinol intake at baseline was based on plant versus non-plant sources of vitamin A. Fortunately, in the case of folic acid, the food composition database did distinguish between naturally occurring food folate and folic acid.

2.5.1 Challenge: The adequacy of the science base supporting the UL for certain nutrients

The ULs have been derived for the various age-gender groups using NOAELs or LOAELs, and UFs. Inherent in the derivation of a UL is the need for scientific judgement when selecting appropriate NOAEL/LOAEL values and UFs. It is recognized that the quality and completeness of the data available to the IOM expert panels was often not ideal, however, the adequacy of the science base supporting the UL for certain nutrients was found to be a challenge when developing the proposed policy.

The UL values were not universally embraced by stakeholders during consultation. The validity of the ULs for certain nutrients, and hence their application in risk categorization and exposure assessment, was questioned. In some cases, this was due to the limited data used in setting the values. For example, for some age and gender groups the UL has been extrapolated either upward or downward on a relative body weight basis from other age groups. Although such extrapolation has been a long-standing practice in setting nutrient requirements, this extrapolation was raised as an objection in the case of some ULs.

The results of dietary assessment studies have shown high proportions of some age-gender groups in the U.S. having usual nutrient intakes in excess of the UL, apparently without adverse effects (e.g. zinc and folic acid in young children). The absence of harm from these levels of intake over at least the past 3-7 years, although not systematically evaluated, raised reservations about the soundness of the UL for certain nutrients. The applicability of a UL based on intake from supplements as well as food sources to the risk of excessive intake from food (e.g., niacin, calcium) was also expressed as a concern.

A lack of data on the NOAEL for some nutrients resulted in the UL being based on a LOAEL with the UF taking into account the uncertainty. The uncertainty factor used in determining ULs varies from 1, great certainty, for certain nutrients, to 36, great uncertainty for others. However, the strength of evidence supporting the use of different uncertainty factors varies, and the rationale for the estimation of some UFs has been questioned by stakeholders. The explanation of the magnitude of UF in the reports was not always satisfactory.

2.5.2 Challenge: Inconsistency in the severity or public health significance of the indicators used to set ULs leads to the need for informed judgement in their application

The first step in the development of a UL is hazard identification. Some degree of scientific judgement is usually required to decide which effects are considered adverse. In addition, adverse effects can differ in severity. The UL may be based on the most sensitive endpoint for a given nutrient in order to ensure protection against all other adverse effects. However, the endpoints used vary across nutrients, as does the severity of the critical adverse effect. This leads to the UL having an inconsistent definition in terms of the risk to health associated with excessive intake. In some cases the critical adverse effect is as sensitive as reduced enzyme activity, e.g., for zinc, and in others, as insensitive as a clinical outcome, e.g., bulging fontanelles in infants from excessive retinol. Informed judgement is thus required when interpreting the results of exposure assessments.

An evaluation of the public health significance of the risk to the population consuming a nutrient in excess of the UL is important. For example, the UL for niacin for adults is 35 mg/d. The adverse effect noted is a relatively benign vasodilation causing flushing of the skin that may be accompanied by a burning, itching or tingling sensation. This effect is readily reversible by a reduction in intake. In comparison, the UL for vitamin B_6 is 100 mg/d and the adverse effect is sensory neuropathy, a serious and irreversible condition. Given the risks to health associated with each critical adverse effect, the level of public health concern over a segment of the population routinely consuming vitamin B_6 in excess of the UL would be greater than the concern if a segment were routinely consuming niacin in excess of the UL.

In addition, certain population lifestage groups are more vulnerable to the adverse effects of excessive intakes than others, and this depends on the nutrient in question, e.g., retinol in children, but folic acid in people over 50. As well, some population subgroups are more exposed to excessive intakes than other groups by virtue of their particular food consumption patterns - the frequency and amounts of certain foods. Although this is often related to total caloric intake, in which case young men tend to be the most exposed, this is not always the case, and reflects back to food consumption patterns as well as the UL determined for the particular group.

3. Case Study 2: Use of the DRIs in the development of the food intake pattern for the revised Canada's Food Guide (2007)

3.1 Introduction

The purpose of Canada's Food Guide is to assist the people of Canada in making food choices that promote health and reduce the risk of nutrition-related chronic disease. The Food Guide describes the amounts and types of foods that make up an overall pattern of healthy eating. Following Canada's Food Guide will result in a high probability of nutrient adequacy and appropriate macronutrient balance, as well as a low probability of nutrient excess, within an appropriate amount of energy.

The nutrient standards and assessment methods provided in the Dietary Reference Intakes reports were a key component of the development of the food intake pattern for the 2007 Food Guide. Ensuring nutritional adequacy as well as avoiding excessive intakes of nutrients is a key concept underpinning dietary guidance to Canadians.

3.2 Modelling process for food intake pattern

A food intake pattern was created using a two step modelling process. DRI values were used as intermediary targets in the first step of modelling, and to evaluate nutrient distributions from simulated diets following the food intake pattern in the second step of modelling.

A brief description of the modelling process and use of the DRIs follows. A more detailed description of the methods and results can be found elsewhere (see http://www.hc-sc.gc.ca/fn-an/pubs/fd_int_pat-ela_mod_alim_e.html). It is emphasized that it was the assessment of the nutrient distributions from simulated diets following the food intake pattern (step two of modelling) that guided decision-making and determination of the adequacy of the food intake pattern.

The first step of modelling used food composites to construct dietary patterns. Amounts of different composites were manipulated until a food intake pattern with satisfactory average nutrient levels was found. Because nutrient requirements vary by age and gender, a separate food intake pattern was developed for each of the DRI age and gender groups for those two years of age and older.

Intermediary targets were used to help guide the development of the dietary pattern. Using a food composite approach to model food intake patterns is, in effect, like working with a single, usual diet, not a "distribution" of diets. The intermediary targets used to guide the development of dietary patterns using composites were thus consistent with the recommended approach to planning for single individuals: the RDA/AI was used for micronutrient content, and macronutrient content was targeted to be within the AMDR. Average nutrient levels were allowed to increase freely beyond the RDA/AI if this occurred when manipulating amounts of food composites. It was presumed that because the variability in nutrient intakes is usually greater than the variability in nutrient

requirements, the median nutrient content of simulated diets would likely need to be greater than the RDA/AI in order to result in a low prevalence of inadequate nutrient content.

The second step of modelling involved testing out the pattern created in step one by simulating 500 diets for each of the DRI age and gender groups and then evaluating the resulting nutrient distributions relative to the appropriate DRI values. When assessment of the nutrient distributions yielded less than satisfactory results, adjustments to the food intake pattern were made, followed by re-assessment of the pattern through the creation of simulated diets.

The nutrient content distributions resulting from the simulated diets were assessed using the recommended approach for nutrient assessment of groups. More specifically, the following criteria were used in assessment:

- For nutrients with an EAR, fewer than 10% of simulated diets in any given DRI age and sex group should have a nutrient content less than the EAR. A threshold of ten percent was used because the simulated nutrient distributions were not adjusted to estimate "usual" nutrient content.

- For nutrients with an AI, the median nutrient content of simulated diets should approximately equal the AI.

- For macronutrients, the majority ($\geq$ 80%) of simulated diets should have carbohydrate, fat, and protein content within the lower and upper bounds of the AMDR. The choice of 80% of diets within the AMDR as a benchmark allows for 10% of diets to have nutrient content below the lower bound and 10% of diets to have nutrient content above the upper bound, given that the simulated nutrient distributions were not adjusted to estimate "usual" nutrient content. The DRI reports do not quantify recommendations for saturated fat and dietary cholesterol, suggesting that diets should be as low as possible in these nutrients without adversely affecting the nutrient adequacy of the diet. Benchmarks of 10% or less of calories from saturated fat and 300 mg or less of dietary cholesterol were used in assessing the median nutrient content of simulated diets.

- For nutrients with a Tolerable Upper Intake Level (UL), there should be an absence of diets with nutrient content at or above the UL.

- For energy, the median energy content of simulated diets should be at or below the Estimated Energy Requirement (EER) calculated for normal-weight reference individuals using a sedentary level of activity. Measured heights and weights from the Canadian Community Health Survey, Cycle 2.2, were used to determine median height and median normal weight for each age and gender group. These were then used as inputs to the EER equations. A sedentary level of activity was considered most appropriate so that there was no overestimation of requirements.

Nutrient, macronutrient, and energy distributions were evaluated at key intervals by expert advisors to the food intake pattern development process. Deviations from the above criteria were tolerated when either the limitations of the DRI value or the databases with which distributions were created (e.g., food composition database) were taken into consideration.

The availability of the DRIs permitted the use of this method of developing a food intake pattern for use in the revised food guide. Indeed, all categories of DRI values were used in some way as part of the food intake pattern development process. In particular, the ability to assess the nutrient content distributions of diets following the food intake pattern adds rigour to the process and provides support for the statement that following Canada's Food Guide will meet nutrient needs.

3.3   Challenges encountered in using the DRIs
There were many challenges encountered in the development of the food intake pattern for the revised Canada's Food Guide. Some of these challenges, such as inadequacies present in the food composition database, had nothing to do with the DRI values per se. Other challenges were related directly to the DRI values.

3.3.1 Challenge: Certain nutrients have DRI values that were considered to be unusable
Certain nutrients have DRI values that were considered to be unusable because of the nature of the values:

The AMDR for n-6 and n-3 fatty acids, in particular the lower bound of the AMDR.
The lower bound of the AMDR for both n-6 (linoleic) and n-3 (alpha-linolenic) fatty acids is based on the percent of energy from these fatty acids needed to provide the AI for these nutrients. The AI, in turn, is based on the median intake of both linoleic and alpha-linolenic acid in the United States, where essential fatty acid deficiency is non-existent in the healthy population. This method of setting the lower boundary of the AMDR differs from the methods used to set AMDRs for carbohydrate, total fat, and protein.

According to the methodology recommended for using the AI in nutrient assessment, when median nutrient content is at the level of the AI, the prevalence of inadequate nutrient intakes is likely to be low, and confidence in this assessment is increased when the AI is based directly on intakes of healthy populations (as is the case for n-6 and n-3 fatty acids).

However, if the median nutrient content was at the level of the AI and the AMDR for n-6 or n-3 fatty acids was used in assessment, 50% of simulated diets would have a nutrient content below the lower bound of the AMDR, indicating that adjustments should be made to improve the nutritional profile of the food intake pattern.
Because of the incongruent results obtained when using both the AI and the AMDR in assessment of n-6 and n-3 fatty acid content of simulated diets, and because the lower

bound of the AMDR for n-6 and n-3 fatty acids was set differently than the AMDRs for other macronutrients, the AMDRs for n-6 and n-3 fatty acids were not used in the assessment of the nutrient content of simulated diets.

Additional macronutrient recommendations for the consumption of saturated fatty acids, trans fatty acids, and dietary cholesterol to be "As low as possible while consuming a nutritionally adequate diet".

There are no known requirements for dietary intake of saturated fatty acids, trans fatty acids, or dietary cholesterol. However, there is a positive linear trend between consumption of these nutrients and increased risk of coronary heart disease (CHD). Tolerable Upper Intake Levels were not set because any incremental increase in intake of these nutrients increases CHD risk. Because these nutrients are unavoidable in ordinary North American diets, the recommendation is that consumption of these nutrients remain as low as possible while consuming a nutritionally adequate diet.

The absence of quantified values precluded using the DRI recommendations in the assessment of the nutrient content of simulated diets. Benchmarks of 10% or less of calories from saturated fat and 300 mg or less of dietary cholesterol were used in assessing the median nutrient content of simulated diets. The trans fat content of simulated diets could not be assessed due to incomplete values in the food composition database used.

3.3.2 Challenge: Informed judgement was required when interpreting results of food intake pattern assessments and considering revisions

Less than perfect results were accepted for certain nutrients following examination of the indicator of adequacy used to set the DRI values.

Through the course of developing the food intake pattern, it was found that adequate nutrient content was achieved quite easily for some nutrients. For other nutrients, specifying the inclusion of particular sub-groups of foods (ex. dark green vegetables) improved the nutrient profile of diet patterns without increasing the total amount of food recommended.

For certain nutrients, however, achieving adequate nutrient content proved to be difficult, and the cost of either adding more food to the pattern, further specifying particular foods (thus making the pattern quite prescriptive), or recommending supplements had to be weighed against the consequences of being at increased risk of nutrient inadequacy. The indicators of adequacy were thus examined for these "difficult to achieve" nutrients – potassium, fibre, and linoleic acid. In the cases of fibre and linoleic acid, food composition data base issues also contributed to the acceptance of less than perfect results.

These "difficult" nutrients are those for which significant changes in the amounts recommended have occurred relative to previous recommendations, and all are nutrients

for which an AI was derived rather than an EAR. AIs have been estimated in a number of different ways using different types of indicators. Because of this, the exact meanings and interpretations of the AIs differ across nutrients, and sometimes across age groups for the same nutrient.

Less than perfect results were only accepted after discussion with experts and advisors. It was generally agreed that nutrients for which the data supporting the reference value are not solid should not drive the modelling process.

Potassium
The AI for potassium is not based on observed intakes, but on data from clinical trials. More specifically, the AI for adults is based on the level found to blunt severe salt sensitivity in African-American men (using supplemental potassium bicarbonate) and to decrease the risk of recurrent kidney stones (using supplemental potassium citrate); as well as the values at the highest quintile of potassium intakes from epidemiological studies showing some benefits on blood pressure, kidney stone formation, and bone loss. The AI for children was extrapolated from the adult AI based on energy intake. Based on the evidence from which the AI for potassium was derived, extra food was not added to the food intake pattern to achieve this intake, especially given the goal of providing adequate nutrients within a reasonable amount of energy.

Fibre
The AI for total fibre is based on epidemiological studies, specifically, the highest quintile of fibre intake in prospective studies of adults showing a significant negative trend between dietary fibre intake and risk of CHD. The recommendation was expressed as a function of energy intake, yielding an AI of 14g/1000 kcal. This level of intake was then applied to all age groups, as there was no information to indicate that fibre intake as a function of energy intake differs during the life cycle.
Given the endpoint from which the AI for total fibre was derived (reduction of CHD risk in adults), the fibre content of the food intake pattern was accepted as satisfactory, particularly for children. In addition, total fibre intakes are probably underestimated somewhat because of some functional fibres not being included in food composition databases.

Linoleic acid
The food composition database used in the food intake pattern development process underestimates the linoleic acid content of certain foods. This underestimation is a contributor to the lower-than-desirable linoleic acid results in the simulated diets.

Furthermore, the AI for linoleic acid is based on observed dietary intakes in the United States, with the reasoning that linoleic acid deficiency is "basically non-existent in the free-living population"; and therefore, current levels of intake should be adequate. However, the Canadian food supply may systematically provide less linoleic acid than in the U.S. due to the greater use of canola oil compared with soybean oil in many foods. Despite the potentially lower linoleic acid content of the Canadian food supply, there are

no indications of linoleic acid deficiency among Canadians. The AI may therefore be more reflective of average food supply levels than of levels associated with adequacy. For these reasons, the linoleic acid content of the food intake pattern was accepted as satisfactory.

3.3.3 Challenge: The Canadian food supply is not conducive to intakes that are in line with the DRI values for certain nutrients

The current sodium and vitamin D content of the Canadian food supply led to difficulties in meeting recommendations for these nutrients. Sodium is ubiquitous in the Canadian food supply, whereas vitamin D is present in only a few foods. Both are nutrients for which an AI was derived rather than an EAR. Both are also nutrients where there are public health consequences associated with excessive (sodium) or inadequate (vitamin D) intakes and thus they were carefully considered through the course of developing the food intake pattern.

Sodium

The current food supply in Canada is such that the majority of food-guide-consistent simulated diets had a sodium content in excess of the UL. The UL is based on the adverse effects of sodium intake on blood pressure. This is an adverse effect with public health consequences, and so further adjustments to the pattern were attempted. These further adjustments to the food intake pattern did not have a large impact on sodium content. The Food Guide does include guidance statements on choosing foods lower in salt and sodium. It is recognized in the DRI reports that the current intake of sodium for most individuals in the U.S. and Canada greatly exceeds both the AI and UL, and that progress in achieving a reduced sodium intake will be challenging and will need to be achieved gradually.

Given that further adjustments to the food intake pattern did not have a large impact on sodium content, and the desire for the Food Guide to retain applicability to the general population (i.e., not be presented as a therapeutic diet, such as a clinical No-Added-Salt diet), less than perfect results were accepted for the sodium content of the food intake pattern.

Vitamin D

Vitamin D is synthesized in the skin upon exposure to ultraviolet B (UVB) radiation. However, in Canada, vitamin D synthesis in the skin is absent during the winter months (October to March), and for an even greater part of the year in far northern latitudes. This means that for a significant portion of the year, Canadians must rely on dietary intake to maintain adequate levels of vitamin D in the body.

The major sources of vitamin D in the Canadian food supply are foods to which vitamin D is added. All cows' milk and margarine are fortified with vitamin D. Because it is a commonly-consumed food, fluid milk is a major dietary source of vitamin D in Canada. For this reason, the food intake pattern in Canada's Food Guide recommends that all

Canadians over 2 years of age have 2 cups of milk (or fortified soy beverage) every day for adequate vitamin D.

The average amount of vitamin D provided by the food intake pattern, however, does not meet the AI for those over 50 years of age. Trying to increase the vitamin D content of the food intake pattern through food sources alone was deemed impractical because it required the pattern contain unrealistic daily amounts of specific foods (for example, four to six cups of fluid milk would be required to satisfy vitamin D requirements in people over the age of 50).

Thus, it was recommended that in addition to following Canada's Food Guide, all adults over the age of 50 should take a daily vitamin D supplement of 10 micrograms (400 IU). With this additional amount of vitamin D, the median vitamin D content of the food intake pattern for people over the age of 50 was at or exceeded the AI for this nutrient.

3.3.4 Challenge: Assessment of the energy content of the food intake pattern - the EER is not recommended for assessment of energy in either groups or individuals

The purpose of Canada's Food Guide is to assist the people of Canada in making food choices that promote health and reduce the risk of nutrition-related chronic disease, including obesity.

The energy content of food-guide-consistent simulated diets was assessed using EER values calculated for normal-weight reference individuals using a sedentary level of activity to ascertain that the food intake pattern did not provide an excessive amount of energy.

This was done even though the use of EER values in assessment of energy adequacy is not recommended in the DRI reports. This recommendation is in part because of the pervasive problem of under-reporting of energy intake, and in part because Body Mass Index (BMI) can be used as a biological indicator of adequacy. The recommended method to assess energy adequacy is to use BMI as an indicator of energy intake. The proportions of a group with BMIs below, within, and above the desirable range reflect the proportions with inadequate, adequate, and excessive energy intakes.

Because the Food Guide modelling process used only simulated diets, and not real people or dietary intakes, BMIs were not available and under-reporting of energy intake was not an issue. Thus, reference EER values were used as benchmarks when examining how much energy the simulated diets contained. However, it is acknowledged that the reference EER values used were exactly that – a reference, calculated using a reference height and a reference weight – and that energy requirements can vary widely between individuals, even those within the same age and gender group.

When calculating reference EER values for use as benchmarks, it was noted that there was a significant jump between the EER values for 18 year olds (calculated using the

equations for 9-18 years) and those for 19 year olds (calculated using the equation for 19 years and older). This jump was more pronounced for females than for males.

Simulated diets for females 14-18 years tended to have median energy content in excess of the reference calculated EER value. This was considered carefully throughout food intake pattern development, but creating a pattern with adequate nutrient content without exceeding the reference EER value proved to be difficult for this age-gender group. Knowledge of the significant jump between the EER values for 18 year olds and those for 19 year olds helped to reduce concern about this result.

4. Options for Modification in the DRI Development Process

Not all of the challenges encountered while using the DRIs in the two case studies described can be resolved through improvements to the DRI development process. However, the number and the extent of challenges to using the DRIs could be reduced if some of the following modifications were made to the DRI development process.

4.1   Rating of the strength of evidence used to derive each of the DRI values

Although the strengths and weaknesses of the individual studies considered in developing the DRI values are often assessed in the nutrient chapters, a formalized rating of the overall strength of the evidence behind each of the DRI values could be helpful. Various systems for rating quality of evidence exist and can be looked to for guidance.

Such a rating would be useful because many of the DRI values were set using considerable scientific judgement. Even when an EAR has been established, the degree of uncertainty associated with the EAR has not been specified. In many cases, the EAR is based on data from a limited number of individuals and has been extrapolated from one lifestage group to another. In addition, the true distribution of requirements is rarely known – the distribution is assumed to be normal, and the standard deviation of requirements is often presumed to be 10% of the EAR, due to insufficient data on the variability in requirements. The strength of evidence supporting UL values also varies.

Having some indication of the level of scientific evidence behind each DRI value would also help provide an indication of the level of expert judgement that may be needed when interpreting and using the DRIs in various applications.

4.2   Replacement of AIs with EARs where possible; defining ULs where possible.

It is recognized that a critical mass of new information is needed to determine EARs and ULs where there currently are none.

4.3   Use of more specific categories of nutrient values when an EAR cannot be determined; consistent definition of "Adequate Intake"

Currently, AIs have been estimated in a number of different ways using different types of indicators. Because of this, the exact meanings and interpretations of the AIs differ across nutrients, and sometimes across age groups for the same nutrient. At present there is no easy way to distinguish between these different types of AIs without going back to the nutrient reports.

Having separate categories of nutrient values – in effect, having different sub-types of AIs – that reflect the type of endpoint used would be useful. These more specific categories would instantly identify a value as being based on a particular type of endpoint, and thus provide an indication as to its use and interpretation.

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For example, rather than having the generic category "Adequate Intake", specific categories of values could be named according to type of endpoint used – e.g. mean intake of healthy population; experimentally derived estimate; threshold/minimum adequate intake; etc.

Alternatively, a single definition for "Adequate Intake" could be agreed upon and used consistently.

4.4 Increased consistency in choosing indicators used to set DRI values

The specific criterion of adequacy used to determine the requirement differs for each nutrient, as does the associated consequence of being "at risk". Similarly, the critical adverse effect used to set the UL varies with each nutrient. Because different types of effects are used as indicators across nutrients, and sometimes across lifestage groups within nutrients, it can be difficult to prioritize which nutrients are of concern when faced with multiple nutrients assessed as having a high prevalence of inadequacy or excess. It is recognized that, in many cases, data addressing the effects of inadequate or excessive intakes on specific indicators of health status are lacking. However, a more standardized approach to determining indicators, and thus increased consistency in the nature of the risk associated with inadequate or excessive intake as determined through assessment using the DRIs, would be useful in interpreting the potential health impacts associated with such intakes.

Alternatively, some kind of ranking of the health impact of the indicator could be employed. The report on *Applications in Dietary Assessment* suggests factors such as the seriousness of the adverse effect, and the extent to which the adverse effect is reversible, should be considered when assessing the risk of adverse effects in those with usual intakes above the UL. A summary of the severity and reversibility of the adverse effect could be used to help describe the nature of the risk in question for each of the DRI values.

4.5 Inclusion of multiple endpoints, where feasible

There is a continuum of outcomes, both beneficial and adverse, associated with various intake levels of a nutrient.

The National Research Council 1986 report *Nutrient Adequacy: Assessment Using Food Consumption Surveys* contained the following recommendation:
"Nutrient requirements based on multiple criteria of adequacy should be developed and applied. For a given nutrient, one might focus on the intake adequate to prevent clinical deficiency, to maintain functional integrity of metabolic systems, and to maintain tissue stores. This would permit multitiered population assessments."

The development of multiple endpoints could expand the scope of scientific information available and would be of use when interpreting and using the DRIs in various applications.

5. Conclusion

The advent of the DRIs has provided those who use nutrient reference values with a greater variety of tools more suited to the diverse ways in which these values are applied. Despite the improvements over previously available Recommended Dietary Allowances and Recommended Nutrient Intakes, challenges related to consistencies in the definitions of the types of values, the strength of evidence supporting the values and uncertainty factors used, and the relationship of the chosen indicators to impact on health have surfaced when applying the DRI values to various activities.