UNCERTAINTY OF THE IODINE-131 INGESTION
DOSE CONVERSION FACTOR

INTRODUCTION

The United States Department of Energy (DOE) has generated special nuclear materials and related by-products for nearly 50 years in support of the Nation's nuclear weapons needs[1]. Across the Complex, radiation dose from iodines and noble gases were significant in the early years due to the practice of processing short-cooled fuel, before volatile short-lived fission and activation products could decay away and before effective measures were created for containing these products. The atmospheric source term at the major production sites is dominated, in terms of dose to the public, by ^{131}I and ^{144}Ce at Hanford[2], uranium and its progeny at Fernald[3], ^{131}I and ^{137}Cs at the Idaho National Engineering Laboratory[4], and ^{3}H and ^{131}I at the Savannah River Site (SRS)[5,6]. Historically, throughout the DOE Complex, ^{131}I released to the atmosphere during the 1950's as a result of fuel processing has been the largest contributor to public exposure. There are also current potential hazards with regard to radioiodines released to the environment from upsets at nuclear power stations; radioiodine was a major contributor to population exposures following the accident at the Chernobyl NPP[7,8,9,10].

Radiation dose to members of the general public living in the vicinity of sites that make up the DOE Complex is dominated by releases to the atmosphere and surface waters in the early years of operation, prior to the development of techniques to reduce emissions of potentially hazardous material. Dose to the offsite populations from atmospheric sources and pathways has a greater impact than surface water releases simply because of the greater number of people affected; surface water releases may result in a higher individual dose, but the total number of people impacted is much lower. In the late 1940's through the early 1960's, offsite dose throughout the DOE Complex from atmospheric releases was dominated by radioiodine, primarily ^{131}I. After the mid-

1960's, when fuel was cooled for longer periods before processing and when effective emission controls were in place, various long-lived fission products began to dominate the annual dose estimates, but total dose was at least an order of magnitude lower and continued to decrease.

Dose reconstruction efforts at DOE's Hanford Site have shown that, for releases of ^{131}I, the consumption pathway accounts for more than 95% of total dose with milk consumption accounting for 80% and beef, eggs, and fruit making up the additional 15%[11]. Uncertainties in the calculation of historical atmospheric concentrations of ^{131}I are on the order of a factor of 2 to 10[12], while the total reconstructed dose of ^{131}I is estimated to have a 90% confidence range of a factor of 15 for the maximum individual[2]. For a representative (average) individual at any given location, however, 90% of the dose estimates are within a factor of 25 at Hanford[13]. Sensitivity analyses showed that the parameter to which the dosimetry models were consistently most sensitive was the iodine dose conversion factor (DCF)[13]. This is not surprising since the DCF is very influential to dose estimates from all pathways, similar to that shown by Hamby[14] with the aggregated atmospheric tritium model. Knowledge of the uncertainties related to the calculation of the ^{131}I ingestion DCF, therefore, will greatly improve our confidence in the dose reconstruction effort and the prediction of the consequences related to radioiodine intake.

METHOD

A probabilistic estimation of the ^{131}I adult ingestion dose conversion factor was generated by multiple calculations of dose to the thyroid following a 1 Bq intake via ingestion. An Excel® spreadsheet was written that contains modules for calculating the S-factor, the integrated activity in the thyroid, and the dose conversion factor. As an add-on to Excel, the Crystal Ball® software package was used to accumulate many iterations of the DCF calculation and to perform statistical analyses on input and output parameter values. The sections that follow present each of the calculational steps in more detail.

Iodine metabolic modeling. Thyroid uptake and iodine metabolism involves extremely complex biological systems. In modeling the metabolic transport of iodine through the body, many simplifying assumptions have to be made. In addition to these assumptions, the presence or absence of dietary iodine plays a significant role in iodine metabolism and thyroid function. There is very little difference in metabolism rates between men and women, and, except during pregnancy, the concentration of hormonal iodine in the bloodstream remains fairly constant throughout life[16].

The uptake of iodine via the ingestion pathway occurs from the consumption of food and fluids. Iodine in these substances is in an inorganic iodide form and is, therefore, absorbed in the bloodstream via all levels of the gastrointestinal tract[17], primarily the intestine[16]. The rate of absorption by the GI tract is about 5% per minute[16] and virtually all ingested iodine is absorbed by the bloodstream[16,18], with very little appearing in the feces[17]. Once in the bloodstream, iodine is rapidly absorbed in the extracellular tissues of the body, with a large fraction, approximately 60-80%, being lost via the urine[16,17]. The majority of body iodine eventually flows through, and is trapped by, the thyroid or is excreted via the kidneys. A small amount is also removed from the bloodstream by the liver and excreted in feces[16]. Equilibrium of the total pool of iodine is achieved within several hours after intake, with iodine selectively concentrating in the thyroid, salivary, and gastric glands[16,17].

Iodine in the body is either in the form of inorganic iodide or organic hormonal iodine. Iodide is converted to an organic state in the thyroid and remains in that state until reincorporated into the bloodstream, at which time it converts back to the inorganic form[16]. The inorganic phase of iodine in the body has a turn-over half-life of about 6-7 hours, and the organic phase of iodine turns over with a half-life of approximately 9.5 days[17].

The uptake of iodine by the thyroid is directly correlated to thyroid mass[19] and decreases only slightly with increasing age[16]. Both mass and uptake fraction vary with dietary intakes of iodine, increasing with low intakes and decreasing with high intakes[19]. The size of the thyroid, and thus, the uptake fraction, is highly dependent on the amount of iodine in the diet[18]. Bair et al.[20] have shown that thyroid uptakes were about 20% in rats with normal iodine diets, but increased to 40-50% with iodine-deficient rats. Dolphin[19] states that, because of its interdependence with thyroid mass, uptake fractions and thyroid masses must be derived from similar cohorts. For example, an appropriate uptake fraction for a cohort from the United States, where iodine is abundant in the normal diet, is about 20%. However, in countries where the iodine abundance in diets is reduced, and thyroid masses are correspondingly larger, average uptakes approach 45%.

The metabolism and transport of iodine in the human body is simulated using a three-compartment, first-order kinetic model (Fig. 1). This model, as developed by Riggs[16] and modified by the ICRP[18], contains one inorganic compartment representing iodide in the blood and two organic compartments representing hormonal iodine in the thyroid gland and in the extracellular tissues of the body. In the model of Fig. 1[16,18], iodide in the blood is either transferred to the thyroid or lost via the urine with a half-life of approximately 6 hours. The ICRP[18] metabolic data for iodine does not consider the blood-to-thyroid transfer to have any holdup time, however, other interpretations of the Riggs model account for this short-term delay[21]. Once in the thyroid, iodide is converted to an organic form and then lost to the extracellular tissues of the body with a half-life of about 120 days. Still in the organic form, iodine in the body is transferred, with a half-life of approximately 12 days, either back to the blood and converted to iodide or lost via feces. During profuse sweating, significant amounts of iodide can be lost by perspiration, but this route is neglected in the model[16,18].

Iodine-131 decays to ^{131}Xe and ^{131m}Xe with yields of about 99% and 1%, respectively[22]. Xenon-131 is a stable isotope, while ^{131m}Xe emits a 164 keV electron via internal conversion. Since

xenon is a noble gas, and because of the low yield and low energy of ^{131m}Xe, it is assumed for estimates of internal dosimetry that its contribution to dose is insignificant. Dose from this nuclide, therefore, is not considered in the estimate of the ^{131}I dose conversion factor[18].

Time-integrated iodine activity. In Riggs'[16] original analysis of the differential equations governing the iodine metabolic model, he suggests that the change in activity in the thyroid gland is approximately equal to the product of the activity in the inorganic compartment and the rate constant describing the transfer from the inorganic compartment to the thyroid. This analysis, however, would rely on several simplifying assumptions. Therefore, a rigorous mathematical treatment is more appropriate. Because of the need to explicitly calculate the dose conversion factor multiple times to determine its variability, the details of the calculation are provided below.

A simplified representation of the three-compartment model for iodine ingestion is presented in Fig. 2. The compartments represent the time-dependent radioiodine activity in the blood, $X(t)$, activity in the thyroid, $Y(t)$, and activity in the rest of the body, $Z(t)$. The rate constants depicted in Fig. 2 account for the transfer of iodine between compartments and the loss of iodine either by excretion or radioactive decay. The rate constants are equal to the following:

$$a = f_{blt}k_{bl}$$
$$b = (1 - f_{blt})k_{bl} + \lambda$$
$$c = k_t$$
$$d = \lambda$$
$$e = (1 - f_{bbl})k_b + \lambda$$
$$f = f_{bbl}k_b$$

where f_{blt} and f_{bbl} represent the fraction of activity in the blood taken up by the thyroid and the fraction of activity in the body going to the blood, respectively. The parameters k_{bl}, k_t, and k_b represent the transfer rate constants for iodine moving out of the blood, out of the thyroid, and out

of the body, respectively. Radiological decay, of ^{131}I in this case, is represented by λ. The differential equations for the three compartments are:

$$\frac{dX(t)}{dt} = fZ(t) - (a+b)X(t),\tag{1}$$

$$\frac{dY(t)}{dt} = aX(t) - (c+d)Y(t), \text{ and}\tag{2}$$

$$\frac{dZ(t)}{dt} = cY(t) - (e+f)Z(t).\tag{3}$$

The solution of these three linear homogeneous first-order differential equations follows from the creation of a single third-order linear homogenous differential equation. This is accomplished by solving eqn (1) for Z(t), where,

$$Z(t) = \frac{\frac{dX(t)}{dt} + (a+b)X(t)}{f}.\tag{4}$$

Then, taking the derivative of eqn (4) with respect to time results in,

$$\frac{dZ(t)}{dt} = \frac{\frac{d^2X(t)}{dt^2} + (a+b)\frac{dX(t)}{dt}}{f}.\tag{5}$$

Solving eqn (3) for Y(t) yields,

$$Y(t) = \frac{\dfrac{dZ(t)}{dt} + (e+f)Z(t)}{c}, \tag{6}$$

and substituting eqns (4) and (5) into eqn (6) results in,

$$Y(t) = \frac{1}{cf}\left[\frac{d^2 X(t)}{dt^2} + (a+b+e+f)\frac{dX(t)}{dt} + (a+b)(e+f)X(t)\right]. \tag{7}$$

Then, the derivative of eqn (7) with respect to time gives,

$$\frac{dY(t)}{dt} = \frac{1}{cf}\left[\frac{d^3 X(t)}{dt^3} + (a+b+e+f)\frac{d^2 X(t)}{dt^2} + (a+b)(e+f)\frac{dX(t)}{dt}\right]. \tag{8}$$

Substituting eqns (7) and (8) into eqn (2) and defining the following parameters,

$$\begin{aligned}
A &= a+b+c+d+e+f, \\
B &= (a+b)(e+f)+(a+b+e+f)(c+d), \text{ and} \\
C &= acf - (a+b)(c+d)(e+f),
\end{aligned} \tag{9}$$

results in the third-order differential equation describing the system of Fig. 2,

$$\frac{d^3 X(t)}{dt^3} + A\frac{d^2 X(t)}{dt^2} + B\frac{dX(t)}{dt} = CX(t). \tag{10}$$

The solution of eqn (10) follows from the solution of the characteristic equation,

$$r^3 + Ar^2 + Br = C, \tag{11}$$

and, therefore, the general solution of eqns (10) and (11) takes the form,

$$X(t) = c_1 e^{r_1 t} + c_2 e^{r_2 t} + c_3 e^{r_3 t} \tag{12}$$

where r_1, r_2, and r_3 are the roots of the characteristic equation and c_1, c_2, and c_3 are integration constants determined from the initial conditions.

In general terms, the roots of eqn (11) are:

$$r_1 = -\frac{A}{3} - \frac{D\sqrt[3]{2}}{3E} + \frac{E}{3\sqrt[3]{2}}, \tag{13}$$

$$r_2 = -\frac{A}{3} - (1 + i\sqrt{3})\frac{D\sqrt[3]{2}}{3E} - (1 - i\sqrt{3})\frac{E}{6\sqrt[3]{2}}, \text{ and} \tag{14}$$

$$r_3 = -\frac{A}{3} + (1 - i\sqrt{3})\frac{D\sqrt[3]{2}}{3E} - (1 + i\sqrt{3})\frac{E}{6\sqrt[3]{2}}, \tag{15}$$

where the parameters, D and E, have been defined as,

$$D = -A^2 + 3B, \text{ and} \tag{16}$$

$$E = \sqrt[3]{-2A^3 + 9AB + 27C + \sqrt{4(-A^2 + 3B)^3 + (-2A^3 + 9AB + 27C)^2}}. \tag{17}$$

8

To solve for c_1, c_2, and c_3, the initial conditions are such that, $X(0) = f_1S$, $Y(0) = 0$, and $Z(0) = 0$, where S is the initial iodine activity ingested and f_1 is the fraction absorbed by the transfer compartment (blood). Using eqn (4), the initial condition of no activity in the body compartment, $Z(0) = 0$, implies that,

$$X'(0) = -(a+b)f_1S, \tag{18}$$

where the single-prime notation represents the first derivative of X with respect to time. Additionally, eqn (6) and the $Y(0) = 0$ initial condition results in,

$$X''(0) = \left[(a+b)(a+b+e+f) - (a+b)(e+f)\right]f_1S. \tag{19}$$

Taking time derivatives of the general solution in eqn (12), the initial conditions can be put into terms of integration constants:

$$c_1 + c_2 + c_3 = f_1S, \tag{20}$$

$$c_1r_1 + c_2r_2 + c_3r_3 = -(a+b)f_1S, \text{ and} \tag{21}$$

$$c_1r_1^2 + c_2r_2^2 + c_3r_3^2 = -\left[(a+b)(a+b+e+f) - (a+b)(e+f)\right]f_1S. \tag{22}$$

The three integration constants can be obtained by simultaneously solving eqns (20)-(22). Then, using eqn (12) as the general solution for X(t), the solutions of Z(t) and Y(t) are obtained through eqns (4) and (6), respectively.

Sample calculations of the roots and integration constants where performed using the following values for the rate constants:

$$\lambda = \frac{\ln(2)}{8.02 \text{ d}} \qquad k_{bl} = \frac{\ln(2)}{0.25 \text{ d}} \qquad k_t = \frac{\ln(2)}{120 \text{ d}} \qquad k_b = \frac{\ln(2)}{12 \text{ d}} \qquad (23)$$

with $f_1 = 1.0$, $f_{blt} = 0.3$, $f_{bbl} = 0.9$, and $S = 1$ Bq of ^{131}I ingested. With these inputs, the roots and integration constants were determined. A high degree of precision was necessary during the numerical calculation of these values due to the large difference in the magnitudes of the three roots as well as taking powers of the roots in eqn (22). The final solutions for the time-dependent iodine activity in the three compartments can be presented at a lower precision. For the base case given here, the iodine activity in each compartment as a function of time, t, can be expressed as,

$$X(t) = 1.00e^{-2.86t} - 0.000613e^{-0.146t} + 0.000588e^{-0.0905t} \text{ Bq}, \qquad (24)$$

$$Y(t) = -0.301e^{-2.86t} - 0.00949e^{-0.146t} + 0.291e^{-0.0905t} \text{ Bq, and} \qquad (25)$$

$$Z(t) = 0.000640e^{-2.86t} - 0.0320e^{-0.146t} + 0.0313e^{-0.0905t} \text{ Bq.} \qquad (26)$$

The activity of other isotopes of radioiodine in the various compartments as a function of time can be calculated rather easily by multiplying eqns (24) - (26) by the factor,

$$e^{-(\lambda_i - 0.0862)t}, \qquad (27)$$

where λ_i is the decay constant (in units of d^{-1}) of the radioiodine in question. The integrated activity in each compartment after ingestion to a time T, in units of d, is determined using,

$$X(T) = 0.352 - 0.350e^{-2.86T} + 0.00420e^{-0.146T} - 0.00650e^{-0.0905T} \text{ Bq - d,} \tag{28}$$

$$Y(T) = 3.18 + 0.105e^{-2.86T} - 0.0650e^{-0.146T} - 3.22e^{-0.0905T} \text{ Bq - d, and} \tag{29}$$

$$Z(T) = 0.127 - 0.000224e^{-2.86T} + 0.219e^{-0.146T} - 0.346e^{-0.0905T} \text{ Bq - d.} \tag{30}$$

For T = 18,250 d (50 y), the integrated activity is 0.35 Bq-d in the blood compartment (X_{50y}), 3.2 Bq-d in the thyroid compartment (Y_{50y}), and 0.13 Bq-d in the body compartment (Z_{50y}). These results are consistent with a previous solution of the iodine ingestion model[16,18], which used an ^{131}I decay half-life of 8.04 d and accounts for the different half-lives of other isotopes.

Calculation of the S-factor. The S-factor, in units of Gy Bq^{-1} d^{-1}, is calculated using,

$$S = \frac{1.6x10^{-13}}{M_T} \sum_i \Delta_i \phi_i \tag{31}$$

where the constant has units of J MeV^{-1} and, for the case of ^{131}I, M_T is the mass of the thyroid (in kg), Δ_i is the product of the fractional yield and the average emission energy per disintegration of radiation I (in MeV), and ϕ_i is the fraction of energy absorbed by the target organ from radiation i originating in a given source (the thyroid is both the source and the target in this case). The mass of the thyroid varies from one person to the next and is correlated to the iodine uptake fraction and its physiological health. Iodine-131 decays by beta emission 100% of the time (Fig. 3). Table 1 shows that it has six significant beta radiations, nine gamma radiations, five capture electrons, and two characteristic x-rays[22]. The specific absorbed fractions, Φ_i, for a thyroid mass of 0.020 kg[24] were used to determine absorbed fractions as a function of photon energy (see Fig. 4). The absorbed fraction, ϕ_i, is related to the specific absorbed fraction by,

$$\phi_i = \Phi_i M_T. \tag{32}$$

Absorbed fractions will be used in the calculation of DCF uncertainty because of the necessity to have variability in the mass of the adult thyroid. Some uncertainty will be introduced into the calculation since the absorbed fractions are derived from specific absorbed fractions which are determined using distinct geometrical shapes related to specific organ masses. This added uncertainty, however, is expected to be insignificant in the overall variability of the DCF. The total yield-weighted energy released per transition is about 0.574 MeV. Of that, approximately 0.204 MeV is absorbed by the thyroid for each transition of ^{131}I that occurs in the thyroid (see Table 1). Therefore, using a standard thyroid mass of 0.020 kg, the S-factor for ^{131}I(thyroid<--thyroid) is 1.64×10^{-12} Gy Bq^{-1} s^{-1}, consistent with that quoted by Eckerman[23]. The quality factor for all radiations emitted by ^{131}I is assumed to be unity.

Calculation of the dose conversion factor. The DCF is the product of the integrated activity and the S-factor. In general terms, the DCF is written as,

$$\overline{D}(T) = \sum_S \tilde{A}_S S(T \leftarrow S). \tag{33}$$

In the case of the thyroid dose from ^{131}I residing in the thyroid, eqn (33) reduces to,

$$DCF = \tilde{A}_s S, \tag{34}$$

since contributions to total dose from all other organs are insignificant compared to thyroid as the target and source[23]. Using the base-case values, the dose conversion factor is equal to 4.5×10^{-7} Sv Bq^{-1}. This value compares to those reported by the DOE (1988), the EPA (1988), and Killough and Eckerman[21], of 4.9×10^{-7}, 4.76×10^{-7}, and 4.6×10^{-7} Sv Bq^{-1}, respectively. The spreadsheets designed

to perform all calculations were hand-checked against reported values[21] and results of Mathematica® calculations.

Monte Carlo technique. Parameter values for multiple calculations of DCF were assigned using a Latin hypercube sampling (LHS) routine. The method considers the range of each parameter to be composed of a given number of non-overlapping intervals of equal probability. For a given parameter, values are selected at random from each interval based on the probability density function in the interval. The Latin hypercube approach is a constrained random sampling technique that results in added precision over conventional random sampling methods (e.g., simple random sampling) since the entire range of the distribution is sampled in a more systematic manner[15]. Thus, fewer iterations are needed in order to provide adequate statistical input for the probabilistic dose estimate. Model input includes the type of distribution (e.g., normal, lognormal, uniform) and parameters describing its range (e.g., mean, standard deviation, minimum, maximum).

One thousand dose estimates were calculated using the dose-conversion-factor model and the parameter assignments described below. The Latin hypercube routine selected 10 parameter values from each of 100 intervals within each parameter distribution. All parameters, except thyroid mass and uptake fraction, were assumed to be independent since data supporting the calculation of correlation coefficients were not found to be available. The Latin hypercube method provided frequency distributions of dose with mean standard errors of less than 1%. Statistics of the dose probability distribution were not significantly improved by increasing the number of trials above 1,000.

PARAMETER DISTRIBUTIONS

Of the parameters varied in the calculation of the ^{131}I ingestion dose factor, very few are known with certainty. Eleven parameters are allowed to vary according to their range and

probability distribution (see Table 2). Because of the lack of certainty, all parameters except thyroid mass, are assigned triangular distributions, the least amount of bias for the information available. Because of early studies on the kinetics of radioiodine in the human body, some information is known about transfer rates, compartmentalization, and transfer fractions, but for the most part, these estimates are either based on studies of persons with thyroid disease or results have been derived from small cohorts[16]. In all but one parameter, the thyroid uptake fraction, the data are limited suggesting the use of uniform or triangular distributions. However, since iodine uptake has been shown to be directly correlated to the mass of one's thyroid[16,17,19], its assigned distribution will mimic, and be closely correlated to, that of the thyroid mass.

Thyroid mass (M_T). Since the mass of ones' thyroid is directly related to its uptake fraction of iodine from the bloodstream[16,19], and since diet has an important influence on fractional uptake and mass, it is extremely important that thyroid mass be correlated with uptake fraction and that the two come from comparable datasets[19]. For example, erroneous dose estimates would result if a dataset from the U.S. for thyroid mass were used with an estimate of fractional uptake from data in a country with iodine-deficient diets. The mass of the adult thyroid (age > 17 years) in Standard Man is determined from data collected in New York[25]. These data have a geometric mean of 0.01778 kg with a geometric standard deviation (GSD) of 1.47. When log-transformed, the distribution is normal with a mean of 1.25 and a standard deviation of 0.1682.

Fractional absorption (f_1). Fractional absorption refers to the fraction of the initial intake that is absorbed into the transfer compartment, i.e., the bloodstream. It is generally assumed that f_1 is equal to unity for iodine[18]. Early investigators report that iodine is rapidly and completely absorbed by the gastrointestinal tract with very little appearing in the feces[16,17]. To allow for the modeling of some excretion via the feces after initial ingestion, the f_1 parameter is assigned a triangular distribution with a mode of 1.0 and a range of 0.9 to 1.0.

Fractional uptake from transfer compartment (f_{blt}). Once in the bloodstream, iodine is taken up by the thyroid with about 20-40% efficiency. This uptake is dependent on thyroid mass, thyroid metabolism and function, and iodine-presence in ones' diet. Dolphin[19] suggests a mass-dependent uptake fraction of 0.015 per gram of thyroid. The ICRP[18] estimate of a fractional uptake of 0.30 is, therefore, consistent with the use of a 0.020 kg thyroid[25]. The early data of Riggs[16] indicates that, based on ratios of rate constants, the uptake fraction for a healthy individual with a "normal" thyroid is approximately 0.33, whereas an individual with "chronic iodine deficiency" has an uptake fraction of about 0.89. Uptake fractions reported by Riggs range from about 0.10 to 0.90.

In order to establish a fractional uptake distribution that is consistent with the distribution of thyroid mass, we have assigned the uptake fraction a lognormal shape with a geometric mean of 0.267 and a GSD of 1.47. The mean is 0.015 times the geometric mean of the thyroid mass (0.01778 kg) and the GSD is equal to the GSD of the thyroid mass distribution.

The parameters of thyroid mass and uptake fraction are directly correlated, however, the numerical relationship is not known. We have chosen to arbitrarily set the correlation coefficient between these two variables to 0.90. This degree of correlation will maximize their influence on each other and on the entire model, as well as provide some degree of flexibility in the selection of values for these two parameters. The value of the correlation coefficient will be investigated to determine its influence on the DCF uncertainty.

Fractional transfer from body to blood (f_{bbl}). The fraction of iodine moving from the extracellular tissues of the body to the blood is more narrowly defined than the thyroid uptake fraction. The body-to-blood fraction does not change from "normal" individuals to those with "acute or chronic iodine deficiency"[16] indicating that the fraction is far less variable between individuals. The iodine leaving the body compartment is assumed to go back to the transfer compartment (bloodstream) or be excreted via the feces. A ratio of rate constants was used to

determine the fractional transfer to the bloodstream. The transfer fraction is taken as the ratio of the rate constant for movement from the body to the blood, k_{bbl}, and the total body loss rate constant, i.e., the transfer to the blood plus the transfer to the feces, k_{bf}, where,

$$f_{bbl} = \frac{k_{bbl}}{k_{bbl} + k_{bf}}. \tag{36}$$

We have assigned f_{bbl} a triangular distribution with a mode of 0.914 and a range of $\pm10\%$ (yet, not to exceed 1.0). The range assigned to this distribution is rather large given the low variability of Riggs' data[16]. This wide range will maximize the parameter's influence on model output; this influence will be quantified if it is shown to be significant.

Radiological half-life ($T_{1/2}$). The estimate of the radiological half-life for ^{131}I, and hence the decay constant, has varied over the years. Depending on which reference is chosen, the range of values in the literature today spans only about 2%. The most current data on the decay of ^{131}I is obtained from the National Nuclear Data Center[22], where the half-life is reported to be 8.02070 days. This value, being carried to six significant figures, is highly precise. We have, therefore, chosen to assign a triangular distribution to this parameter with a mode of 8.0207 d and a range of $\pm0.1\%$. Because its value is so well known, it is expected that this parameter will have very little influence on total DCF uncertainty.

Thyroid-loss rate constant (k_T). Iodine is lost from the thyroid in "normal" individuals (with regard to thyroid function) with a half-life of about 113 days[16]. It is from Riggs' data that the ICRP[18] obtain their estimate of 120 days. The half-life in patients with "chronic iodine deficiency" increases to 156 days and drops to as low as 20 days in patients with hyperthyroidism[16]. Given this range of possible values over a large population, a triangular distribution has been assigned with a mode of 113 days and a range of $\pm40\%$. Radioiodine is also

lost from the thyroid compartment by radiological decay, and in the case of the short-lived iodines, radiological decay dominates the loss from the thyroid.

Body-loss rate constant (k_b). Loss of iodine from the extracellular tissues occurs by transfer to the blood, excretion via feces, and radiological decay. Riggs[16] estimates a half-life of 11.9 days in this compartment for both blood transfer and fecal excretion. As with the blood-to-body fractional transfer, the loss rate does not change in individuals with "acute or chronic iodine deficiency" and the lowest value for patients with hyperthyroidism is 3.9 days[16]. Based on Riggs' data, therefore, a triangular distribution with a mode of 12 days and a range of ±20% was chosen to describe k_b.

Blood-loss rate constant (k_{blt}). The ICRP 30 model[18] makes no mention of gradual loss of iodine from the transfer compartment. Taken explicitly, the model suggests that the transfer of iodine from the blood to the thyroid and out of the body via the urine is instantaneous. However, when examining the original model development[16] and exercises by Killough and Eckerman[21] and Eckerman[23], it is evident that iodine is lost from the blood with a half-life of about 6 hours. Riggs[16] estimates this value to be 5.8 hours, varying between 1 and 13.9 hours depending on iodine deficiency and thyroid function. Therefore, we have chosen a triangular distribution with a mode of 0.25 days and a range of ±99% to describe the loss of iodine from the blood.

Radiation yield (Δ_i). The fraction of the time a given radiation is emitted per transition of ^{131}I is taken from data provided by the NNDC[22] and is reproduced in Table 1. These values are reported to three significant figures, and as such, each have been assigned a triangular distribution with a mode equal to the reported value and a range of ±1%.

Average energy per transition (E_i). Also given in Table 1 are the NNDC's values for the energy of each radiation emitted by ^{131}I, average energies for beta particles[22]. Radiation energies

are reported to four significant digits, and as such, each have been assigned triangular distributions with ranges of ±0.1% and modes equal to the reported values.

Absorbed fraction (ϕ_i). The value of absorbed fraction is unity for beta particles and conversion electrons, but varies as a function of energy for photons. Variability of this parameter is not handled explicitly, but is linked to the variability established for E_i. The values of absorbed fraction are linear-interpolated from the data[24] of Figure 4 for each iteration and each photon energy.

RESULTS

The sensitivity of the iodine-DCF model to its input parameters was determined using both rank correlation and contribution to variance methods[14,26]. Estimates of several distributions have been made at a few intermediate steps through the calculation of dose conversion factor, i.e., energy per transition, S-factor, and time-integrated activity. No correlations between parameters were considered for the calculation of these distributions. However, since both uptake fraction and thyroid mass are used in the calculation of dose conversion factor, these two input distributions were assumed to be correlated with a coefficient of 0.9. The influence on DCF output of choosing this value for the correlation is investigated below.

Energy per transition. The energy-per-transition distribution is calculated to assess the impact that radiation yield and radiation energy have on the parameter, $\sum_i \Delta_i \phi_i$, used in the calculation of S-factor. The resulting distribution is triangular in shape with a range of no more than 2% from the minimum to the maximum value. The variability in the distribution is almost entirely explained by the B4 beta yield parameter to a degree of 93% and the B4 beta energy by an additional 1%. Beyond that, no other single parameter of energy or yield contributes more than 1% to the variability of $\sum_i \Delta_i \phi_i$. Given that essentially one input parameter contributes to the uncertainty of

this output parameter, the radiation energy and yield parameters are excluded from further consideration in the results that follow. Their slight contribution to the variability of the dose conversion factor, however, will be maintained throughout the estimation of total uncertainty in the DCF.

S-factor. The mass of the thyroid shows a complete inverse correlation (-1.0) with the ^{131}I S-factor distribution (Fig. 5) and contributes 96% to the total variance. The estimated S-factor distribution is lognormal with a geometric mean (GM) of 1.9×10^{-12} Gray per nuclear transition (Gy nt^{-1}) and a GSD of 1.47. The maximum value is about 14 times larger than the minimum value and the historical MIRD estimation of 1.7×10^{-12} Gy nt^{-1}[27] falls at the 38th percentile.

Time-integrated activity. The distribution for time-integrated activity is lognormal with a geometric mean of 1.0×10^{5} Bq d^{-1} and a GSD of 1.46, and its range spans a factor of 12 (Fig. 6). The uptake fraction accounts for 96% of the total variance (Table 3). The other input parameters play a minor role in the total variability of integrated activity in the thyroid.

Dose conversion factor. The dose conversion factor model is equally sensitive to thyroid mass and uptake fraction (Table 4), primarily due to their high degree of correlation, but also because the thyroid mass drives the estimate of the S-factor and the uptake fraction drives the estimate of the integrated activity. Although the distribution appears to be normally distributed (Fig. 7), the DCF best fits a lognormal distribution with a GM of 4.3×10^{-7} Sv Bq^{-1} and a GSD of 1.19. The range of output values resulted in the maximum being a factor of about 3.7 times the minimum and the DOE and EPA estimates[28,29] fall at about the 78th percentile. The recent estimate of 3.5×10^{-7} Sv Bq^{-1} by the National Cancer Institute[30] falls at the 13th percentile.

DISCUSSION

The thyroid mass is of extreme importance in determining the S-factor for self-irradiation of the thyroid and the uptake fraction completely dominates the estimate of the thyroid's integrated activity. And, in general, these two parameters dominate the uncertainty of the ^{131}I ingestion dose conversion factor. In calculating the dose conversion factor, two more parameters provide some influence, those being the blood absorption fraction, f_1, and the thyroid loss constant, k_t. The absorption fraction varied from 0.9 to 1.0, with increasing emphasis placed on values closer to unity. When this parameter was allowed to vary from 0.8 to 1.0, with the same distributional emphasis, f_1 became the most influential parameter with regard to DCF model sensitivity, but otherwise the distribution was essentially unchanged with only a 3% decrease in the median value. The thyroid loss constant was varied by 40% on either side of 113 days. Even though this is a considerable range, the parameter was still only marginally important in the calculation of DCF, being responsible for only 2% of the total variance.

The emission yield of the B4 beta particle (see Table 1) is very important in the calculation of the absorbed energy and only marginally for the S-factor, but in light of the major influence of thyroid mass and uptake fraction, its influence on the total DCF uncertainty is vanishingly small.

The correlation between thyroid mass and uptake fraction plays a significant role in estimating the DCF probability distribution. The degree to which the correlation affects the DCF was judged by estimating certain statistical parameters while varying the correlation coefficient (CC) from zero to 1.0 (Fig. 8). Generally, with decreasing correlation, the range between the maximum and minimum values estimated in the probabilistic DCF distribution is increased. Likewise, with decreasing correlation, the skewness increases, indicating that the lognormal distribution is getting more skewed to the right, and the kurtosis increases, indicating that the peakedness of the distribution is increasing. However, regardless of the degree of correlation, the median of the DCF distribution remains the same, with a standard deviation of the calculated median values of less than 1%. Correlation coefficients between about 0.2 and 0.95 result in roughly the same DCF distribution,

except that the range of possible values increases from about 4 to 15 with decreasing correlation. For CCs between 0.6 and 0.95, the distributions are virtually unchanged. At a CC of 1.0, the DCF distribution changes shape dramatically, becoming skewed to the left. This degree of correlation is mathematically equivalent to requiring that the uptake fraction equal the product of 0.015 and the thyroid mass. It is not prudent to expect that thyroid mass and uptake are perfectly correlated across any population. Therefore, it appears that the selection of a CC of 0.9 is a valid assumption and has minimal impact on the results presented herein.

The overall uncertainty of the iodine dose conversion factor is actually decreased because of the correlation between thyroid mass and uptake fraction. The individual variability in the S-factor and integrated activity distributions is considerably greater than the uncertainty of the two combined. This is due to the fact that the uncertainties of mass and uptake dominate the uncertainties of the S-factor and the integrated activity, respectively, and that those two parameters are highly correlated. Accordingly, the range of possible values is only about a factor of 4 for the ^{131}I DCF, compared to a factor of 15 for the tritium dose factor[31]. By comparison, when the correlation is removed (CC=0), the range of values for the iodine DCF increases to more than a factor of 40.

CONCLUSIONS

The ^{131}I dose conversion factor is lognormally distributed with a median of 4.3×10^{-7} Sv Bq^{-1} and a geometric standard deviation of 1.19. The distribution has a range of a factor of approximately 4. Thyroid mass and the fractional uptake of iodine from the blood are the two most important parameters in the calculation of the iodine DCF. These parameters are known to be correlated, but not to what degree. Dose estimates to individuals and populations exposed to radioiodine can be made more accurate with an increased understanding of the correlation between thyroid mass and uptake fraction and the development of a more extensive database of these two parameters.

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FIGURE CAPTIONS

Fig. 1.   ICRP 30 iodine ingestion biokinetic model[18].   Radioiodine is also lost from each compartment by radiological decay.

Fig. 2. Simplified iodine biokinetic model.

Fig. 3. Iodine-131 decay scheme (taken from Ref. 22).

Fig. 4. Absorbed fraction as a function of energy with the thyroid as both source and target (from Ref. 24).

Fig. 5. Estimated probability distribution for the ^{131}I S-factor with the thyroid as both source and target (in units of Gy per nuclear transition).

Fig. 6. Estimated probability distribution for the ^{131}I time-integrated activity in the thyroid.

Fig. 7. Estimated probability distribution for the ^{131}I dose conversion factor.

Fig. 8.   Statistical descriptors for distributional shape of the ^{131}I dose conversion factor as a function of correlation between thyroid mass and thyroid uptake fraction.

Table 1. Nuclear data and absorbed fractions for the transition of ^{131}I with the thyroid as source and target (adapted from Ref. 22).

Radiations	Yield (Bq^{-1} s^{-1})	Energy, E_i (MeV)	E_i per transition (MeV Bq^{-1} s^{-1})	Absorbed fraction	Absorbed E_i (MeV Bq^{-1} s^{-1})
β^- 1	0.0210	0.06936	0.00146	1	0.00146
β^- 2	0.00651	0.08694	0.000566	1	0.000566
β^- 3	0.0727	0.09662	0.00702	1	0.00702
β^- 4	0.899	0.1916	0.172	1	0.172
β^- 6	0.00480	0.2832	0.00136	1	0.00136
γ 1	0.0262	0.08019	0.00210	0.0331	0.0000695
ce-K, γ 1	0.0354	0.04562	0.00161	1	0.00161
ce-L, γ 1	0.00464	0.07473	0.000347	1	0.000347
γ 3	0.00270	0.1772	0.000478	0.0283	0.0000135
γ 6	0.0614	0.2843	0.0175	0.0314	0.000548
ce-K, γ 6	0.00252	0.2497	0.000629	1	0.000629
γ 11	0.00274	0.3258	0.000893	0.0312	0.0000279
γ 13	0.817	0.3645	0.298	0.0310	0.00924
ce-K, γ 13	0.0155	0.3299	0.00511	1	0.00511
ce-L, γ 13	0.00246	0.3590	0.000883	1	0.000883
γ 16	0.00360	0.5030	0.00181	0.0319	0.0000577
γ 17	0.0717	0.6370	0.0457	0.0310	0.00142
γ 18	0.00217	0.6427	0.00139	0.0310	0.0000432
γ 19	0.0177	0.7229	0.0128	0.0306	0.000392
Kα_1 X-ray	0.0256	0.02978	0.000762	0.1515	0.000115
Kα_2 X-ray	0.0138	0.02946	0.000407	0.1551	0.0000631
Omitted β, ce and Auger radiations			0.00132	1	0.00132
Omitted X-ray and γ radiations			0.00114	<1	<0.00114
SUM			0.574		0.204

Table 2. Input parameter distributions.

Symbol	Parameter	Distribution[a]	Reference(s)
M_T	Thyroid mass	LN (0.01778; 1.47)	20
f_1	Fractional absorption	T (0.9; 1.0; 1.0)	11,12,13
f_{blt}	Uptake fraction	LN (0.267; 1.47)	11,14
f_{bbl}	Body-blood transfer	T (0.823; 0.914; 1.000)	11
$T_{1/2}$	^{131}I Radiological half-life	T (8.0127; 8.0207; 8.0287)	17
k_T	Thyroid loss constant	T (67.8; 113; 158)	11
k_b	Body loss constant	T (9.6; 12; 14.4)	11
k_{blt}	Blood loss constant	T (0.0025; 0.25; 0.4975)	11
Δ_i	Radiation yield	see Table 2	-
E_i	Energy per transition	see Table 2	-
ϕ_i	Absorbed fraction	see Figure 4	-

[a]LN = lognormal (GM; GSD); T = triangular (minimum value; mode; maximum value)

Table 3. Sensitivity analysis results for the time-integrated thyroid activity.

Parameter	Symbol	Rank Correlation	Contribution to Variance (%)[a]
Uptake fraction	f_{blt}	1.00	95.7
Body loss constant	k_b	-0.08	0.6
Radiological half-life	$T_{1/2}$	0.04	0.1
Absorption fraction	f_1	0.03	0.1
Fraction body-to-blood	f_{bbl}	0.03	0.1
Blood loss constant	k_{bl}	0.00	0.0
Thyroid loss constant	k_t	0.00	0.0

[a]the remainder of the variance corresponds to the correlations with radiation yield and average energy.

Table 4. Sensitivity analysis results for the ^{131}I dose conversion factor model.

Parameter	Symbol	Rank Correlation	Contribution to Variance (%)[a]
Thyroid mass	M_T	-0.21	30.1
Uptake fraction	f_{blt}	0.21	30.3
Absorption fraction	f_1	0.13	6.5
Thyroid loss constant	k_t	0.08	2.2
Radiological half-life	$T_{1/2}$	-0.02	0.9
Blood loss constant	k_{bl}	0.02	0.3
Fraction body-to-blood	f_{bbl}	-0.02	0.1
Body loss constant	k_b	0.00	0.0

[a]the remainder of the variance corresponds to the correlations with radiation yield and average energy.