Risk Estimates for Deterministic Health Effects of Inhaled Weapons Grade Plutonium

Bobby R. Scott[a] and Vern L. Peterson[b]

Abstract

Risk estimates for deterministic effects of inhaled weapons-grade plutonium (WG Pu) are needed to evaluate potential serious harm to: (1) U. S. Department of Energy nuclear workers from accidental or other work-place releases of WG Pu; and (2) the public from terrorist actions resulting in the release of WG Pu to the environment. Deterministic health effects (the most serious radiobiological consequences to humans) can arise when large amounts of WG Pu are taken into the body. Inhalation is considered the most likely route of intake during work-place accidents or during a nuclear terrorism incident releasing WG Pu to the environment. Our current knowledge about radiation-related harm is insufficient for generating precise estimates of risk for a given WG Pu exposure scenario. This relates largely to uncertainties associated with currently available risk and dosimetry models. Thus, rather than generating point estimates of risk, distributions that account for variability/uncertainty are needed to properly characterize potential harm to humans from a given WG Pu exposure scenario. In this manuscript, we generate and summarize risk distributions for deterministic radiation effects in the lungs of nuclear workers from inhaled WG Pu particles (standard isotopic mix). These distributions were developed using NUREG/CR-4214 risk models and time-dependent, dose conversion factor (DCF) data based on Publication 30 of the International Commission on Radiological Protection (ICRP). DCFs based on ICRP Publication 30 are more relevant to deterministic effects than are the DCFs based on ICRP Publication 66, which relate to targets for stochastic effects. Risk distributions that account for NUREG/CR-4214 parameter and model uncertainties were generated using the Monte Carlo method. Risks were evaluated for both lethality (from radiation pneumonitis) and morbidity (due to radiation-induced respiratory dysfunction) and were found to depend strongly on absorbed-dose-rate history (which depends on WG Pu solubility). The results obtained were compared to new data from animal and epidemiological studies. Our findings suggest that NUREG/CR-4214 models for assessing lethality risk from inhaled radionuclides may need some modest revision in light the new data. However, for assessing morbidity risks, major revisions may be needed.

Introduction

Department of Energy (DOE) workers at the Rocky Flats Environmental Technology Site (RFETS) involved in deactivation and decommissioning activities could be at risk of inhaling significant amounts of weapons-grade Pu (WG Pu) during accidents. Further, since the tragic events on September 11, 2001, perpetrated by foreign terrorists and subsequent events associated with anthrax, the public has realized that they could also be exposed because of a nuclear terrorist act. Deposition of WG Pu in the respiratory tract (especially the lung) can lead to serious health impairment and possibly death within a few years.

[a] Lovelace Respiratory Research Institute, 2425 Ridgecrest Drive SE, Albuquerque, NM 87108-5127, Bscott@lrri.org
[b] AB Consulting, Inc., 4616 Ipswich Street, Boulder, CO 80301, vlrep@msn.com

Deterministic health effects (the most serious radiobiological consequences) can arise when large amounts of WG Pu are taken into the body. Inhalation is considered the most likely route of intake during work-place accidents or during a nuclear terrorism incident releasing WG Pu to the environment. Our current knowledge about radiation-related harm is insufficient for generating precise estimates of risk for a given WG Pu exposure scenario. This relates largely to uncertainties associated with currently available risk and dosimetry models. Thus, rather than generating a point estimate of risk, distributions that account for variability/uncertainty are needed to properly characterize potential harm to humans from a given WG Pu exposure scenario.

Weapons-grade Pu contains several alpha-particle-emitting radionuclides (^{238}Pu, ^{239}Pu, ^{240}Pu, ^{242}Pu, and ^{241}Am) as well as the beta emitter ^{241}Pu. The main contributors to radiation dose and biological harm are the alpha-emitting radionuclides. Unlike for gamma-emitting radionuclides, induction of adverse biological effects depends on the alpha-emitting radionuclides entering the body and depositing in radiosensitive tissue (Voelz and Buican, 2000). The indicated alpha-emitting radionuclides are not readily absorbed from the gastrointestinal tract and are even less readily absorbed through the intact skin (National Research Council/National Academy of Science 1988). Further, because of the short range of the alpha particles emitted, they do not penetrate the dead, external layer of the skin.

For airborne WG Pu, the aerodynamic particle size, which depends on particle real size, density, and shape, influences the fractional deposition and location of deposition in the respiratory tract. Inhaled WG Pu would be expected to lead to significant alpha radiation doses to four critical sites (lung, lung-associated lymph nodes, liver, and bone) (Hahn et al. 1999; Muggenburg et al. 1996, 1999). Low intakes and associated low radiation doses could lead to stochastic effects (mainly lung, liver, and bone cancers), while large intakes could lead to serious deterministic effects that arise when large numbers of cells are destroyed in an organ/tissue by radiation. Deterministic effects include organ dysfunction (morbidity) and lethality (e.g., from radiation pneumonitis in the lung).

In the former Soviet Union during the Cold War, large amounts of ^{239}Pu/^{241}Am were inhaled and deposited in the respiratory tracts of Russian workers at the Mayak Production Association (PA), which produced WG Pu. Many workers developed lung, bone, and liver cancer as well as other serious health effects (Gilbert et al. 2000; Grogan et al. 2001; Khokhryakov and Romanov 1994; Khokhryakov et al. 1998; Koshurnikova et al. 2000; Kreisheimer et al. 2000; Tokarskaya et al. 1995, 1997). The large intakes in many cases also lead to radiation-induced deterministic effects, including respiratory dysfunction and death and morbidity from what was called pneumosclerosis (translated to mean radiation pneumonitis and pulmonary fibrosis) (Okladnikova et al. 1994).

The DOE standards (e.g., U.S. DOE, 1994) require evaluating consequences to their workers from health effects other than cancer (in addition to evaluating cancer hazard). Two such effects related to the lung are death from radiation pneumonitis (a high consequence) and

respiratory dysfunction due to significant pulmonary injury (considered a moderate consequence) (USNRC 1993a, b). These effects are considered deterministic effects of irradiation because their induction requires doses in excess of specific thresholds, and severity increases as dose increases (USNRC 1989, 1990, 1993a). The thresholds depend on how the radiation dose builds up over time in the lung (dose and dose rate history) and its distribution throughout the lung (Scott et al. 1990; USNRC 1993b). Deterministic effects among DOE workers (and members of the public) could also arise following a nuclear terrorism incident. Results derived in this manuscript for inhalation exposure of DOE workers during WG Pu incidents may be used as an approximation for adult members of the public exposed by inhalation to WG Pu because of a nuclear terrorism incident. However, estimates that are more precise could be derived by applying methods presented here to specific exposure scenarios that relate to a nuclear terrorism incident of interest.

It is of interest to estimate the mass of WG Pu that needs to be inhaled in order to induce serious deterministic effects in the lung. This is because the mass of WG Pu inhaled can, in principle, be calculated based on the concentration of WG Pu in air and the amount of air a person is expected to inhale during a given incident. Ideally, one would like to relate risk for a specific deterministic effect to the mass of WG Pu inhaled. While this can be done for a specific exposure scenario (i.e., specific particle size distribution, level of physical exertion, duration of intake, etc.), the risk coefficient derived may not apply to other exposure scenarios.

The terms "acute" and "prompt" have been used to describe deterministic effects that occur within a few weeks after brief, high-dose-rate, and high-dose exposure to radiation. However, we apply these terms to any deterministic effect that occurs within several years of first contact with radiation. In animal studies in which dogs inhaled $^{238}PuO_2$, deterministic effects were reported to occur in the lung as long as 5 years after first contact (Muggenburg et al. 1996). At the time the NUREG/CR-4214 models for deterministic effects were developed, the dog studies were just being initiated, so only limited information was available for use in developing those models. DOE standards are based on the terms acute and prompt. Thus, modifying the use of the terms to include deterministic effects that occur within several years after first contact with radiation allows application of our research results to DOE standards as they relate to WG Pu.

Risk Models for Deterministic Health Effects

The Lovelace Respiratory Research Institute (LRRI) in Albuquerque, NM, has developed risk models for deterministic health effects (lethality and morbidity) of irradiation of the lung for the Nuclear Regulatory Commission. The models are described in a series of NUREG/CR-4214 reports (USNRC 1989, 1990, 1993a, b) and are here called NUREG/CR-4214 models. The low- and high-LET radiation doses were combined via the RBE-weighting method. When evaluating deterministic effects, the relative biological effectiveness (RBE)-weighted dose is called the **adjusted dose** (USNRC 1993b) and has units of Gy (or a similar unit)[c]. With the NUREG/CR-

c The RBE is the ratio D_R/D_T for the same level of biological effect from test dose D_T and reference dose D_R. The reference is usually X rays or gamma rays. The RBE-weighted dose, $RBE*D_T$, is an adjusted dose.

4214 risk models for deterministic health effects, the thresholds and the so-called shape factor (explained below) depend on the mix of high- and low-LET radiations.

The NUREG/CR-4214 models for deterministic health effects are based on a two-parameter, Weibull-type hazard function given by

$$H = [\ln(2)]\,(D/D_{50})^{V} = [\ln(2)]\,X^{V}, \tag{1}$$

where D is the absorbed dose (averaged over the lung), D_{50} is the corresponding absorbed dose that theoretically affects 50% of those exposed, and V is called the shape factor because it determines the steepness of the dose-response curve (Scott et al. 1988, 1990). Eqn (1) mainly applies to constant dose-rate exposures and single radiations. The variable X is called the normalized dose and is in units of D_{50} (e.g., $X=0.5$ represents half of a D_{50} exposure). Only for the constant dose rate does $X = D/D_{50}$. For a variable dose rate, obtaining X is more complicated (discussed later).

Although D_{50} is a dose-rate-dependent function, it can be treated as a parameter. For variable dose rate, evaluation of D_{50} is complicated as the value obtained depends on the dose rate history (i.e., how the dose rate changes over time) (Scott et al. 1988, 1990).

The interpretation of the D_{50} depends upon whether lethality or morbidity is being considered. For lethality, D_{50} represents the median lethal dose (LD_{50}). For morbidity, D_{50} represents the median effective dose (ED_{50}).

With NUREG/CR-4214 models, risk R is evaluated as a function of H based on the equation (USNRC 1989):

$$R = 1 - e^{-H}. \tag{2}$$

The dependent variable R determines the fraction of the population that would be expected to experience the specified health effect of interest given H when each individual has the same dose and dose rate history. If the dose, D, is below a threshold, D_{thresh}, H is evaluated as zero in NUREG/CR-4214 models and thus R would also be zero.

For a combined exposure to high-LET alpha and low-LET beta and/or gamma radiations, the adjusted dose (RBE-weighted dose) replaces the absorbed dose in NUREG/CR-4214 models. The adjusted dose has only been used for deterministic effects. Other doses (e.g., equivalent dose, effective dose) apply to stochastic effects as they are based on weighting factors specific for stochastic effects (ICRP 1975, 1979, 1994, 1995).

In the calculation of the H in eqn (2), both D and D_{50} should be either absorbed doses (single radiation) or adjusted doses (mixed radiations), not a combination of the two.

The D_{50} for a specific deterministic effect in the lung depends on the dose rate history. If the rate of delivery of the dose is constant, D_{50} is calculated with NUREG/CR-4214 lethality and morbidity models using the empirical equation

$$D_{50} = (\theta_1 /d) + \theta_\infty , \quad (3)$$

where d is the instantaneous absorbed dose rate (Gy/h), θ_∞ (Gy) represents the asymptotic value of D_{50} for high dose rates (such as 100 Gy/h), and θ_1 (Gy^2/h) represents the increase in the D_{50} above θ_∞ evaluated at $d = 1$ *Gy/h*.

For combined high-LET alpha and low-LET beta and/or gamma irradiation, the situation is more complex because adjusted doses are used in NUREG/CR-4214 models rather than absorbed doses (USNRC 1993b). NUREG/CR-4214 model parameters θ_1 and θ_∞ evaluated in terms of adjusted dose are indicated here by $\theta_1\{\beta\gamma\}$, $\theta_\infty\{\beta\gamma\}$, respectively. This is because the parameters take on the same values as for exposure to beta and/or gamma radiation when adjusted dose and adjusted dose rate are used. The brackets "*{}*" are used so as not to indicate a functional relationship with an argument. Along with the indicated parameters, one also needs values for alpha radiation RBE, $RBE\{\alpha\}$, and the Weibull model shape parameter, V, for the deterministic effect of interest.

Generally, the larger the value for D_{50} for different deterministic effects, the larger the value for V. Values of V > 3 represent steep dose-response relationships. For such relationships, generally the ratio D_{50}/D_{thresh} is less than 2. $RBE\{\alpha\}$ is at least weakly dose-rate dependent. It can be much larger for chronic exposure than for brief exposure (CEC/USNRC 1997). This relates largely to a strong dose-rate sparing effect for low-LET radiation as compared to a weak, dose-rate sparing effect for high-LET radiation (USNRC 1993a, b).

Estimates for $\theta_1\{\beta\gamma\}$, $\theta_\infty\{\beta\gamma\}$, $RBE\{\alpha\}$, and the shape factor V for deterministic effects in the lungs are given in Table 1 and are based on NUREG/CR-4214 reports (USNRC 1989, 1990, 1993a, b). These parameters have uncertainty that is represented by subjective triangular distributions (CEC/USNRC 1997). The triangular distribution is characterized by three parameters: minimum (min) or lower estimate; mode or central estimate; and maximum (max) or upper estimate. NUREG/CR-4214 models are based on the combination (lower, central, upper estimates). The central estimate was intended for use in generating central risk estimates. Upper and lower estimates were intended to account for all key uncertainties. Central estimates, however, do not necessarily represent the best estimates. Parameter estimates for the NUREG/CR-4214 models were largely based on animal data available at the time the models were developed. However, the animal data only involved 1.5 to about 3 y follow-up after briefly inhaling radionuclides. For alpha-emitting radionuclides, it is likely that longer follow-up would have been better. In spite of such concerns, we consider it important to proceed with the use of the NUREG/CR-4214 models to generate risk estimates that can be compared to currently available data for deterministic effects of irradiation. This helps in judging the extent to which model revisions are necessary.

In this study, we have considered two types of particle size distributions and two solubility classes (W and Y) for airborne WG Pu particles: (1) monodisperse particles with an aerodynamic diameter from 1- to 10-μm; and, (2) a polydisperse (lognormal) distribution with an activity median aerodynamic diameter (AMAD) of 5-μm and a geometric standard deviation (σ_g) of 2.5. We are aware that new solubility classes have been established in ICRP Publication 66

(1994). However, for the lung, the solubility-class-associated dose coefficients are more related to radiation-induced stochastic effects than to deterministic effects. This is because the target volume over which dose is evaluated in ICRP Publication 66 for stochastic effects is inappropriate for deterministic effects. Further, the dose coefficients are not time dependent. For deterministic effects, ICRP 30 (1979) dose coefficients, which are time dependent and allow evaluation of the average dose to the pulmonary region, are considered more relevant.

For the current study, only radiation damage to the lungs is considered. The minimum inhalation intake (mg of WG Pu and associated uncertainty) to cause deterministic health effects is estimated. However, results are specific for the exposure scenario considered.

Table 1. Triangular distributions of input parameters.

Parameter	Lower Estimate	Central Estimate	Upper Estimate
RBE $\{\alpha\}$	5	12	20
V$\{\alpha\}$	4	5	6
θ_1 $\{\beta\gamma\}$, lethality, Gy^2/h	15	30	45
θ_1 $\{\beta\gamma\}$, morbidity, Gy^2/h	7.5	15	22.5
θ_∞ $\{\beta\gamma\}$, lethality, Gy	8	10	12
θ_∞ $\{\beta\gamma\}$, morbidity, Gy	4	5	6

The uncertainty indicated in Table 1 for the *RBE{α}* is large mainly because of a lack of knowledge about how the RBE changes with dose rate. Presently available information indicates that the *RBE{α}* could be quite large (much greater than 10) when the dose is delivered over many years as occurred for Mayak PA workers (CEC/USNRC 1997).

In the calculation risk of deterministic health effects, the uncertainties reflected in Table 1 are taken into account by using Monte Carlo (MC) simulations implemented with Crystal Ball© (add-in software to Microsoft Excel©) (Decisioneering 2000). The appropriate equations were set up in an Excel© spreadsheet, and the triangular distributions in Table 1 were assigned. The MC simulations consisted of 40,000 random combinations of values from the assigned distributions. This was considered more than enough to ensure convergence in the final results. The M C simulations are discussed in more detail below.

The evaluations of LD_{50}, ED_{50}, and their thresholds are based on the calculation of the normalized dose, *X*, introduced earlier. Although eqn (3) is appropriate for β- and γ-radiation *(both have RBE=1)*, it must be modified for application to combined alpha and beta irradiation as arises from WG Pu because of the presence of the beta emitter ^{241}Pu. The higher RBE (>1) for alpha radiation is accounted for using the adjusted dose rate (*ADR*) and adjusted dose. The absorbed dose rate, *d*, in eqn (3) is replaced with the *ADR*, and the modified form of eqn (3) for combined α/β irradiation from WG Pu becomes

$$\theta_{ADR} = (\theta_1\{\beta\gamma\}/ ADR) + \theta_\infty\{\beta\gamma\}, \qquad (4)$$

where the *ADR* for alpha radiation is the absorbed alpha dose rate multiplied by $RBE\{\alpha\}$. This product is added to the absorbed beta dose rate to obtain the total ADR. Because the *ADR* varies with radiation exposure time and because θ_{ADR} depends on *ADR*, the normalized dose is calculated as in NUREG/CR-4214 reports using

$$X = \int (ADR / \theta_{ADR})\, dt, \tag{5}$$

where the integral is over a sufficiently long period to encompass the deterministic health effects of interest. This period is presently taken as 5 y based on observations in dogs that briefly inhaled $^{238}PuO_2$ and were subsequently followed for about 5 y (Muggenburg et al. 1996). The radiation dose continued to accumulate in the lung over years even though the period of inhalation exposure to ^{238}Pu was brief. Because of the high specific activity of the $^{238}PuO_2$, particle breakup occurred in the lung due to the alpha energy deposited in the particle matrix. This lead to rapid translocation of ^{238}Pu to the liver and bone. We considered the 5-y follow-up period to be adequate for solubility class W compounds in the lung. However, results presented in this manuscript suggest that a longer follow-up period may be needed for solubility class Y compounds.

The values of LD_{50} and ED_{50} correspond to $X = 1$, by definition. (This yields $H = \ln 2$ and $R = 0.5$, which means that 50% of the irradiated population would be expected to suffer the effect of interest.) Thus, the inhalation intakes (in mg) that yield $X = 1$ are the intakes associated with LD_{50} and ED_{50} estimates. Here intake means the mass of material inhaled. However, not all material inhaled deposits in the respiratory tract. Further, different amounts deposit in the different regions of the respiratory tract depending on the particle aerodynamic characteristics, geometry of the respiratory tract, quantity of contaminated air inhaled, and contributions of nose and mouth breathing. *The LD_{50} and ED_{50} estimates differ when the corresponding θ_1 and θ_∞ values differ. Note that estimates of θ used for morbidity are half those used for lethality.* The corresponding thresholds are taken to correspond to $X = 0.5$ (USNRC 1993a, b). Thus, the inhalation intakes that yield $X = 0.5$ are threshold intakes (estimates) for a specific deterministic effect. Again, the intakes represent material inhaled rather than material deposited in the respiratory tract. Because the spatial distribution and amount of inhaled material deposited in the respiratory tract depend strongly on particle size distribution, respiratory tract geometry, level of exertion (e.g., light vs. heavy exercise), percentage of nose (vs. mouth) breathing, intake is not the usual choice for predicting risk.

Calculational Methods

In order to calculate *ADR* and θ_{ADR} as a function of time, the variation in the dose conversion factor (DCF) with time is needed. These DCFs have been obtained from the dose factor file DOSD87, which was distributed with the MACCS2 code and used to derive the DCFs for cancer used in MACCS/MACCS2 (Chanin et al. 1990; DOSD87, which was produced by Keith Eckerman at Oak Ridge, is documented with MACCS2). The DCFs derived below for Pu for 1-μm aerodynamic diameter particles are identical with those given in Federal Guidance Report 11 (FGR11, EPA 1988), once the difference between *RBE* and W_R (radiation weighting

factor) is taken into account, as well as the difference in integration time (5 vs. 50 y). No variability or uncertainty is presently assigned to the DCFs.

DOSD87 contains dose factor increments for periods of 0 – 1 d, 2 – 7 d, 7 – 14 d, etc. out to 50 y. Dose factor increments are given for 60 radionuclides and 21 organs for three respiratory compartments – NP (nasal passage and pharynx), TB (trachea and bronchial passages), and P (pulmonary). The ultimate value of DCF depends on particle size, for which regional deposition fractions (RDFs) are assigned to each respiratory compartment. For example, for 1-μm particles, the RDFs are 0.30 for NP, 0.08 for the TB, and 0.25 for the P regions; they are the deposition efficiencies used in this calculation (for 1-μm particles), as well as in FGR11 and the MACCS DCF database.[d] For particles, these dose-factor increments are given for three solubility classes – D, W, and Y, corresponding to very soluble, moderately soluble, and insoluble compounds. In addition, separate dose factors are given for low-LET and high-LET radiation, as both types of radiation are emitted for many isotopes. For example, for ^{239}Pu the dominant α-radiation is accompanied by γ-radiation. In this case, the γ-radiation is a minor contributor to dose. In the case of ^{241}Pu, a β-emitter, the low-LET dose factor increments dominate, but there is also a high-LET component because ^{241}Pu decays to ^{241}Am, which is an α-emitter. These dose factor increments thus take into account daughter products formed in the organ or tissue by decay of the parent isotope following intake. The dose factor increments for the relevant Pu isotopes and ^{241}Am were extracted from DOSD87 and copied into the Excel© spreadsheet.

The method to determine LD_{50}, ED_{50}, and their associated thresholds is comprised of the following steps:

1. For each radionuclide, calculate the time-interval specific absorbed dose factor increment (Gy/Bq) by multiplying the dose factor increments for each respiratory compartment by their RDFs and summing the results. Do this for both the low-LET and high-LET components. Multiply the high-LET result by the RBE and add it to the low-LET result to derive the adjusted dose factor increment. FGR11 and MACCS/MACCS2 include all three respiratory compartments (NP, TB, and P). All three compartments were included in this study for completeness, as well as the P compartment alone. The latter is of primary interest because the deterministic health effects considered here occur in the pulmonary region (Okladnikova et al. 1994). The results presented below are for the "P-region" only. (However, the results are nearly identical to those that included all three respiratory compartments.)
2. For a given isotopic mix, the adjusted dose increments (Gy) are calculated by multiplying each isotope's activity (Bq/g-mix) by the inhalation intake (g-mix) and its dose factor increment from step 1 (Gy/Bq), and summing over all isotopes.

[d] Note that the term "inhalation intake" used in this study refers to the amount of WG Pu in the air inhaled. The amount deposited in a given respiratory region is less, as given by its RDF. The pulmonary burden, for example, is 25% of the inhalation intake for 1-μm particles. The difference between one and the sum of the RDFs (0.37 for 1-μm particles) is the fraction of the inhalation intake that is exhaled.

3. The cumulative adjusted dose (Gy) is calculated by integrating the adjusted dose increments out to 5 y. This integration is simply the sum of the increments over the selected period.
4. The ADR (Gy/h) is calculated by dividing the adjusted dose increment (from step 2) by the corresponding period (in hours).
5. The θ_{ADR} is calculated by using eqn (4) for both lethality and morbidity.
6. The normalized dose increments, ΔX, for both lethality and morbidity, are calculated by dividing the adjusted dose increment (step 3) by the respective values of θ_{ADR} for each increment, then summing these increments out to 5 y to determine X.
7. The LD_{50}, ED_{50}, and their thresholds were determined by adjusting the inhalation intake until the normalized dose is $X = 1$ or $X = 0.5$.

Once the LD_{50}, ED_{50}, and their thresholds have been estimated, the hazard function and risk can be calculated for any inhalation intake, using eqn (1) and (2). However, for the MC simulations, the input parameters (particle size, RBE, V, and the θs for lethality and morbidity) are selected randomly within their assigned distributions in order to determine distributions of hazard and risk for any given inhalation intake. The LD_{50} and ED_{50} estimates and the associated threshold estimates are different for each combination of these input parameters. Equations giving the dependence of LD_{50}, ED_{50}, and their thresholds on the input parameters were therefore required before the M C simulations could be run. Therefore, LD_{50}, ED_{50}, and their thresholds have been evaluated (see step 7, above) for many combinations of the input parameters. The Excel© curve-fitting capability has been used along with empirical relationships to fit the indicated data (i.e., derive appropriate parameterizations). It is found that the dependences of the adjusted dose values of LD_{50}, ED_{50}, and their thresholds on particle size, RBE, and θ_∞ are so weak that they can be ignored. This results from the fact that the θ_1/ADR term in eqn (4) is much larger than the θ_∞ term for most intervals. The resulting dependence on θ_1 is nearly linear, but a quadratic equation was used to maintain accuracy. The weak dependence on RBE is a result of the constraint of $X = 1$ or $X = 0.5$ and the weak dependence on θ_∞.

Although the risk for deterministic health effects have been calculated for three isotopic mixes commonly used at RFETS, only that of WG Pu is reported here. The calculations were done for solubility classes W and Y. Plutonium oxides and hydroxides are of class Y; the other Pu compounds considered are of class W. The specific activities of WG Pu are shown in Table 2. Note that ^{242}Pu is not included in this table because it is not included in the DOSD87 file. This omission leads to a trivial error because ^{242}Pu is a minor constituent (less than 0.0003% of overall activity) and contributes little to the overall radiation dose.

Table 2. Radionuclide-specific activities for WG Pu.

Radionuclide	Activity (Bq/g-mix)
^{238}Pu	1.85E+08
^{239}Pu	2.13E+09
^{240}Pu	4.77E+08
^{241}Pu	1.24E+10
^{241}Am	2.22E+07

Estimates of LD_{50}, ED_{50}, and associated thresholds were first derived for various combinations of θ_1 and θ_∞ for RBE = 5, 12, and 20 for particle sizes (monodisperse) of 1-, 5-, and 10-µm aerodynamic diameters. The variation of LD_{50}, ED_{50}, and their thresholds in terms of adjusted dose were found to have a very weak dependence on RBE and θ_∞, but the corresponding intake in gram and absorbed doses varies inversely as RBE for LD_{50} and ED_{50}. For example, for a 5-µm particle size, WG Pu Class W, θ_1 = 30, and θ_∞ = 10, the LD_{50} as adjusted dose remains nearly constant at 342 Gy from RBE = 5 to RBE = 20, which shows the very weak dependence on RBE. (The values for 1-µm and 10-µm particle sizes are nearly the same.) In contrast, the LD_{50} when expressed as absorbed dose varies from 68 Gy for RBE = 5 to 17 Gy for RBE = 20, and the corresponding inhalation intakes vary from 0.0813 g for RBE = 5 to 0.0204 g for RBE = 20, a factor of four variation, the same as the RBE variation. Thus, the LD_{50}, ED_{50}, and thresholds are almost independent of RBE when expressed as adjusted doses, but the corresponding absorbed doses and inhaled amounts vary inversely to the RBE. Recall that the absorbed dose is the adjusted dose divided by the RBE when the entire absorbed dose is due to alpha radiation. This is essentially the case here, as the beta dose from ^{241}Pu was negligible. Thus, the LD_{50}, ED_{50}, and thresholds expressed as absorbed doses are proportional to the corresponding inhalation intakes; the corresponding adjusted dose values, however, are not. Note that the intake in milligrams corresponding to LD_{50}, ED_{50}, and thresholds vary strongly with particle size even though the corresponding adjusted doses do not.

The MC simulations were made for seven levels in inhalation intake (5-, 7-, 10-, 15-, 20-, 30-, and 50-mg) and two solubility classes (W and Y). Two types of probabilities are evaluated using Crystal Ball©. The first is "risk," which is a measure of the proportion of exposed persons that would be expected to suffer a given health effect for the specified dose and dose rate history. For example, a risk of 0.5 for death from deterministic effects means that half the people that receive the specified exposure are expected to die from the deterministic effect. With our MC simulations, many risk estimates are generated for a given intake of WG Pu. Thus, we speak of a risk distribution (i.e., distribution of risk estimates). The second probability we describe is expressed as a percent and relates to the cumulative distribution associated with the risk distribution generated via the MC method. This second probability we called a "computational distribution statistic" because it refers to a single point on the cumulative distribution curve for a generated risk distribution (see later, for example, the vertical axis of Fig. 3). The cumulative

distribution curve (for a risk distribution) as used here reflects uncertainties associated with the risk model employed.

The median, or 50th percentile risk estimate, represents our "central estimate" of the actual risk because it corresponds to the risk value for which half of MC-generated risk estimates are larger and half are smaller than the selected estimate. Similarly, central estimates of LD_{50} and ED_{50} are based on medians of MC-generated distributions that reflect uncertainty associated with NUREG/CR-4214 models used.

Results and Discussion

The distributions of LD_{50}, ED_{50}, and their thresholds were obtained based on our MC evaluations. When these dose percentiles are expressed as adjusted doses, the resulting distributions are nearly triangular. An example is shown in Fig. 1 for the LD_{50} estimate for Class W, WG Pu. *[This display happens to be taken from the calculation for an inhalation intake of 10 mg, but the results do not depend on the amount inhaled. The results are the same (within the randomness of the MC sampling) for other intakes. The term "outliers" in the figure refers to the samples not shown, that is, the display range does not cover the full range of results.]* The probabilities are slightly depressed from linear for values below the median (left side of triangle) and slightly inflated above linear for values above the median (right side of triangle).

Parameters representative of the nearly triangular distributions of adjusted dose measures from the MC simulations are shown in Table 3. The central values given in the table are the median values, but the mean and mode are nearly the same (within 1%) and could have been used as well. (The values shown are taken from the calculations for 5-μm particles, but the results are nearly the same for 1-μm or 10-μm particles.) Note that the thresholds are about 70% of the corresponding LD_{50} or ED_{50} values, not 50% as might have been anticipated from the fact that LD_{50} and ED_{50} correspond to $X = 1$, whereas the thresholds correspond to $X = 0.5$. The 50% rule does not apply because the expression for X is not linearly proportional to inhalation intake. On the other hand, the ED_{50} values (morbidity) are the same as the threshold values for lethality, which is a direct result of the θ values for morbidity being half those of lethality. Note that the morbidity thresholds are about half of the LD_{50} values. This is because the thresholds are about 70% of the LD_{50} or ED_{50}, and the lethality threshold is the same as ED_{50}; thus, the morbidity threshold is about $0.7 \times 0.7 \approx 0.5$ of the LD_{50}.

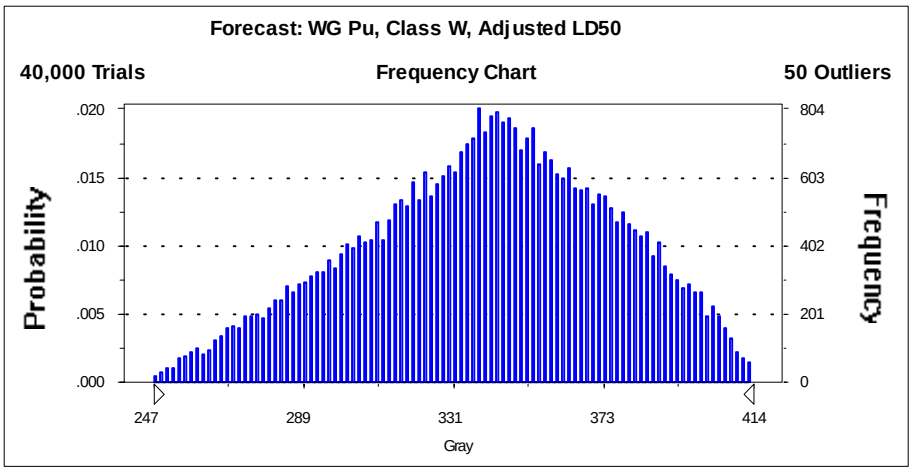

Fig. 1. Distribution of LD_{50} (adjusted dose) estimates from Monte Carlo simulation for Class W WG Pu for 5-µm particles.

Table 3. Triangular distribution parameters for adjusted dose measures (Gray).

Isotopic Mix, Class	Min	Median	Max	Min	Median	Max
	Lethality, LD_{50} (Gy)			**Lethality, Threshold (Gy)**		
WG Pu, Class W	244	343	417	171	241	293
WG Pu, Class Y	673	948	1,155	476	672	820
	Morbidity, ED_{50} (Gy)			**Morbidity, Threshold (Gy)**		
WG Pu, Class W	171	240	294	120	169	207
WG Pu, Class Y	476	671	820	336	473	579

The absorbed dose measures show distributions that more resemble lognormal than triangular. An example is shown in Fig. 2 for the LD_{50} estimate for Class W WG Pu. (As with adjusted dose, the example happens to be for an inhalation intake of 10 mg, but the results do not depend on the amount inhaled. The results are the same (within the randomness of the Monte Carlo sampling) for other intakes. These distributions are not truly lognormal in that they have minimum and maximum values that are determined by the limits on the triangular distribution of input parameters and limited by the finite number of samples in the simulation.

Parameters related to the absorbed dose distributions are presented in Table 4. Note that, again, the threshold values are about 70% of the corresponding LD_{50} or ED_{50}. Again, the morbidity threshold values are about half of the LD_{50} values. (As before, these values are taken from the calculations for 5-µm AMAD polydisperse particles, but the results are nearly the same as for monodisperse 1-µm particles.)

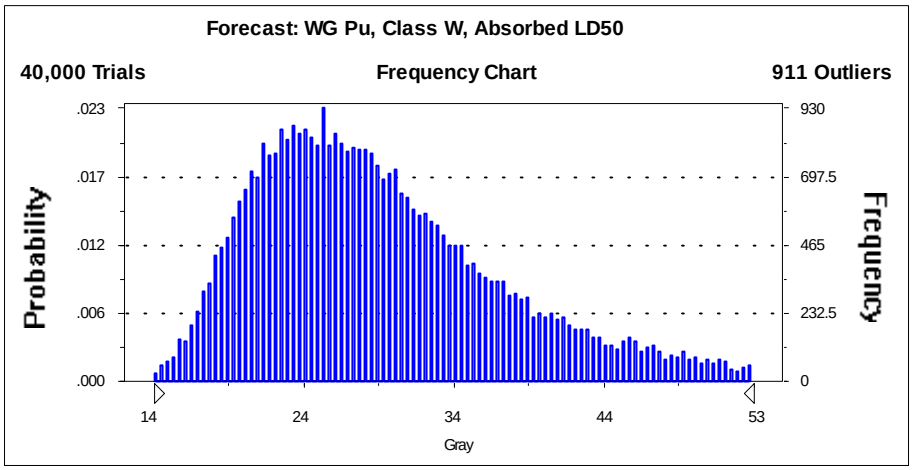

Fig. 2. Distribution of LD_{50} (absorbed dose) estimates from Monte Carlo simulation for Class W WG Pu for 5-µm particles.

Table 4. Absorbed dose measures (Gy).

Isotopic Mix, Class	Min	Median	Max	Min	Median	Max
	Lethality, LD_{50} (Gy)			**Lethality, Threshold (Gy)**		
WG Pu, Class W	13	28	80	9	19	56
WG Pu, Class Y	37	77	222	26	54	158
	Morbidity, ED_{50} (Gy)			**Morbidity, Threshold (Gy)**		
WG Pu, Class W	9	19	54	6	14	38
WG Pu, Class Y	26	54	151	18	38	107

The ratios of the adjusted-dose LD_{50} (or ED_{50}) to the corresponding absorbed-dose LD_{50} (or ED_{50}) in Tables 3 and 4 are about 20 for the minima, 12 for the medians, and 5 for the maxima, which are the same as the range of RBEs. This accounts for the shape of the LD_{50} or ED_{50} distributions when expressed as absorbed doses – the distributions are skewed toward the lower values because absorbed dose is adjusted dose divided by the RBE, the larger values of RBE producing the smaller absorbed doses. This method of obtaining absorbed doses is, however, only of value when the low-LET component of the dose is negligible, as is the case here. Results in Table 4 are somewhat higher than would be expected based on new data from studies in which dogs briefly inhaled $^{239}PuO_2$ and were followed for about 12 y (Hahn et al. 1999; Muggenburg et al. 1999). The dog data suggest an LD_{50} on the order of 40 Gy and a threshold for lethality from radiation pneumonitis on the order of 6 Gy for Class Y sources.

A key finding in this study is that alpha-radiation dose-rate history could be very important related to the induction of deterministic effects in the lungs. Soluble forms of WG Pu would be expected to translocate from the lung to bone and liver faster than insoluble forms. Thus, dose rate to the lung will decrease faster for soluble than insoluble forms of WG Pu. To have enough radiation dose to produce deterministic effects, initial dose rates will need to be relatively high compared to insoluble forms of WG Pu; that is, the intake of the soluble form

would have to be higher than the insoluble form to give the same risk. The higher dose rates (on average) from the more soluble forms of WG Pu will lead to higher normalized doses X and higher risks than for insoluble forms of WG Pu. This can be seen from medians presented in Table 4 by comparing numbers for solubility class W with those for solubility class Y; the LD_{50} and ED_{50} values are smaller for class W than for class Y. These findings apply only to brief, single inhalation intake. For chronic intake, the situation is more complex.

The risk distributions for deterministic effects in the lung from inhaled WG Pu (solubility classes W and Y), as calculated in the MC simulations are shown in Figs. 3-6 for a polydisperse size distribution with AMAD = 5 μm and σ_g = 2.5. Again, the results apply to a brief, single inhalation intake. Some of the curves in these figures are not obvious because they coincide with the abscissa or ordinate axis. The curves presented in Figs. 3-6 are for fixed intakes (i.e., isointake) of WG Pu. These curves can be understood based on the explanations that follow related to Fig. 3.

The top three curves in Fig. 3 represent computational risk distributions for the fixed intakes of 5, 7, and 10 mg of WG Pu. Risk (as indicated on the horizontal axis) represents a given value for a risk estimate for lethality obtained from our many MC iterations. For the top three curves in Fig. 3, a risk of zero was obtained about 95% of the time (see where curves intersect the vertical axis) for the fixed intakes considered. This indicates that the actual risk is probably very small and likely zero. For the three indicated curves, the central risk estimate (median of the risk distribution) is zero. For a 20-mg intake (fifth curve from the top), about 70% of the risk estimates obtained with the MC simulations were less than 0.2. This can be seen by selecting a risk of 0.2 on the horizontal axis and reading the corresponding value on the vertical axis for the 20-mg curve. The value is approximately 70%.

The curves in Figs. 3-6 show the large variability in the risk estimates associated with a given intake of WG Pu. This variability reflects the large uncertainty associated with the NUREG/CR-4214 risk models used. The 50th percentile (i.e., median) risks are considered central estimates as previously indicated. As an example, for a polydisperse distribution with the AMAD = 5 μm and σ_g = 2.5, the central estimate of risk for lethality from inhaled WG Pu, Class W for an intake of 30 mg is 0.45. Forty-five percent of the people with this intake would be expected to die within 5 y, whereas that for 50 mg, it is 1.0 (no survivors expected), and for 10 mg it is 0.0 (no deaths expected). For serious injury (morbidity), the central estimate of risk for an intake of 30 mg is 0.97 (97% of the people would be expected to suffer from serious lung injury), whereas for a 50-mg intake, it is 1.0, and for 20 mg it is 0.366. However, based on results presented later, the NUREG/CR-4214 model used to generate these results may need to be revised in light of newly available data on radiation deterministic effects.

For purposes of risk comparisons, the inhalation intakes that yield the 50th percentile risks of 0.5 are shown in Table 5. Results presented are specific for the exposure scenario considered. Similar evaluations could be carried out for nuclear terrorism incidents involving WG Pu or other radioactive materials.

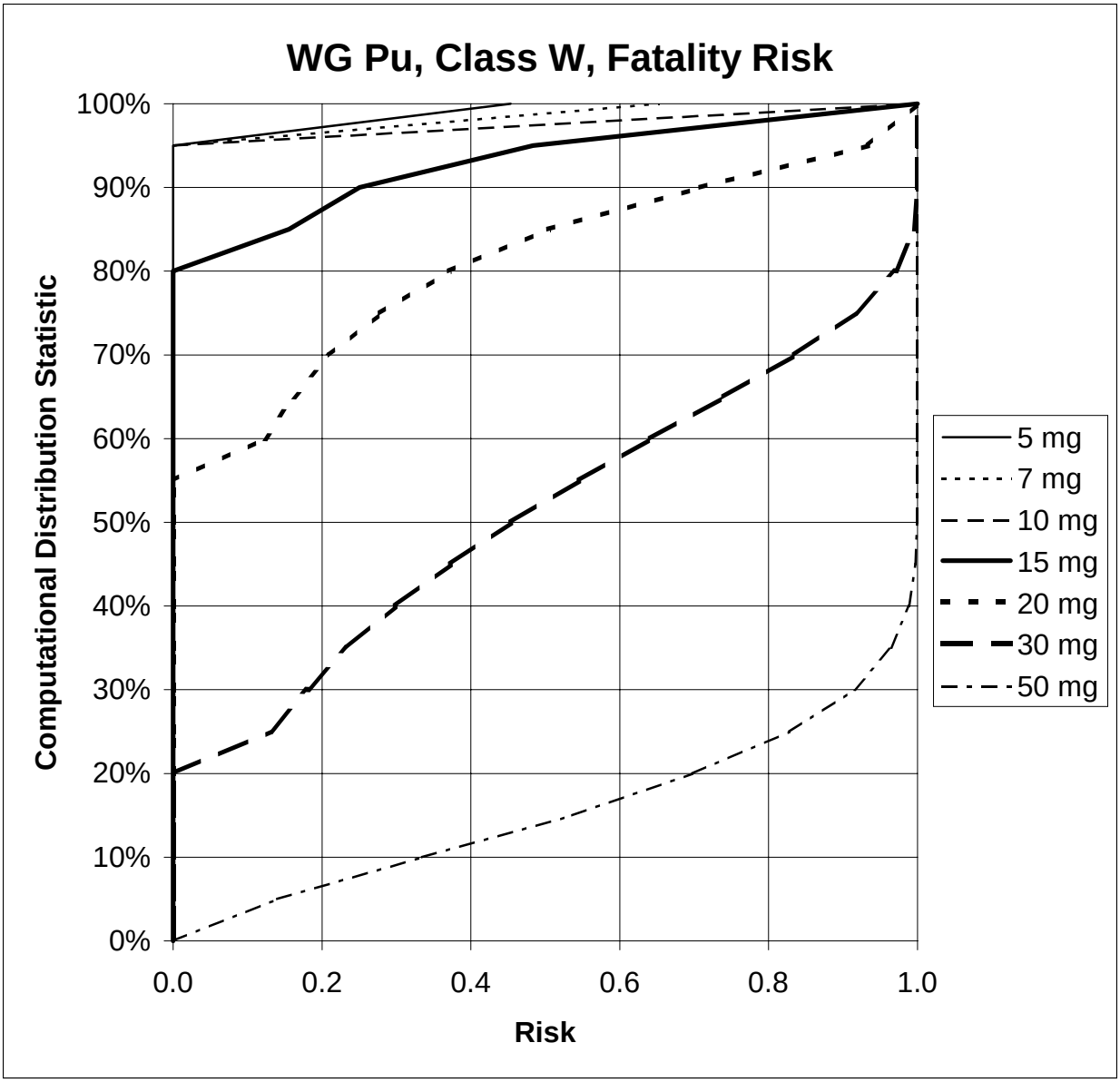

Fig. 3. Computational distribution statistic for the risk of lethality for specific inhalation intakes (5 to 50 mg) of polydisperse WG Pu (Class W) particles with AMAD = 5 μm and σ_g = 2.5.

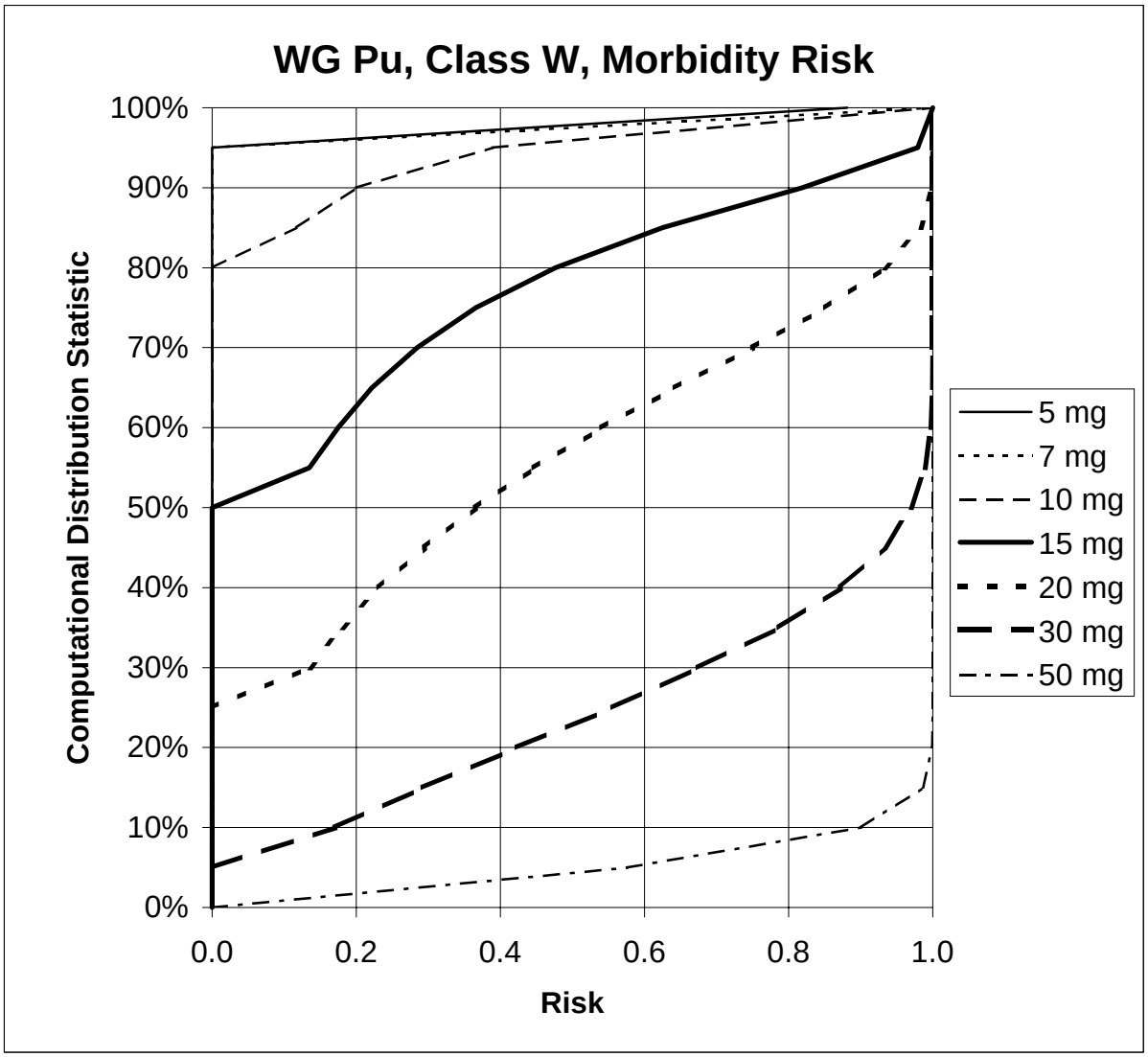

Fig. 4. Computational distribution statistic for the risk of morbidity for specific inhalation intakes (5 to 50 mg) of polydisperse WG Pu (Class W) particles with AMAD = 5 μm and σ_g = 2.5.

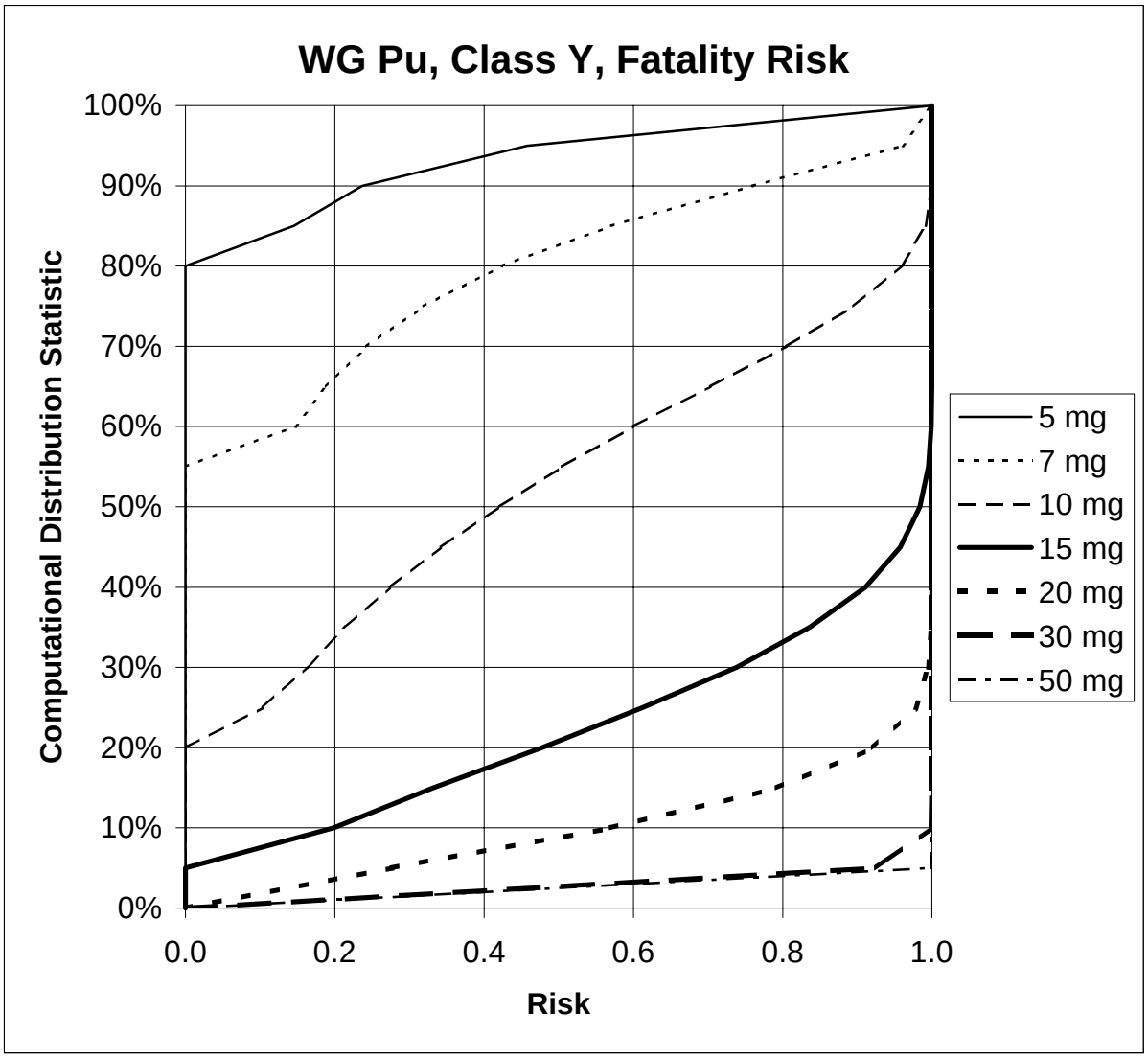

Fig. 5. Computational distribution statistic for the risk of lethality for specific inhalation intakes (5 to 50 mg) of polydisperse WG Pu (Class Y) particles with AMAD = 5 μm and σ_g = 2.5.

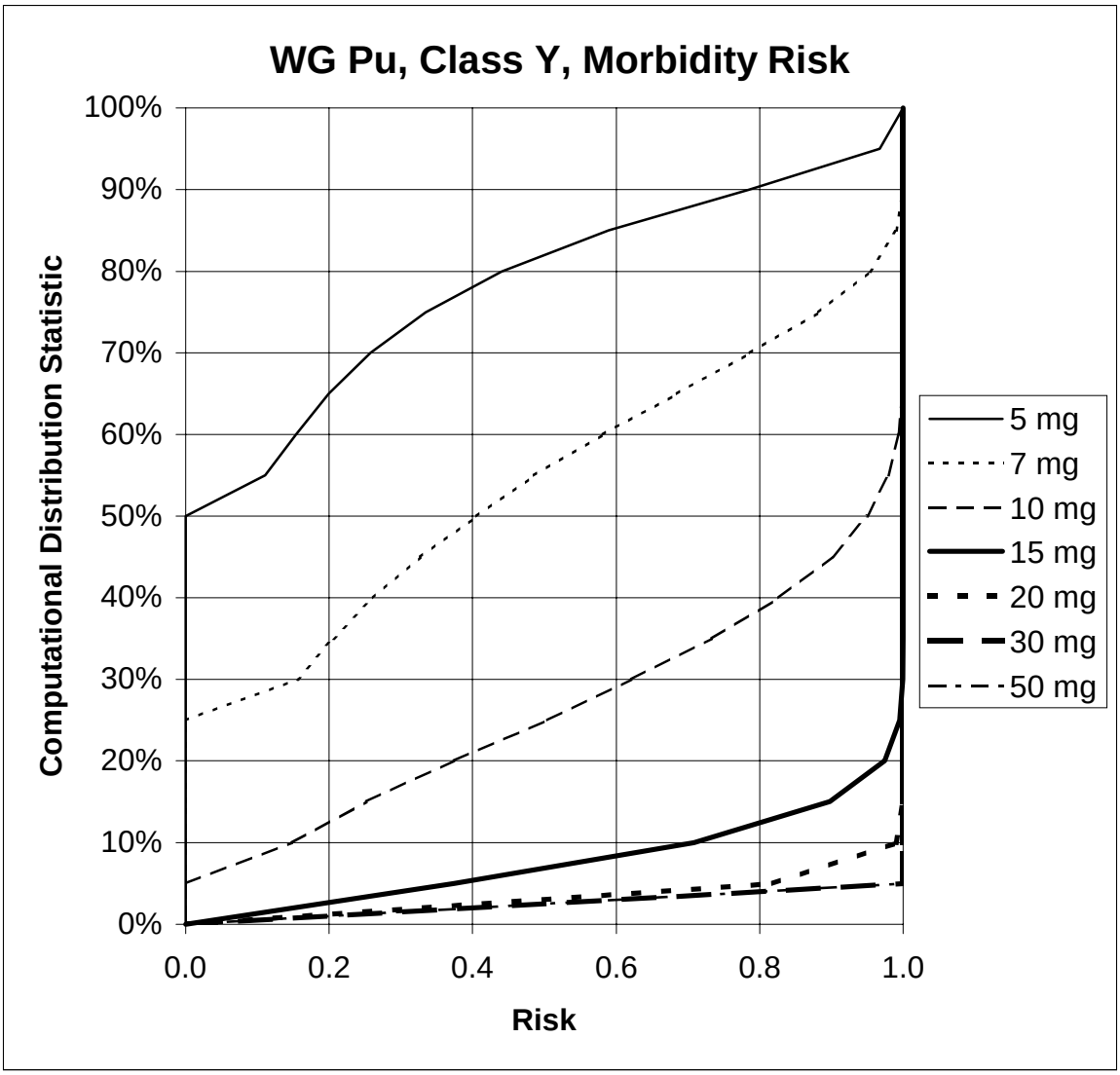

Fig. 6. Computational distribution statistic for the risk of morbidity for specific inhalation intakes (5 to 50 mg) of polydisperse WG Pu (Class Y) particles with AMAD = 5 μm and σ_g = 2.5.

Table 5. Inhalation intakes (mg) corresponding to 50th percentile risks of 0.5 for lethality or morbidity.

Isotopic Mix / Class	Lethality	Morbidity
WG Pu, Class W, 1-μm monodisperse	12	8.2
WG Pu, Class Y, 1-μm monodisperse	4	2.8
WG Pu, Class W, 5-μm polydisperse	31	22
WG Pu, Class Y, 5-μm polydisperse	11	7.5

The DCFs used in these analyses were taken – the ICRP-30 database. The ICRP-30 doses are averaged over the lung. This is more relevant to our study of deterministic effects than doses developed in ICRP 66. In that report, absorbed doses are averaged over a tissue volume appropriate for stochastic but inappropriate for deterministic effects.

Results obtained for morbidity risk are based on models developed largely with data from animal studies that involved 450 to 1,100 d follow-up after briefly inhaling radioactive aerosols. Animal (dog) data are now available for much longer follow-up (to about 6,000 d) after brief inhalation exposure to $^{238}PuO_2$ (Muggenburg et al. 1996). Surprisingly, these data show the occurrence of high numbers of cases of pulmonary fibrosis for follow-up times in excess of about 1,100 d. Not only was fibrosis reported for dogs with lung doses less than 2 Gy, but also for a large proportion of the controls. This suggests that the late-occurring fibrosis may not have been caused by radiation but rather by particle loading in the lungs. This means that morbidity risks based on NUREG/CR-4214 models (which are based on respiratory function data) may be highly unreliable in light of these new data. It is plausible that the NUREG/CR-4214 models for respiratory dysfunction may accurately reflect radiation-associated risks but not account for total risks associated with inhaled particles. New animal data are also now available for 12-y follow-up of dogs that briefly inhaled $^{239}PuO_2$ Muggenburg et al. 1999; Hahn et al. 1999). However, LD_{50} and ED_{50} estimates developed here based on the NUREG/CR-4214 risk models are somewhat higher than would be expected based on the new data. In addition, morbidity and lethality data are now available for humans (Mayak workers) that inhaled soluble and insoluble forms of ^{239}Pu. These data should be used in testing the NUREG/CR-4214 morbidity and lethality risk models and for investigating the possibility that late-occurring fibrosis (and possibly other effects) could arise from a non-radiation-related cause (namely deposition of metal [Pu] in the lung).

The results in Table 5 can be used as the basis for identifying hazards to Pu workers. For an inhalation intake of > 10 mg of WG Pu, the worker would be at considerable risk for radiation deterministic effects within a few years if there were no medical intervention. Death from radiation pneumonitis is also considered highly likely without medical intervention. For intakes from 1 to 10 mg, death from radiation pneumonitis is possible, and respiratory dysfunction is considered highly likely without medical intervention. For intakes < 1 mg, death from radiation pneumonitis is considered unlikely.

In obtaining the indicated results, dose uncertainty was not considered. Further, the NUREG/CR-4214 models that were used to conduct these evaluations were developed at a time where little information was available about Pu health effects based on actual human exposures, and only limited data were available from animal studies for long-term follow-up (> 5 y). Now it is known that thousands of nuclear workers in Russia were exposed via inhalation to ^{239}Pu at the Mayak Pu Facility. Health-effects data for these workers should be used to further evaluate the validity of the NUREG/CR-4214 models presented here. New data from animal studies also suggest that late-occurring fibrosis could arise simply from metal deposition in the lung (Muggenburg et al. 1996). If so, considering fibrosis to be a deterministic effect, it is important to consider that deterministic effects could be observed at low radiation doses after inhaling high-density WG Pu metal. This may explain the observations of pneumosclerosis in Mayak workers that received alpha-radiation doses to the lung of less than 4 Gy (Okladnikova et al. 1994).

Summary and Conclusions

We have generated risk distributions for deterministic radiation effects in the lung of nuclear workers from inhaled WG Pu particles (standard isotopic mix). These distributions were developed using NUREG/CR-4214 risk models and time-dependent DCF data based on Publication 30 of the ICRP. DCFs based on ICRP Publication 30 are more relevant to deterministic effects than are the DCFs based on ICRP Publication 66, which relate to targets for stochastic effects. Results presented apply to single inhalation intakes but not chronic intakes.

Risks were evaluated for both lethality (from radiation pneumonitis) and morbidity (due to radiation-induced respiratory dysfunction) and were found to depend strongly on absorbed-dose-rate history (which depends on WG Pu solubility). Risk distributions that account for NUREG/CR-4214 parameter and model uncertainties were generated using the MC method. Dose variability/uncertainty, however, was not addressed. Central risk estimates were based on the 50th percentiles of the risk distributions. Evaluations were carried out for 1- to 10-μm monodisperse and for polydisperse WG Pu particles for solubility classes W and Y. The risks were evaluated based on pulmonary region absorbed doses (5-y doses).

Central estimates of the median effective (ED50 for respiratory dysfunction) and median lethal (LD50 for pulmonary-mode death) absorbed doses to the P region for solubility class W are 19 and 28 Gy, respectively. Central estimates of corresponding absorbed dose thresholds are 14 and 19 Gy, respectively, for solubility class W. The LD_{50} and associated dose threshold estimates for solubility class W are consistent with absorbed doses reported to cause death from radiation pneumonitis in dogs that inhaled $^{238}PuO_2$ and were followed for about 5 y. For solubility class Y, central estimates of the ED_{50} and LD_{50} are 54 and 77 Gy, respectively; the corresponding central estimates for thresholds are 38 and 54 Gy, respectively. The central estimates of LD_{50} and associated threshold doses for solubility class Y are somewhat higher than would be expected based on recently reported observations in dogs that briefly inhaled $^{239}PuO_2$ and were then followed for about 12 y. In addition, central estimates of the ED_{50} and associated threshold for solubility classes W and Y are greater by a factor of 10 or more than alpha radiation doses reported to cause pneumosclerosis (interpreted to be radiation pneumonitis and pulmonary fibrosis) in Russian Mayak workers that inhaled large amounts of $^{239}Pu/^{241}Am$ over many years during the Cold War. The Mayak workers were, however, also exposed to gamma rays, which needs to be considered.

The NUREG/CR-4214 model parameters are largely based on animal data that were available at the time the models were developed. These data included follow-up times from 1.5 to about 3 y after inhalation exposure to radioactive aerosols. Our findings suggests that NUREG/CR-4214 models for assessing lethality risk from inhaled radionuclides may need some modest revision in light of newly available data from animal, epidemiological, and clinical studies. However, for assessing morbidity risks, major revisions may be needed in light of these data.

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References

Chanin, D. I.; Sprung, J. L.; Ritchie, L. T.; Jow, H-N., MELCOR Accident Consequence Code System (MACCS), User's Guide, NUREG/CR-4691, SAND86-1562, Vol. 1, Sandia National Laboratories, Albuquerque, NM, 87185, February 1990.

Commission of European Communities; U.S. Nuclear Regulatory Commission (CEC/USNRC). Probabilistic accident consequence uncertainty analysis. Early health effects uncertainty assessment. Luxembourg: Report NUREG/CR-6545 EUR-16775 SAND97-2689; Expert B; pp. C-31 – C-60; 1997.

Decisionerring Inc., Crystal Ball 2000, 1515 Arapahoe Street, Suite 1311, Denver, CO 80202, 2000.

Gilbert, E. S.; Koshurnikova, N. A.; Sokolnikov, M.; Khokhryakov, V. F.; Miller, S.; Preston, D. L.; Romanov, S. A.; Shilnikova, N. S.; Suslova, K. G.; Vostrotin, V. V. Liver cancer in Mayak workers. Radiat. Res. 154:246-252; 2000.

Grogan, H. A.; Sinclair, W. K. ; Vollequé, P. G. Risks of fatal cancer from inhalation of ^{239,240}Pu by humans: A combined four-method approach with uncertainty evaluation. Health Phys. 80(5):447-461; 2001.

Hahn, F. F.; Muggenburg, B. A.; Guilmette, R. A.; Boecker, B. B. Comparative stochastic effects of inhaled alpha- and beta-particle-emitting radionuclides in Beagle dogs. Radiat. Res. 152:S19-S22; 1999.

International Commission on Radiological Protection (ICRP). Age-dependent doses to members of the public from intake of radionuclides: Part 4—inhalation dose coefficients. Elmsford, NY: International Commission on Radiological Protection; ICRP Publication 71; 1995.

International Commission on Radiological Protection (ICRP). Human respiratory tract model for radiological protection. Oxford:Pergamon Press: ICRP Publication 66; 1994.

International Commission on Radiological Protection (ICRP). Limits for intakes of radionuclides by workers. Oxford: Pergamon; ICRP Publication 30; 1979.

International Commission on Radiological Protection (ICRP). Report of the Task Group on Reference Man. Oxford: ICRP Publication 23, 1975.

Khokhryakov, V. F.; Kellerer, A. M.; Kreisheimer, M.; Romanov, S. A. Lung cancer in nuclear workers of Mayak. Radiat. Environ. Biophys. 37:11-17; 1998.Khokhryakov, V. F.; Romanov, S. A. Lung cancer in radiochemical industry workers. Sci. Total Environ.142:25-28; 1994.

Koshurnikova, N. A.; Gilbert, E. S; Sokolnikov, M., Khrokhryakov, V. F.; Miller, S.; Preston, D. L.; Romanov, S. A.; Shilnikova, N. S.; Suslova, K. G.; Vostrotin, V. V. Bone cancer in Mayak workers. Radiat. Res. 154:237-245; 2000.

Kreisheimer, M.; Koshurnikova, N. A.; Nekolla, E.; Khokhryakov, V. F.; Romanov, S. A.; Sokolnikov, M. E.; Shilnikova, N. S.; Okatenko, P. V.; Kellerer, A. M. Lung cancer mortality among male nuclear workers of the Mayak facilities in the former Soviet Union. Radiat. Res. 154:3-11; 2000.

Muggenburg, B. A.; Guilmette, R. A. ; Mewhinney, J. A. ; Gillett, N. A. Mauderly, J. L.; Griffith, W. C.; Diel, J. H.; Scott, B. R.; Hahn, F. F.; Boecker, B. B. Toxicity of inhaled plutonium dioxide in Beagle dogs. Radiat. Res. 145:361-381; 1996.

Muggenburg, B. A.; Hahn, F. F.; Ménache, M. G., Guilmette, R. A.; Boecker, B. B. Comparative deterministic effects of inhaled, insoluble alpha- and beta-particle-emitting radionuclides in dogs. Radiat. Res. 152:S23-S26; 1999.

National Research Council/National Academy of Science. Health risks of radon and other internally deposited alpha-emitters. BEIR- IV. National Academy Press, 1988.

Okladnikova, N.D.; Pesternikova, V. S.; Sumina, M. V.; Doshchenko, V. N. Occupational diseases from radiation exposure at the first nuclear plant in the USSR. Sci. Total Environ. 142:9-17; 1994.

Scott, B. R.; Hahn, F. F.; McClellan, R. O.; Seiler, F. A. Risk estimators for radiation-induced bone marrow syndrome lethality in humans. Risk Anal. 8:393-402; 1988.

Scott, B. R.; Hahn, F. F.; Snipes, M. B; Newton, G. J.; Eidson, A. F.; Mauderly, J. L.; Boecker, B. B. Predicted and observed early effects of combined alpha and beta lung irradiation. Health Phys. 59:791-805; 1990.

Tokarskaya, Z. B.; Okladnikova, N. D.; Belyaeva, Z. D.; Drozhko E. G. Multifactorial analysis of lung cancer dose-response relationships for workers at the Mayak nuclear enterprise. Health Phys. 73:899–905; 1997.

Tokarskaya, Z. B.; Okladnikova, N. D.; Belyaeva, Z. D.; Drozhko, E. G. The influence of radiation and nonradiation factors on the lung cancer incidence among the workers of the nuclear enterprise Mayak. Health Phys. 69:356–366; 1995.

U.S. Department of Energy (DOE), Guidance for Preparation of DOE-5480.22 (TSR) and DOE 5480.23 (SAR) Implementation Plans, DOE-STD-3011-94, U.S. Department of Energy, Washington, DC; 1994.

U.S. Nuclear Regulatory Commission (USNRC). Health effects models for nuclear power plant accident consequence analysis. Part I: Introduction, integration, and summary. Washington, DC: Report NUREG/CR-4214 ITRI-141 Rev. 2 Part I; 1993a.

U.S. Nuclear Regulatory Commission (USNRC). Health effects models for nuclear power plant accident consequence analysis. Modifications of models resulting from addition of effects of exposure to alpha-emitting radionuclides. Part II: Scientific bases for health effects models. Washington, DC: Report NUREG/CR-4214 LMF-136 Rev. 1 Part II Addendum 2; 1993b.

U.S. Nuclear Regulatory Commission (USNRC). Health effects models for nuclear power plant accident consequence analysis. Low LET radiation. Part I: Introduction, integration, and summary. Washington, DC: Report NUREG/CR-4214 SAND85-7185 Rev. 1 Part I; 1990.

U.S. Nuclear Regulatory Commission (USNRC). Health effects models for nuclear power plant accident consequence analysis. Low LET radiation. Part II: Scientific basis for health effects models. Washington, DC: Report NUREG/CR-4214 Rev. 1 Part II; 1989.

U.S. Environmental Protection Agency (EPA). Limiting values of radionuclide intake and air concentration and dose conversion factors for inhalation, submersion, and ingestion. Washington, DC: Report EPA-5201/1-88-020; 1988.

Voelz, G. L.; Buican, I. G. Plutonium and health—how great is the risk? Los Alamos Science 26:74-89; 2000.