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**Probabilistic Accident
Consequence Uncertainty Analysis**

Early Health Effects Uncertainty Assessment

Appendices

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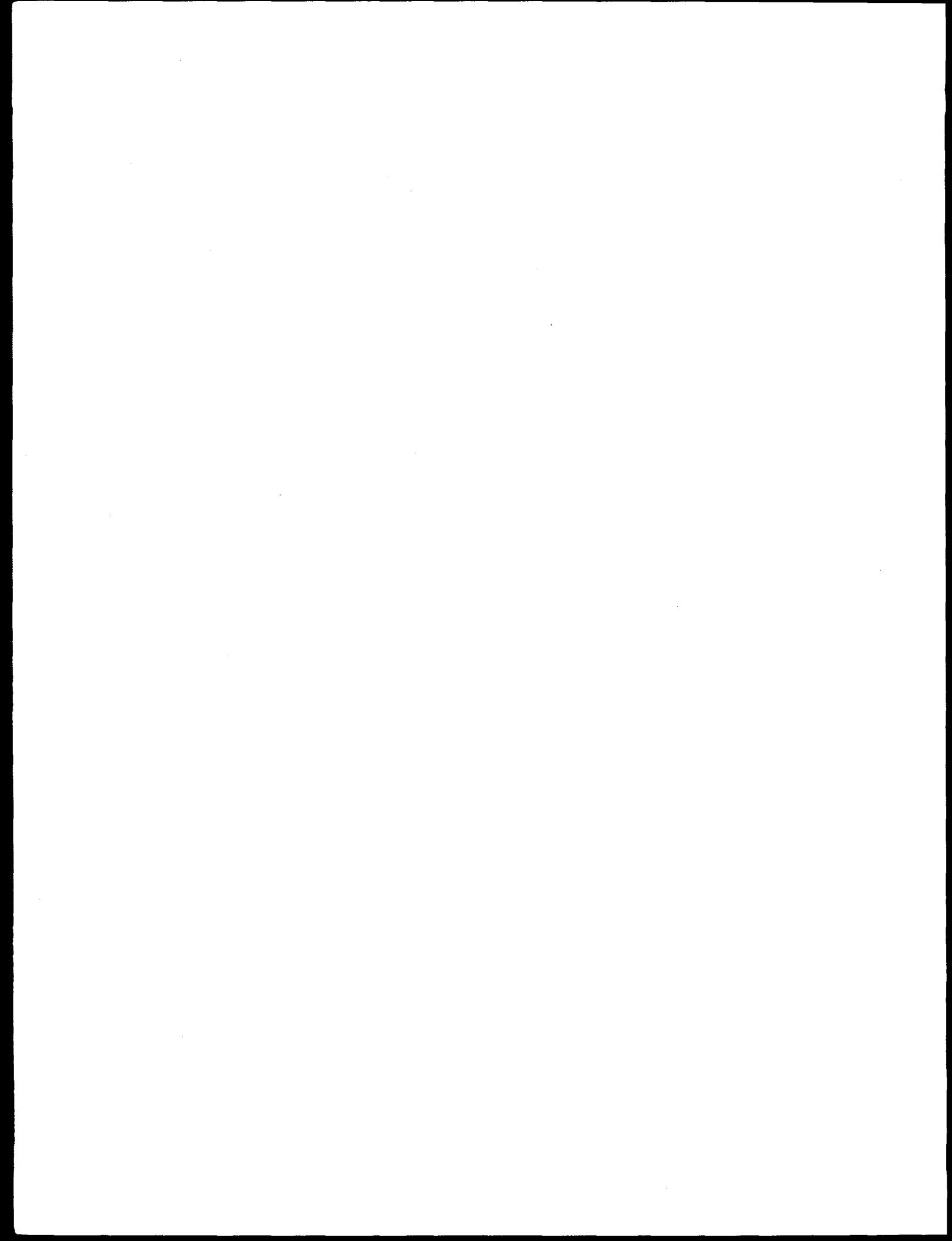
Abstract

The development of two new probabilistic accident consequence codes, MACCS and COSYMA, was completed in 1990. These codes estimate the risks presented by nuclear installations based on postulated frequencies and magnitudes of potential accidents. In 1991, the US Nuclear Regulatory Commission (NRC) and the European Commission (EC) began a joint uncertainty analysis of the two codes. The ultimate objective was to develop credible and traceable uncertainty distributions for the input variables of the codes.

The study was formulated jointly and was limited to the current code models and to physical quantities that could be measured in experiments. An elicitation procedure was devised from previous US and EC studies with refinements based on recent experience. Elicitation questions were developed, tested, and clarified. Internationally recognized experts were selected using a common set of criteria. Probability training exercises were conducted to establish ground rules and set the initial and boundary conditions. Experts developed their distributions independently.

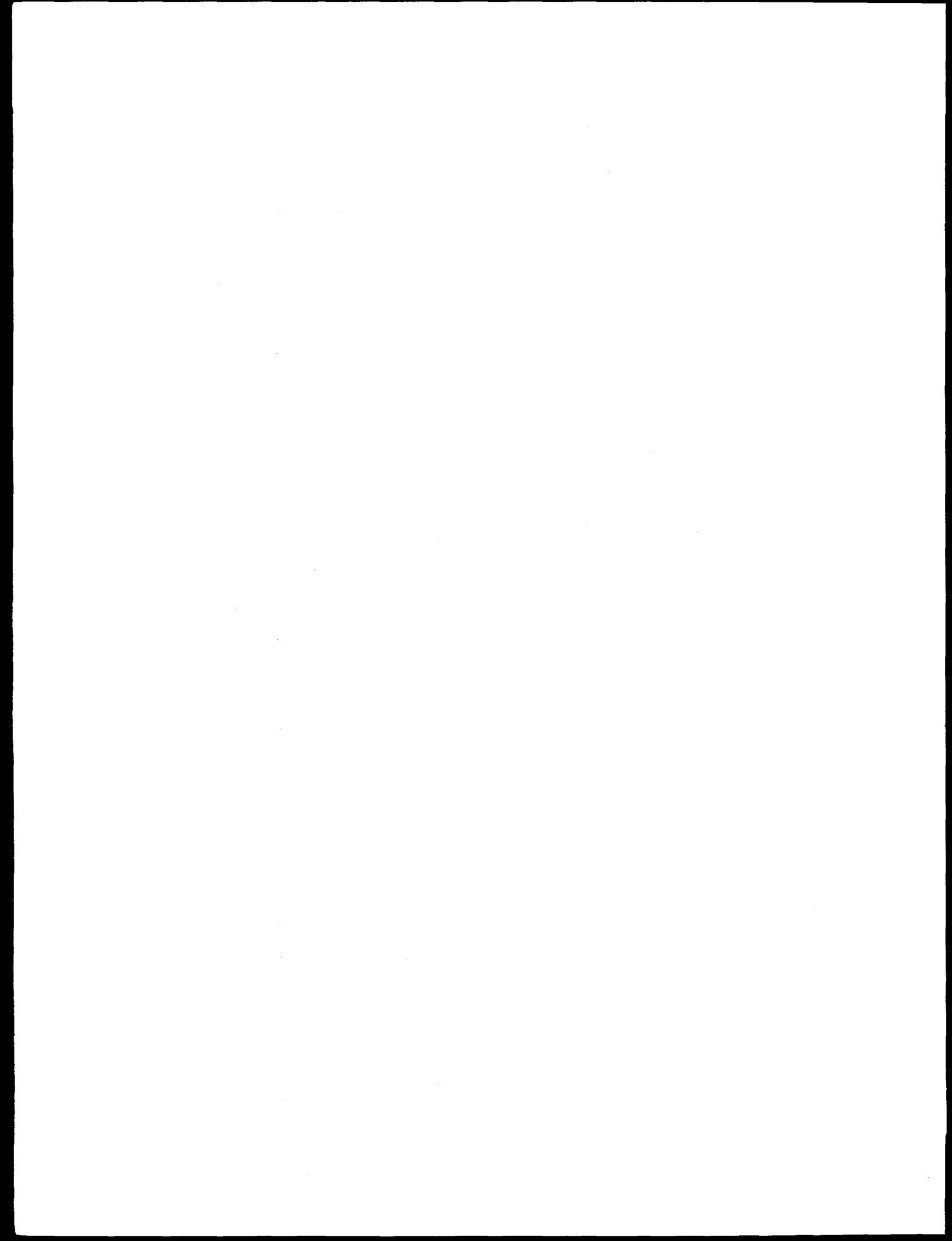
After the first feasibility study on atmospheric dispersion and deposition parameters, further expert judgment exercises were carried out. This report is on the early health effects part of the study. The goal again was to develop a library of uncertainty distributions for the selected consequence parameters. Nine experts were selected for the early health effects panel. Their results were processed with an equal-weighting aggregation method, and the aggregated distributions will be processed into the code input variables of the early health effects in COSYMA and MACCS.

Further expert judgment studies are being undertaken to examine the uncertainty in other aspects of probabilistic accident consequence codes. Finally, the uncertainties will be propagated through the codes and the uncertainty in the code predictions will be quantified.



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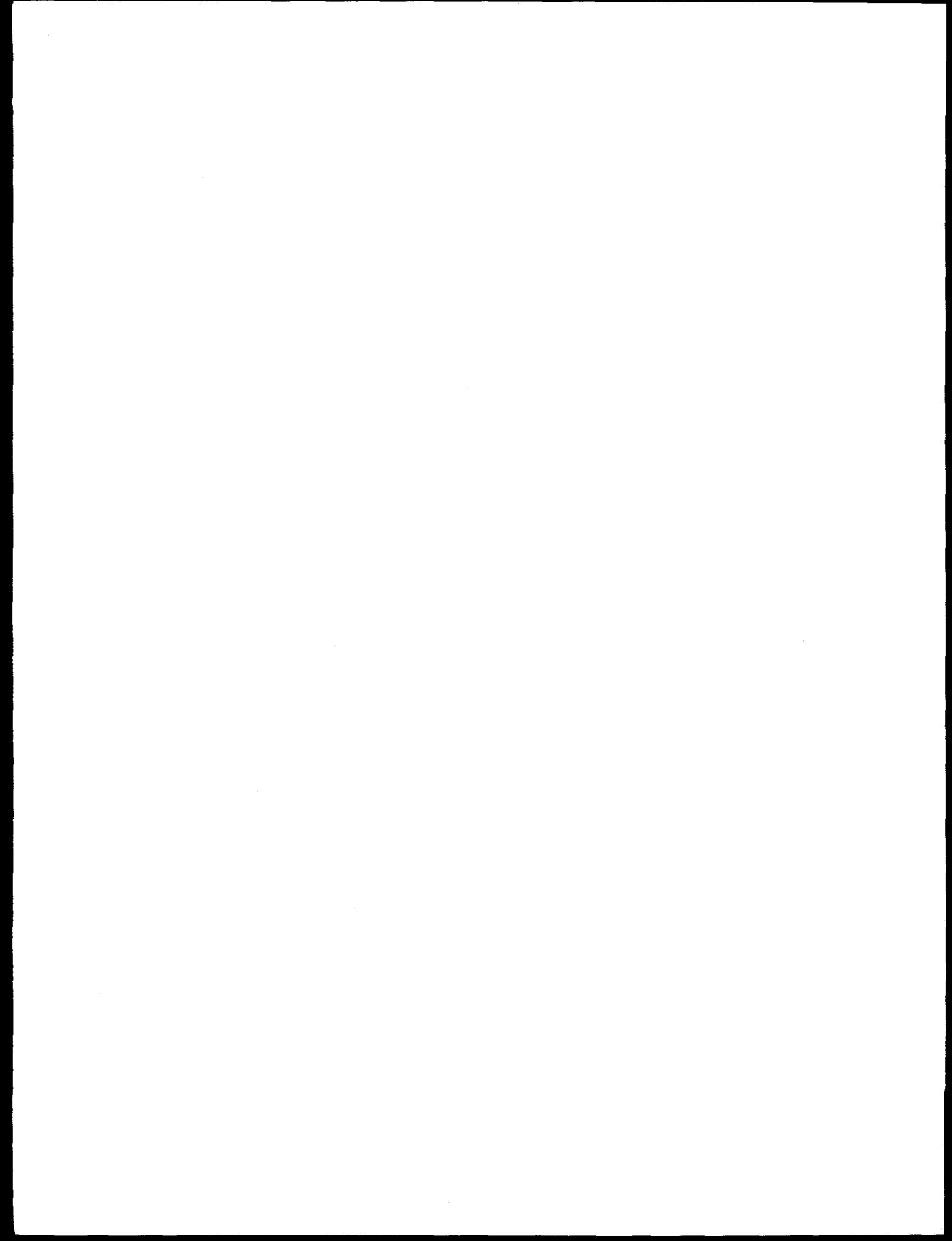
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Preface

This volume is the second of a two-volume document that summarizes a joint project conducted by the US Nuclear Regulatory Commission and the European Commission to assess uncertainties in the MACCS and COSYMA probabilistic accident consequence codes. These codes were developed primarily for estimating the risks presented by nuclear reactors based on postulated frequencies and magnitudes of potential accidents. This document reports on an ongoing project to assess uncertainty in the MACCS and COSYMA calculations for the offsite consequences of radionuclide releases by hypothetical nuclear power plant accidents. A panel of nine experts was formed to compile credible and traceable uncertainty distributions for the early health effects variables that affect calculations of offsite consequences. The expert judgment elicitation procedure and its outcomes are described in these volumes. Other panels were formed to consider uncertainty in other aspects of the codes. Their results are described in companion reports.

Volume 1 contains background information and a complete description of the joint consequence uncertainty study along with a summary of the results of this aspect of the study. Volume 2 contains appendices that include (1) a summary of the MACCS and COSYMA consequence codes, (2) the elicitation questionnaires and case structures, (3) the rationales and results for the panel on early health effects, (4) short biographies of the experts, and (5) the aggregated results of their responses.



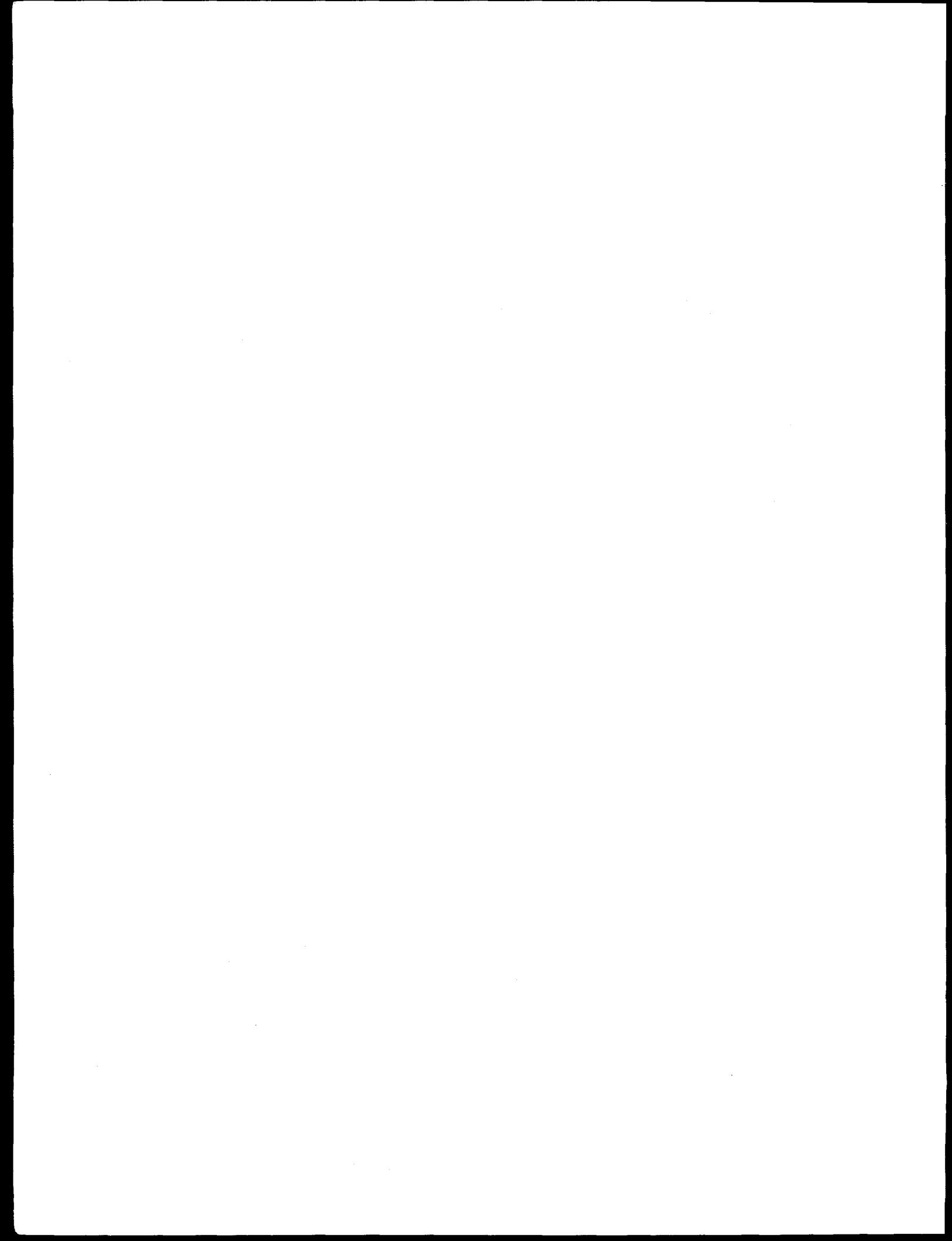
Acknowledgments

The authors would like to acknowledge all the participants in the expert judgment elicitation process, in particular the expert panel on early health effects. While we organized the process, processed the results, and wrote and edited the report, the experts provided the technical content that is the foundation of this report. Dr. Steven C. Hora and Dr. Detlof von Winterfeldt are acknowledged for their contributions as elicitors.

We would like to acknowledge several institutes that facilitated the collection of unpublished experimental information used in the probabilistic training and evaluation of the experts. In particular we want to thank Prof. Th. Fliedner and co-workers at the University of Ulm in Germany. We also want to thank Dr. Hermans and Dr. Kal for their support of Dr. Broerse's assessments and rationale.

We also greatly appreciate the technical assistance of Ms. Ina Bos of Delft University of Technology, The Netherlands; the editorial help of Ruth Haas and Sally Kmetz at Tech Reps, the support of Judy Jones at Sandia National Laboratories, and the guidance provided by Ms. Reeta Garber of Sandia National Laboratories in preparing this report.

On Monday January 22, 1996, Peter Roelofsen, manager of the risk analysis group at the Netherlands Energy Research Foundation (ECN), died after a long period of illness. Peter prepared the first discussion documents for the early health effects expert panel, and provided valuable comments on early versions of the documents on deposited materials and related doses. He will be missed by the project staff, and in particular by the staff at ECN.

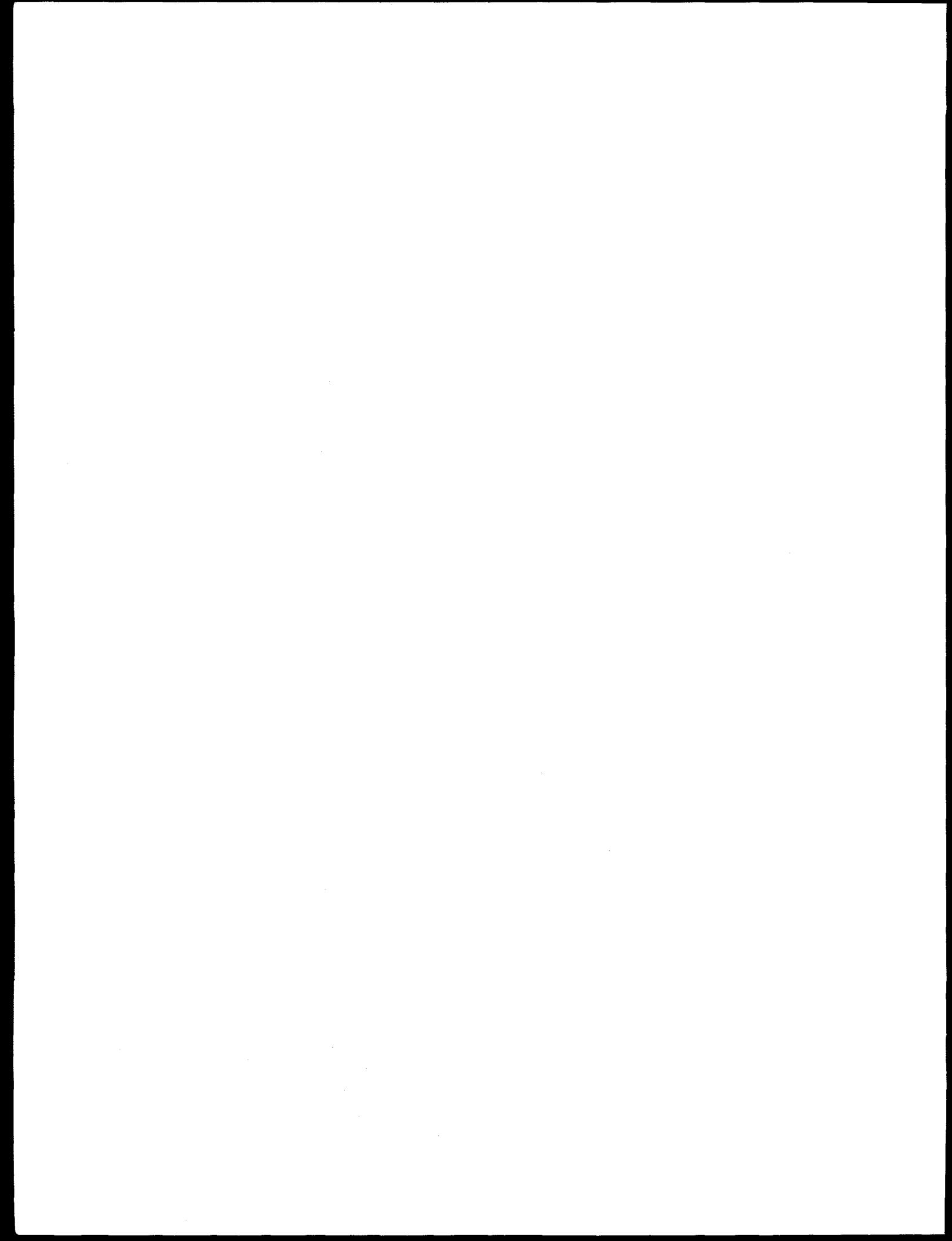


List of Acronyms

ARD	acute radiation disease
ARS	acute radiation sickness
BMS	bone marrow syndrome
CNS	central nervous system
DDREF	dose and dose rate effectiveness factor
DREF	dose rate effectiveness factor
ERR	excess relative risk
IAEA	International Atomic Energy Agency
IS	intestinal syndrome
LRSI	local radiation skin injuries
LSS	Life Span Study
OPS	oropharyngeal syndrome
RB	radiation burns
RBE	relative biological effectiveness
TBI	whole-body irradiation
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation

APPENDIX A

Summary of the MACCS and COSYMA Consequence Codes



Summary of the MACCS and COSYMA Consequence Codes

Introduction

The information developed in this study will be used to perform uncertainty studies using the European Commission (EC) consequence code COSYMA and the US Nuclear Regulatory Commission (USNRC) code MACCS. COSYMA and MACCS model the offsite consequences of postulated severe reactor accidents that release a plume of radioactive material to the atmosphere. These codes model the transport and deposition of radioactive gases and aerosols into the environment and the potential resulting human health and economic consequences. They calculate the health effects, impact of countermeasures and economic costs of the releases. The processes considered in the calculations, and the routes of exposure following accidental releases to atmosphere, are illustrated in Figure A-1. The calculations are divided into a number of steps, illustrated in Figure A-2. COSYMA and MACCS are modular codes, with different modules addressing the different stages of the calculation. However, while Figure A-1 illustrates the steps in the calculation, the modules of the codes do not correspond exactly with the boxes shown.

The following sections give brief descriptions of the COSYMA and MACCS codes.

Brief Description of MACCS and COSYMA Dispersion and Deposition Models

COSYMA and MACCS both employ a Gaussian plume model (GPM) for atmospheric dispersion. At a given downwind distance and given atmospheric conditions, the Gaussian model predicts the time-integrated concentration at various horizontal and vertical displacements from the center-line of the plume. When the plume is not constrained by the ground or the inversion layer, the basic Gaussian plume equation for determining the concentration relative to the release rate is:

$$\frac{\chi}{Q} = \frac{1}{2\pi\sigma_y\sigma_z\bar{U}} \exp\left(-\frac{y^2}{2\sigma_y^2}\right) \exp\left(-\frac{(z-h)^2}{2\sigma_z^2}\right)$$

where:

χ = time-integrated air concentration,

Q = the source strength,

y = the horizontal displacement relative to the plume centerline,

z = the vertical displacement,

h = the vertical height of the plume centerline,

\bar{U} = the average wind velocity, and

σ_y and σ_z are plume expansion parameters.

In MACCS and COSYMA, the plume expansion parameters, σ_y and σ_z , are modeled by the following power law:

$$\sigma_y = a_y x^{b_y}; \sigma_z = a_z x^{b_z}$$

where x = the downwind distance from the plume release point.

Currently, constant values for a_y , b_y and a_z , b_z are provided in the codes. The values for the parameters are determined by the atmospheric stability class and the roughness length of the terrain.

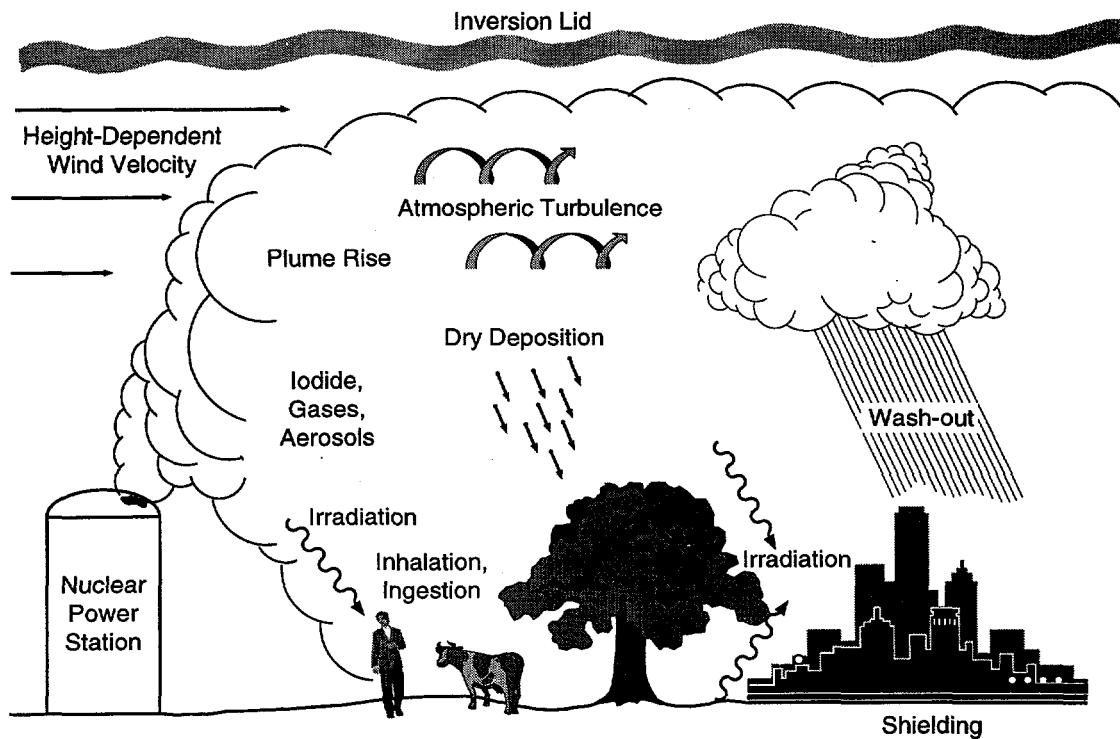
Two types of deposition are modeled in the MACCS and COSYMA codes: wet and dry. Dry deposition incorporates removal from the plume by diffusion, impaction, and settling; it is modeled through a dry deposition velocity, which is a user input. The dry deposition velocity depends on particle size; therefore, if the aerosol size distribution is divided into ranges, a dry deposition velocity must be specified for each range. The washout of radioactive material from the plume, wet deposition, is modeled as dependent on the rain intensity. The fraction of material, f_w , that remains in the plume is given by:

$$f_w = \exp\{-a I^b \Delta t\}$$

where I is the rain intensity and Δt is the amount of time the plume is exposed to the rain. The parameters a and b are the user-specified parameters that determine the amount of material washed from the plume as a result of rain intensity. Rainout, in which droplets nucleate on the aerosol particles, is not modeled.

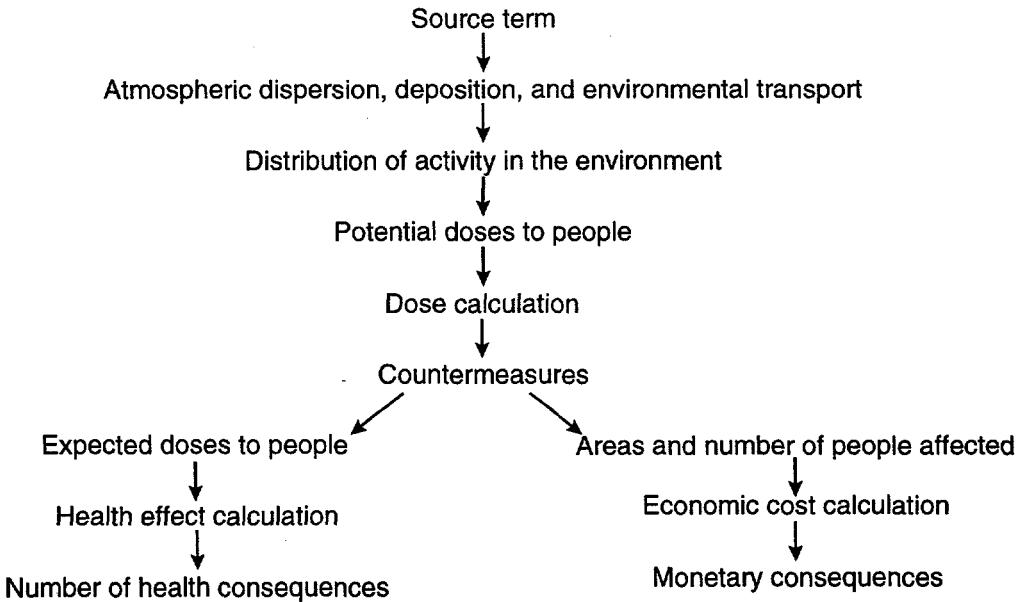
Summary of the MACCS Radiological Consequence Code

The MACCS code was originally developed under NRC sponsorship to estimate the offsite consequences of



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Figure A-1. Dispersion and deposition phenomena considered in an accident consequence analysis.



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Figure A-2. Basic features and relationships of an accident consequence analysis.

potential severe accidents at nuclear power plants by using meteorological data that vary on an hourly basis. The code models the transport and dispersion of plumes of radioactive material released from the facility to the atmosphere. As the plumes travel through the atmosphere, material may be deposited on the ground via wet and dry deposition processes. There are seven pathways through which the general population can be exposed: cloudshine, groundshine, direct inhalation, resuspension inhalation, ingestion of contaminated food, ingestion of contaminated water, and deposition on skin. Emergency response and protective action guides for both the short and long term are also considered as means for mitigating the extent of the exposures. As a final step, the economic costs that would result from the mitigative actions are estimated. Variability in consequences as a result of weather may be obtained in the form of a complementary cumulative distribution function.

MACCS is organized into three modules. The ATMOS module performs the atmospheric transport and deposition portion of the calculation. The EARLY module estimates the consequences of the accident immediately following the incident (usually within the first week), and the CHRONC module estimates the long-term consequences of the accident. A schematic representation of these modules and the input files that provide information to them is shown in Figure A-3. The following sections describe the phenomena modeled in MACCS in more detail.

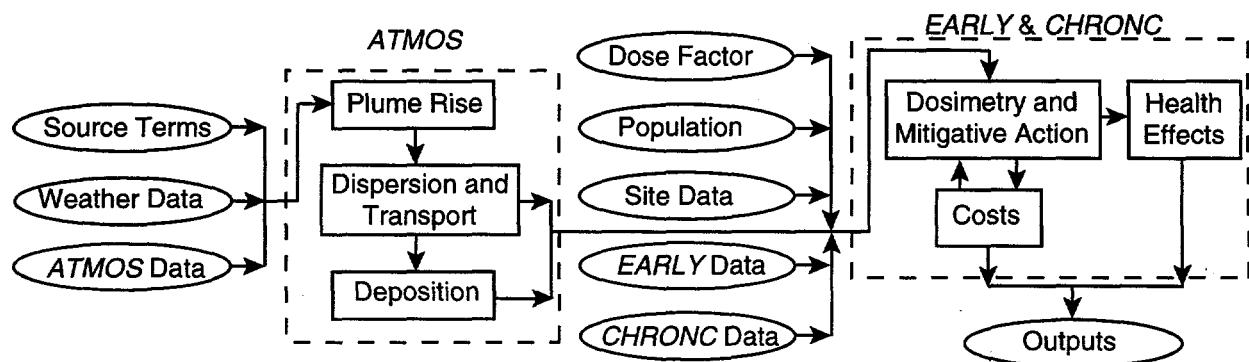
Atmospheric Dispersion and Transport

The release of radioactive materials to the atmosphere can be divided into successive plume segments, which can have different compositions, release times, durations, release

heights, and amounts of sensible heats. The plume segment lengths are determined by the product of the segment's release duration and the average windspeed during release. The initial vertical and horizontal dimensions of each plume segment are user-specified.

A lift-off criterion based on a critical windspeed determines whether or not a plume is subject to buoyant plume rise. Momentum plume rise is not modeled. If the windspeed at release is greater than the critical windspeed, plume rise is prevented.

After release from the facility, windspeed determines the rates at which plume segments transport in the downwind direction, and the wind direction at the time of release determines the direction of travel. MACCS neglects wind trajectories, as do most other consequence codes. Sixteen compass-sector population distributions are assumed to constitute a representative set of downwind exposed populations. The exposure probability of each of the 16 compass-sector population distributions is assumed to be given by the frequency with which the wind blows from the site into the sector. During transport, dispersion of the plume in the vertical and horizontal directions is estimated using an empirical model, the GPM. In this model, dispersion depends on atmospheric stability and windspeed. Horizontal dispersion of the plume segments is unconstrained. However, vertical dispersion is bounded by the ground and by the mixing layer, which are both modeled as totally reflecting layers. A single value for the mixing layer is specified by the user for each season of the year and is constant during a calculation. Eventually the vertical distribution of each plume segment becomes uniform and is so modeled.



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Figure A-3. Progression of a MACCS consequence calculation.

Deposition, Weathering, Resuspension, and Decay

As noted earlier, two types of deposition are modeled in MACCS: wet deposition and dry deposition. Weathering, resuspension, washoff, and radioactive decay decrease the deposited concentrations of radioactive materials. Radioactive decay treats only first generation daughter products.

Weather

Plume rise, dispersion, downwind transport, and deposition depend on the prevailing meteorological conditions. These conditions can be modeled as time-invariant or as varying hour-by-hour. If they are modeled as variable, the user may specify them directly or through an input file.

Dosimetry

The MACCS dosimetry model consists of three interacting processes: (1) the projection of individual exposures to radioactive contamination for each of the seven exposure pathways modeled over a user-specified time, (2) mitigation of these exposures by protective-measure actions, and (3) calculation of the actual exposures incurred after mitigation by protective-measure actions. For each exposure pathway, MACCS models the radiological burden for the pathway as reduced by the actions taken to mitigate that pathway dose. The total dose to an organ is obtained by summing the doses delivered by each of the individual pathways.

Dose Mitigation

The time after accident initiation is divided into three phases: (1) an emergency phase, (2) an optional intermediate phase, and (3) a long-term phase. During the emergency phase, which can last up to seven days, doses are reduced by evacuation, sheltering, and temporary relocation of people. During the intermediate phase, doses may be avoided by temporary relocation of people. During the long-term phase, doses are reduced by decontamination of property that is not habitable, by temporary interdiction of property that cannot be restored to habitability by decontamination alone, by condemnation of property that cannot be restored to habitability at a cost below or equal to the worth of the property, by disposal of contaminated crops, and by banning farming on contaminated farmland.

Exposure Pathways

MACCS models seven exposure pathways: (1) exposure to the passing plume (cloudshine), (2) exposure to materials

deposited on the ground (groundshine), (3) exposure to materials deposited on skin, (4) inhalation of materials directly from the passing plume (inhalation), (5) inhalation of materials resuspended from the ground by natural and mechanical process (resuspension inhalation), (6) ingestion of contaminated foodstuffs (food ingestion), and (7) ingestion of contaminated water (water ingestion). Ingestion doses do not contribute to the doses calculated for the emergency phase of the accident. Only groundshine and inhalation of resuspended materials produce doses during the optional intermediate phase of the accident. Long-term doses are caused by groundshine, resuspension inhalation, water ingestion, and food ingestion. Ingestion of contaminated food or water generates doses to people who reside at unknown locations both on and off of the computational grid.

Population Cohorts

People on the computational grid are assigned to three groups: (1) evacuees, (2) people actively taking shelter, and (3) people who continue normal activities. Shielding factors for each of the groups are specified by the user.

Health Effects

Health effects are calculated from doses to specific organs using dose conversion factors. Early injuries and fatalities (those occurring within one year of the accident) are estimated using nonlinear dose-response models. Latent cancers are estimated using a piecewise linear dose-response model that is discontinuous. Two equations are implemented in the code, one for high exposures and one for low exposures.

Economic Effects

Economic consequences result from the implementation of mitigative actions. The following costs are considered in this estimate: (1) evacuation costs, (2) temporary relocation costs, (3) costs of decontaminating land and buildings, (4) lost return-on-investments from temporarily interdicted properties, (5) value of crops destroyed or not grown, and (6) value of condemned property. Costs associated with damage to the reactor, the purchase of replacement power, medical care, life-shortening, and litigation are not considered.

Summary of COSYMA Radiological Consequence Code

COSYMA was developed by the National Radiological Protection Board (NRPB) of the UK and Forschun-

gszentrum Karlsruhe (FZK) of Germany, as part of the European Commission's MARIA project (FZK and NRPB, 1991). It represents a fusion of ideas from the NRPB program MARC (Hill et al., 1988), the FZK program system UFOMOD (Ehrhardt et al., 1988) and input from other MARIA contractors. The program package was first made available in 1990 for use on mainframe computers, and several updates have been released since then. A PC version was first released in 1993 and has since been updated (Jones et al., 1995).

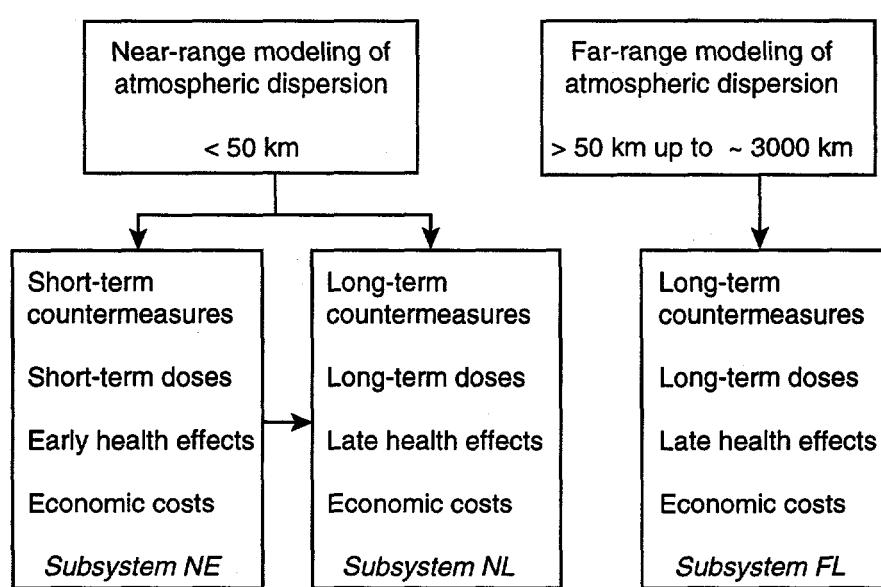
COSYMA is a system of programs and data bases, rather than a single program. The mainframe version contains three main accident consequence assessment programs together with a number of preprocessing and evaluation programs. The three main sub-systems of COSYMA are known as the NE, NL, and FL sub-systems (Figure A-4). The NE (near, early) sub-system is limited to calculating early health effects and the influence of emergency actions to reduce those effects and applies to the region near the accident site. The NL (near, late) subsystem is limited to calculating late health effects and the associated countermeasures, and applies mainly to the region near the site. The FL (far, late) sub-system calculates late health effects and appropriate countermeasures at greater distances from the site. Each of these programs is subdivided into a series of modules for the various steps in the calculation.

PC COSYMA incorporates the NE and NL sub-systems of the mainframe version.

The main endpoints of COSYMA are the numbers of health effects, the impact of countermeasures, and the economic costs resulting from the accidental release. A large number of intermediate results are obtained in the process of calculating the major endpoints; these results include activity concentrations, individual and collective doses, and the countermeasures assumed at different locations. COSYMA contains a series of evaluation programs that allow these results to be presented in a variety of ways.

Following an accidental release to atmosphere, people can be irradiated by a number of exposure paths. Those considered in COSYMA are cloudshine, groundshine, exposure to materials deposited on skin, direct inhalation of plume material, inhalation of resuspended materials, and ingestion of contaminated foods.

COSYMA includes some models directly within the various modules or subsidiary programs, such as atmospheric dispersion models. In other cases, COSYMA uses data libraries giving the results of other models which are not part of COSYMA itself, but whose uncertainty is considered within the current study.



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Figure A-4. General structure of the COSYMA program system.

Atmospheric dispersion and deposition

Mainframe COSYMA contains five different models of atmospheric dispersion that are appropriate for different applications or are based on different assumptions and approximations (Panitz et al., 1989).

The NE and NL sub-system include the MUSEMET (Straka et al., 1981) model, originally written at Forschungsanlage Julich and extensively modified at FZK for use with COSYMA. This is a segmented Gaussian plume model allowing for changes of atmospheric conditions and wind direction during plume travel. This model derives the sequences of atmospheric conditions affecting the plume from hourly averages for wind speed and direction, stability category, precipitation intensity and mixing layer depth. It allows for the effects on the subsequent dispersion of plume rise and buildings near the release point. It also includes the effects of wet and dry deposition of the dispersing material. This model is also included in PC COSYMA.

The NE and NL sub-systems can also be used with the COSGAP or RIMPUFF dispersion models, which are provided as separate programs. COSGAP (Jones and Charles, 1982) is a Gaussian plume dispersion model, which is similar to MUSEMET but does not consider changes of wind direction during plume travel. It is based on the dispersion model in MARC. RIMPUFF (Mikkelsen et al., 1984), developed by Risø National Laboratory, Denmark, is a Gaussian puff trajectory model which derives the atmospheric conditions affecting the plume by interpolating between data from a number of meteorological stations in the region of interest.

The NL sub-system also contains the ISOLA (Hübschmann and Raskob) model for very long release durations. This uses statistics of atmospheric conditions and is only appropriate for releases that are sufficiently small that no countermeasures and no early health effects would be expected.

The FL sub-system is linked to the Mesos model (ApSimon and Goddard, 1983), developed by Imperial College, UK. This is a trajectory model for dispersion over long distances using meteorological data for a large area, such as the whole of Europe.

Accident consequence assessment programs need to consider that the accident could occur in any of a wide range of atmospheric conditions. It is not possible to calculate the consequences for every sequence of conditions that might arise, so a method of sampling a representative set of

conditions from those possible is needed. Both the mainframe and PC versions of COSYMA include a flexible program to conduct this sampling.

Dose calculations

As stated earlier, COSYMA does not include dosimetric models but uses information from data libraries which are calculated with these models. The libraries include information on doses from 197 nuclides.

The data library used for calculating external exposure from activity deposited on the ground contains outdoor doses per unit deposit for a series of times. These doses are mitigated by location factors describing the reduction in exposure due to shielding by buildings. The library is drawn from a number of sources, using results of models developed at NRPB (Charles et al., 1982; Crick and Brown, 1990) and Forschungszentrum für Umwelt und Gesundheit (GSF) (Jacob et al., 1988), Germany. The doses for major contributing nuclides in a fission reactor accident are derived from a model describing the deposition patterns in urban areas and the subsequent transfer of material between the different surfaces.

The doses from internal irradiation following ingestion or inhalation are calculated using data libraries of dose per unit intake derived using models which are consistent with those in International Commission on Radiological Protection (ICRP) publications 56, 67 and 69 (ICRP, 1990, 1994, 1995). COSYMA requires information on the dose received during different periods after the accident, which is included in the data libraries. Because the method used for calculating doses and risks of health effects in the mainframe version of COSYMA allows for the variation of dose per unit intake with age at intake, the libraries contain information on doses for different age groups in the population. The PC version, however, uses a simpler method which considers only the doses to adults.

Food chain models

COSYMA requires information on the concentration of material in foods as a function of time after the accident. It does not include a food chain model, but uses the results of such models through data libraries which give concentrations for a range of radionuclides in a number of foods at a series of times following unit deposition. The concentration of material in foods depends on the time of year at which the deposition occurs. COSYMA uses two data libraries for deposition in summer and in winter.

COSYMA uses libraries derived from the NRPB model FARMLAND (Brown and Simmonds, 1995) and the GSF model ECOSYS (Matthies et al., 1982). The libraries were created using accepted values for the food chain parameters for application within the EC, but differences exist because of other modeling assumptions made and because of the foods considered in each. The foods which can be considered with FARMLAND are: milk; meat and liver from cattle; pork; meat and liver from sheep; green vegetables; grain products; and potatoes and other root vegetables. The foods which can be considered with ECOSYS are: milk; beef; pork; grain products; potatoes and other root vegetables; and leafy and non-leafy green vegetables.

The intakes of these foods are calculated within COSYMA using one of two assumptions about the distribution of food between harvest and consumption. One method assumes that all food consumed is produced locally, and is used in calculating individual ingestion doses. The other method uses information on the amount of food produced in the area of interest, and calculates collective doses on the assumption that all food produced is consumed somewhere.

Countermeasures

COSYMA allows the user to consider the effects of a wide range of countermeasures in reducing the exposure of the population, and gives the user considerable freedom in specifying the criteria at which the actions will be imposed or withdrawn (Hasemann and Ehrhardt, 1994).

Sheltering alone or combined with evacuation may be implemented automatically or on the basis of dose. The distribution of iodine tablets, automatically or on the basis of dose, can also be considered. These actions are assumed to be implemented sufficiently rapidly to reduce the risks of both early and late health effects. Relocation is considered as an action to reduce doses and risks over longer time periods. It can be implemented on a dose criterion, as can return from evacuation or relocation. The effects of decontamination in reducing the period of relocation can be considered. If these actions are initiated on the basis of dose, the user can specify the intervention levels, organs and pathways to be considered, and the time over which the dose is to be integrated. The behavior of the population considered in the dose criteria can also be described using location factors.

Food bans can also be considered (Steinhauer, 1992). They can be implemented or withdrawn on the basis of doses

received within specified time periods or on the basis of the instantaneous concentration of radionuclides in foods.

Health effects

COSYMA considers both early and late health effects in the population, using methods recommended by NRPB (Edwards, pers. comm; NRPB, 1993), the USNRC (Evans et al., 1990) and GSF (Paretzke et al., 1991).

The risk of early health effects is calculated using "hazard functions." The method allows for the variation of risk with the rate at which dose is accumulated over the first few days following the accident. Ten different fatal and non-fatal effects are considered.

The risk of late health effects is calculated using the linear dose response relationship. COSYMA considers the risk of fatal and non-fatal cancers in ten organs, as well as the risk of leukemia. It also considers the risk of hereditary effects. The method adopted in the mainframe version of COSYMA allows for the variation of risk with age at exposure (Ehrhardt et al., 1995). PC COSYMA uses a simpler method which only considers the doses and risks to adults. The mainframe version of COSYMA can provide information on the numbers of cancers in the people alive at the time of the accident, and in their descendants. It also gives information on the times at which the cancers occur.

Economic effects

COSYMA can calculate the off-site economic effects of the accident, considering the costs arising from the countermeasures and the costs of health effects. The assumptions and models are described in Haywood et al. (1991) and Faude (1992). The countermeasures for which costs are considered are movement of the population, food restrictions, and decontamination. The costs arising from lost production in the area from which people are moved can be assessed in terms of the per capita contribution of the relocated population to gross domestic product (GDP) or in terms of the value of the land affected. For longer periods of relocation, the lost capital value of the land and its assets may be calculated. The costs of food bans include contributions to GDP as well as the lost capital value and the disposal costs of the food affected. The cost arising from health effects may be calculated in terms of the treatment costs and the lost economic productivity of the affected individuals, or an estimation of the cost of health effects may be obtained using a more subjective approach to the valuation of life.

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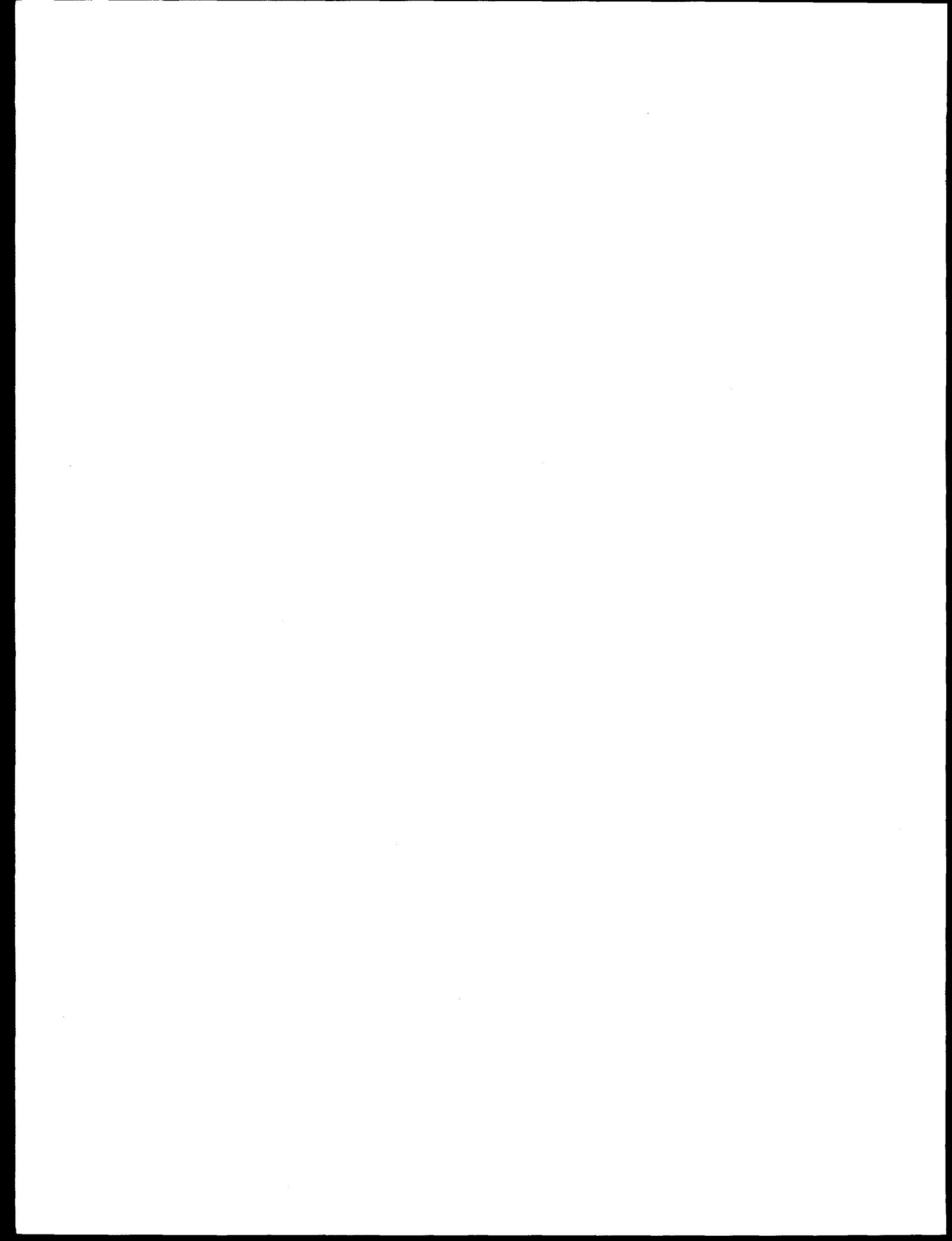
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APPENDIX B

Structure Document and Elicitation Questionnaire for the Expert Panel on Early Health Effects



ELICITATION QUESTIONS

Expert Panel on Early Health Effects

CEC/USNRC Joint Project on
Uncertainty Analysis of Consequence Assessment Programs

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1. Introduction

The CEC/USNRC Joint Study has been initiated to develop further and apply expert judgment elicitation techniques to estimate the uncertainties associated with the predictions of probabilistic risk assessment (PRA), or accident consequence assessment (ACA) codes. The uncertainties in the various aspects of consequence assessment modeling are being considered separately by several expert panels. These panels are to be formed jointly, where possible between experts from the European Union (EU) and the United States of America.

Codes for PRA analysis, such as COSYMA and MACCS, incorporate estimates of the early health effects following radiation exposure. In this document, the adjective *early* is synonymous with the adjectives *deterministic* and *non-stochastic*. In the BIER V report, *non-stochastic* effects are defined as those for which the severity of the effect is regarded as a function of dose and a threshold may exist. In this context, no fixed time interval is associated with the adjective early. Generally, deterministic effects are observable in days to weeks following brief exposure; however, when the radiation dose is protracted over a long time period, the effect in question may occur much later.

This document provides introductory information for the members of the early health effects panel relevant to the parameters of interest. The questions for expert elicitation are then listed.

2. Objectives of the Study

The overall aim of the Joint Study is to assess the uncertainties associated with consequence calculations for accidental releases of radionuclides from nuclear power plants. It is envisaged that the uncertainty analyses of at least two ACA codes (COSYMA from the EU, MACCS from the US) will make use of information derived from this project. (The physical "processes" modeled in ACA codes, such as COSYMA and MACCS, are identical, even though the models representing the processes in the codes may be different.) The results of the Joint Study will also be used to develop a library of uncertainty that can be used for many different uncertainty studies in the future.

One of the guiding principles of this expert elicitation exercise is that the experts should be asked to respond only to questions about physically observable or measurable quantities, even though the actual measurement of these quantities may be impractical due to resource constraints. Therefore, the experts are not asked to answer questions on the mathematical models themselves, to which they may not be able to easily relate, particularly when the models have been derived empirically. The advantages of this approach are that all ACA codes may make use of the information derived from the elicitation questions posed to the experts, since they are somewhat divorced from the basic modeling. The disadvantage, however, is that the uncertainty distributions suggested by the experts have to be processed in order to derive the distributions for those model parameters used within a particular program.

The Joint Study is limited to those issues where alternative sources of information, such as experimental or observational data or even validated computer models, are not available to directly calculate early effect risks, or where multiple sources of information provide conflicting or incomplete evidence of the uncertainties.

3. Choice of Experts and Elicitation Process

The experts have been chosen in such a way as to provide a wide diversity of expertise and experience. Alternative points of view are encouraged and the experts have the opportunity to discuss the issues together at the initial training meeting (December 11-13, 1995). Following this meeting, the experts are given time to assess the problems contained in the elicitation questions. They are not asked to use the methods contained in the consequence codes, but are free to use whatever models or tools they feel are appropriate to answer the questions. They are encouraged, however, to write down all the assumptions made and methods used during this process, together with a clear statement of all the uncertainties they have considered in the assessments (in the so-called rationale). The actual elicitations occur during a private meeting between each expert and up to two analysts, one specializing in probability assessment and the other in the specific aspect of consequence modeling under consideration.

4. Formal Expert Elicitation Process

Expert judgements applicable for uncertainty analysis must be cast in the form of subjective probability distributions. Subjective probability measures degree of belief with respect to possible observations. Subjective measures of uncertainty should be contrasted with the rather narrower range of uncertainties due to purely observational error (e.g., Poisson error in the number of early fatalities observed) which are usually reported in experimental studies.

Quantiles

Degree of belief is elicited in the form of 5%, 50%, and 95% quantiles of subjective probability distributions. The 5% quantile of the distribution for an uncertain quantity X is the number $x_{0.05}$ such that

$$\text{Prob}[X \leq x_{0.05}] = 0.05$$

and similarly for the other quantiles. For each assessment, certain background information is supplied. It is not our intent to provide all physically relevant information; rather the information provided corresponds to the information the ACA codes require.

Dependencies

In some cases, information is sought regarding dependencies that may (or may not) exist among two elicited quantities, call them X and Y . The marginal distributions of X and Y are assumed to have already been assessed. We consider an experiment for assessing the (rank) correlation between X and Y .

The (rank) correlation is a way of summarizing how the true values of X and Y might appear together. If X and Y are positively (rank) correlated, a large value of X might be expected to appear together with a large value of Y , and a small value of X might be expected to appear together with a small value of Y . If X and Y are negatively correlated then the reverse holds: a large value of X would be expected to appear with a small value of Y .

Imagine now that many, many possible realizations are examined, and that the values for X and Y in each realization are recorded on a slip of paper. The paper slips are deposited in a large urn. We draw, say, 1000 slips of paper from this urn (without replacement). We now discard all slips for which the X value is less than the median X value. We now have roughly 500 slips of paper, since the probability of X being less than its median is (by definition) 1/2. Suppose we have exactly 500 slips left on which X is greater than its median value. We now ask: on how many of these slips is Y greater than the median Y value?

If the answer is "250", then the probability is 1/2 that Y is bigger than its median, given that X is bigger than its median. This would be the case if X and Y were independent.

If the answer is "more than 250," then there is a tendency for large X 's and large Y 's to appear together, and this would be the case if X and Y were positively rank correlated.

If the answer is "less than 250," then there is a tendency for large X 's and small Y 's to appear together, and this would be the case if X and Y were negatively correlated.

The expert can describe his/her feeling for correlation by number N between 0 and 500. This number can then be substituted into the following equation to obtain the requested probability:

$$Pr(Y > median \mid X > median) = \frac{N}{500}$$

An appropriate joint distribution can then be selected which has the assessed marginal distributions, satisfies the above equation, and has minimal information among all distributions satisfying the above.

Some information regarding dependencies is requested explicitly in Section 9. In addition, each expert is asked to identify any other major dependencies (*i.e.*, cases in which $Pr(Y > median \mid X > median)$ is greater than say 0.75) between elicited quantities. Such dependencies should be discussed in the expert's rationale.

5. Combining Expert Judgements

There are two reasons for using panels of experts in this study. First, eliciting differing viewpoints gives a better representation of the true uncertainty about the physical phenomena under consideration. A single expert would normally offer only one viewpoint. Second, empirical evidence shows that when the judgments of a number of experts, expressed in the form of probabilities, are combined using some reasonable aggregation procedure, the resulting probability distributions are more reliable. Such aggregated distributions better express the true uncertainty than the probability distribution of a single expert.

Two concepts are important when evaluating probability distributions:

Calibration

Calibration refers to the faithfulness of probabilities. In principle events that are assigned a given probability should occur with a relative frequency equal to that probability. For example, an expert who assigns probability distributions to a set of uncertain quantities should find that 5% of quantities fall below the 5% quantile of his or her subjective distribution, half below the 50% quantile etc.

Calibration is a concept that applies to sets of distributions, not to individual probabilities. An expert is said to be well calibrated if, over a large number of assessments, the probabilities assigned are correctly reflected in the relative frequencies. Of course, the measurement of calibration can occur only when the true values of the uncertain quantities become known. Calibration can be measured, in a statistical sense, through goodness-of-fit statistics and relative entropy.

Informativeness

Informativeness refers to how well probabilities define the value of a variable or the likelihood of an event. Probabilities near zero and one better resolve uncertainty than probabilities near one half. Similarly, sharp or peaked density functions better resolve uncertainty than flat or diffuse densities.

Calibration and high informativeness may not be compatible, however. A set of probability distributions may be very peaked but very wrong. In fact, there is a common tendency for elicited probability distributions to be more "informative" than is warranted. Combined judgements tend to be better calibrated but less informative (more diffuse).

Many ways of combining judgements have been suggested. The simplest rule for combining expert judgements is to take a simple average of their probability distributions. Another method is to weight the experts on the basis of how well they perform on questions of which the true values are known. This approach is known as performance based weighting.

6. Calculations in ACA Codes Related to Early Health Effects

The inputs to the early health effects calculation routines in COSYMA and MACCS are the exposures from various pathways (e.g., cloudshine, groundshine inhalation, ingestion) of specified radionuclides in various time periods. The output from the early health effects routines consists of numbers of radiation-induced fatalities and injuries.

In order to derive the numbers of radiation-induced early health effects, COSYMA and MACCS evaluate risks using hazard functions. The risk of a specific radiation-induced early health effect resulting from a dose to a specific organ is calculated using the equation

$$Risk = 1 - \exp(-H)$$

Lethality or morbidity hazards (i.e., cumulative hazard functions), H , are calculated as

$$H = \ln(2) X^V$$

where X is dose received divided by the dose that would produce the effect in 50% of the exposed population. When the dose D is delivered at a constant rate,

$$X = D/D_{50}$$

In many cases, D_{50} varies with dose rate. V is a shape parameter that determines the steepness of the dose-response curve. Methods of estimating risks of early health effects arising from doses to multiple organs at rates that vary with time have been devised. Experts are not constrained to use ACA code models in performing calculations of risks.

7. Scope of the Early Health Effects Panel

Assessment of the risks of radiation-induced early health effects depends upon a number of factors, such as the different doses delivered to various organs, the effects of dose rate, the linear energy transfer (LET) of the radiation giving rise to the dose, the degree of medical treatment received, and the age and health of the exposed individuals. The expert panel on early health effects characterizes the degree of uncertainty in estimates of radiation-induced health effects taking into account of the correlations introduced by the variables listed above.

In their first meeting, the members of the early health effects panel generated the following list of factors that contribute to uncertainty and agreed on the column within the following table where each potential contributor belongs for the purpose of their elicitations.

Table 1.

Initial Condition Does Not Contribute to Uncertainty	In Case Structure Contributes to Uncertainty	Out of Scope Not to be considered in uncertainty
doses and dose rates as functions of time	uncertainties in dose reconstruction (e.g., for A-bomb survivors)	sample to sample variabilities of population subgroups
population distribution	under-reporting in database	impact of intensive treatment
minimal versus supportive medical treatment	sparse database some data are for injured persons average population with varying health states of members of population efficacy of medical treatment extrapolating from animal data limited data on synergistic effects	psychological and psychosomatic effects death due to concomitant illness

8. Guidance and Assumptions for Uncertainty Assessments

Doses and Dose Rates

All doses are to be quantified in Gray, and all dose rates in Gray/hour.

Elicited Quantities

Most of the elicited quantities are doses at which a certain fraction of a population would be expected to experience a specified health effect. For example, when the effect is early fatality, information is elicited regarding LD₅₀, which is the dose at which 50% of the exposed population would succumb. Specifically, we request the 5-th, 50-th, and 95-th percentile values that characterize an expert's uncertainty in LD₅₀ for the stated exposure conditions. Random samples of equal size from the overall population would, when subjected to the specified exposure conditions, be expected to result in different numbers of fatalities. Information regarding such sample to sample variability is not sought. Rather, we seek the expert's uncertainty in the dose that would cause fatalities to half of the people in the overall population. It may be useful to envision successive random samples from the overall population being exposed to different doses in order to "measure" LD₅₀. If so, the sample size envisioned should be very large (say $\geq 10,000,000$) in order to make sample-to-sample variabilities negligible. Clearly, this is Gedanken.

Population

The basis for the questions below is exposure of a hypothetical "average" EU/US population of all ages and both sexes. In a few questions, this overall population is divided into over-40 and under-40 age groups. Envisioned samples should be randomly selected from the people within the respective age group. The Appendix lists numbers of persons and baseline mortality rates, by sex and in five-year age groups. This is the same population information being used by the late health effects panel.

Minimal and Supportive Treatment

In some questions information is sought for two different levels of medical treatment: minimal and supportive. In other questions, where the level of treatment is not deemed as important, supportive medical treatment is to be assumed. Minimal medical treatment involves basic first aid. Supportive medical treatment includes decontamination of skin and clothing, hospitalization with routine isolation procedures (i.e., not including laminar airflow), wound dressings, electrolyte replacement, administration of blood products (especially fresh platelets), treatment with broad-spectrum antibiotics, antifungals and antivirals, and parenteral feeding.

9. Elicitation Questions

The actual elicitation questions are divided into four parts.

Section 9.1 Questions 1 through 5 involve constant dose rates

Section 9.2 Questions 6a, 6b and 6c involve two distinct exposure periods

Section 9.3 Questions 7a and 7b involve multiple exposed organs and exposure periods

Section 9.4 Seed question(s)

9.1 Questions Involving Constant Dose Rates

Question 1a – Early Fatalities Due to Whole Body Dose

People are exposed to a uniform external source of gamma radiation. This is a whole body exposure. The gamma energy spectrum (0.2 to 2 MeV) is such that the dose rates to major organs including red bone marrow, small intestine, and lungs are assumed to be equal. We call this rate the whole body dose rate and its integral the whole body dose. For the indicated whole body dose rates, provide your 5%, 50%, and 95% values for

- a) the threshold whole body dose below which early fatalities are not observed.
- b) LD₁₀, the whole body dose that will result in fatalities in 10% of exposed individuals.
- c) LD₅₀, the whole body dose that will result in fatalities in 50% of exposed individuals.
- d) LD₉₀, the whole body dose that will result in fatalities in 90% of exposed individuals.

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

NOTE: NUREG/CR-4214, Figure 3.3 indicates that above 1 Gy/hr, LD₅₀ for the hematopoietic syndrome is within 20% of its limiting value. If you feel your 5%, 50%, and 95% values at any of the following dose rates are the same as at 100 Gy/hr, simply note this at the top of the table—there is no need to put the same numbers in more than one table.

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Dose Rate at Which LD₅₀ Doubles

Provide your 5%, 50%, and 95% estimates of the dose rate at which LD₅₀ would be twice its value at 100 Gy/hr.

5%	50%	95%

Minimal Versus Supportive Treatment: Given that the true LD₅₀ with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ with minimal treatment is also above your 50% value? Give your response by dose rate:

100 Gy/hr _____
 10 Gy/hr _____
 1 Gy/hr _____
 0.2 Gy/hr _____

Dose Rate Effects: Given that the true LD₅₀ is determined to be above your 50% value at the higher dose rate, what is the probability that the true LD₅₀ is also above your 50% value for the lower dose rate? Answer for both treatment levels.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr		
10 Gy/hr	1 Gy/hr		
1 Gy/hr	0.2 Gy/hr		

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

As in Question 1a, people are exposed to a uniform external source of gamma radiation. Again, the energy spectrum (0.2 to 2 MeV) is such that dose rates to major organs are approximately equal. For the indicated whole body dose rates and treatment levels, provide your 5%, 50%, and 95% values for

- the threshold whole body dose below which early fatalities due to the gastrointestinal syndrome are not observed.
- LD_{10GI}, the whole body dose that will result in fatalities in 10% of exposed individuals as a result of the gastrointestinal syndrome.
- LD_{50GI}, the whole body dose that will result in fatalities in 50% of exposed individuals as a result of the gastrointestinal syndrome.
- LD_{90GI}, the whole body dose that will result in fatalities in 90% of exposed individuals as a result of the gastrointestinal syndrome.

Any potential effects to the central nervous system and cardiovascular system should be ignored (the exposed individual either survived or did not experience such effects). See section 8 for the explanations of minimal and supportive treatment.)

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD _{10GI}						
LD _{50GI}						
LD _{90GI}						

NOTE: If you feel your 5%, 50%, and 95% values at any of the following dose rates are the same as at 100 Gy/hr, simply note this at the top of the table—there is no need to put the same numbers in more than one table.

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD _{10GI}						
LD _{50GI}						
LD _{90GI}						

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD _{10GI}						
LD _{50GI}						
LD _{90GI}						

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD _{10GI}						
LD _{50GI}						
LD _{90GI}						

Dose Rate Where LD_{50GI} Doubles

Provide your 5%, 50%, and 95% estimates of the whole body dose rate at which LD_{50GI} would be twice its value at 100 Gy/hr.

5%	50%	95%

Dependencies:

Minimal and Supportive Treatment: Given that the true LD_{50GI} with supportive treatment is determined to be above your 50% value, what is the probability that the true LD_{50GI} with minimal treatment is also above your 50% value? Give your response by dose rate:

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Dose Rate Effects: Given that the true LD_{50GI} is determined to be above your 50% value at the higher dose rate, what is the probability that the true LD_{50GI} is also above your 50% value for the lower dose rate? Answer for both treatment levels.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr		
10 Gy/hr	1 Gy/hr		
1 Gy/hr	0.2 Gy/hr		

LD_{50GI} Versus LD_{50} : Given that the true LD_{50GI} is determined to be above your 50% value, what is the probability that the true LD_{50} for Question 1a (all causes of death) is also above your 50% value? Answer by dose rate for both treatment levels.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr		
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Question 2a – Early Fatalities Due to Beta Lung Dose

People breath air that contains chemically inert beta emitters. The resulting lung dose rate is constant over the exposure period. Doses to organs other than the lung are negligible. The beta energies range from 0 to 2 MeV with an average of 0.6 MeV. Assume supportive medical treatment. For the indicated lung dose rates, provide your 5%, 50%, and 95% values for

- the threshold lung dose below which early fatalities are not observed.
- LD_{10} , the lung dose that will result in fatalities in 10% of exposed individuals.
- LD_{50} , the lung dose that will result in fatalities in 50% of exposed individuals.
- LD_{90} , the lung dose that will result in fatalities in 90% of exposed individuals.

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

NOTE: If you feel your 5%, 50%, and 95% values at any of the following dose rates are the same as at 100 Gy/hr, simply note this at the top of the table—there is no need to put the same numbers in more than one table.

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Dependencies:

Age Groups: Given that the true LD₅₀ for individuals over 40 years old is determined to be above your 50% value, what is the probability that the true LD₅₀ for individuals under 40 years old is also above your 50% value? Give your response by dose rate:

100 Gy/hr	_____
10 Gy/hr	_____
1 Gy/hr	_____
0.2 Gy/hr	_____

Dose Rate: Given that the true LD₅₀ is determined to be above your 50% value for the higher dose rate, what is the probability that the true LD₅₀ is also above your 50% value for the lower dose rate? Give your estimates by age group.

	Under 40	Over 40
100 Gy/hr	10 Gy/hr	_____
10 Gy/hr	1 Gy/hr	_____
1 Gy/hr	0.2 Gy/hr	_____

Beta Lung Dose Versus Whole Body Dose: Given that the true LD₅₀ for the whole body exposure in Question 1a with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ for this question is also above your 50% value? Give your response by dose rate and age group:

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 2b – Morbidity Due to Beta Lung Dose

As in Question 2a, people breath air that contains an inert beta emitter. The resulting lung dose rate is constant over the exposure period. Doses to organs other than the lung are negligible. The beta energies range from 0 to 2 MeV with an average of 0.6 MeV.

Let respiratory-functional morbidity be defined as having combinations of any three of the following radiation-induced effects in the lung [NUREG/CR-4214, Rev 1, Part II, p.50]: (1) a reduced volume, (2) an increased stiffness, (3) a nonuniform gas distribution, or (4) a reduced alveolar-capillary gas exchange efficiency.

Assume supportive medical treatment. For the indicated lung dose rates, provide your 5%, 50%, and 95% values for

- a) the threshold lung dose below which respiratory-functional morbidity is not observed.
- b) ED₁₀, the lung dose that will result in respiratory-functional morbidity in 10% of exposed individuals.
- c) ED₅₀, the lung dose that will result in respiratory-functional morbidity in 50% of exposed individuals.
- d) ED₉₀, the lung dose that will result in respiratory-functional morbidity in 90% of exposed individuals.

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED ₁₀						
ED ₅₀						
ED ₉₀						

NOTE: If you feel your 5%, 50%, and 95% values at any of the following dose rates are the same as at 100 Gy/hr, simply note this at the top of the table—there is no need to put the same numbers in more than one table.

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED ₁₀						
ED ₅₀						
ED ₉₀						

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED ₁₀						
ED ₅₀						
ED ₉₀						

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED ₁₀						
ED ₅₀						
ED ₉₀						

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

People inhale aerosols that contain transuranic radionuclides. The inhalation period is very brief, so the dose during inhalation is negligible. The lung dose rate resulting from deposited aerosols is nearly constant following inhalation.

Assume supportive medical treatment. Provide your 5%, 50%, and 95% values for

- a) the threshold lung dose rate below which no deterministic fatalities are observed within three years,
- b) the lung dose rate that will result in deterministic fatalities in 10% of exposed individuals within three years,
- c) the lung dose rate that will result in deterministic fatalities in 50% of exposed individuals within three years,
- d) the lung dose rate that will result in deterministic fatalities in 90% of exposed individuals within three years.

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
DR ₁₀						
DR ₅₀						
DR ₉₀						

Under-40 Versus Over-40: Given that the true LD₅₀ for individuals over 40 years old is determined to be above your 50% value, what is the probability that the true LD₅₀ for individuals under 40 years old is also above your 50% value? Give your response by dose rate:

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Alpha Versus Beta Lung Dose: Given that the true LD₅₀ for beta irradiation in Question 2a is determined to be above your 50% value, what is the probability that the true LD₅₀ for alphas in this question is also above your 50% value? Give your response by dose rate and age group:

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 4a – DELETED

Question 4b – DELETED

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

Individuals are subjected to deposition on skin and clothing from a cloud of beta emitters. Gamma doses in this scenario are negligible. Beta doses to areas protected by clothing are negligible. Assume that the deposition per area of exposed skin is uniform. Uncertainty in the fraction of skin exposed is not part of this question. All exposed individuals have the same fraction of skin exposed irrespective of age or gender.

For this question, skin doses and dose rates are to be quantified at a depth of 7 mg/cm^2 . Factors for converting doses and dose rates at 7 mg/cm^2 are provided in the following table.

Skin Depth (mg/cm^2)	Relative Skin Dose Rate
1	1.72
2	1.50
3	1.27
4	1.16
5	1.12
6	1.06
7	1.00
8	0.920
9	0.864
10	0.819
11	0.779
12	0.744
13	0.731
14	0.706
15	0.696
16	0.671
17	0.659
18	0.635
19	0.615
20	0.611
30	0.546
40	0.493
50	0.456
60	0.427
70	0.405
80	0.387
90	0.371
100	0.31
110	0.27
120	0.26
130	0.26
140	0.25
150	0.24

Acute breakdown of the skin can occur after beta irradiation. The most severe types of lesions as defined in ICRP-59 are

- Acute ulceration (<14 days): an early loss of the epidermis and to a varying degree deeper dermal tissue that results from the death of fibroblasts and endothelial cells in interphase.
- Acute epidermal necrosis (<10 days): interphase death of post mitotic keratinocytes in the upper viable layers of the epidermis. This type of lesion may occur with high-dose, low-energy β irradiation.

Assuming supportive medical treatment and a 24-hour exposure period, provide your 5%, 50%, and 95% values for

- a) the threshold beta skin dose below which acute ulceration is not observed,
- b) the beta skin dose that will result in acute ulceration to 10% of the exposed skin area,
- c) the beta skin dose that will result in acute ulceration to 50% of the exposed skin area,
- d) the beta skin dose that will result in acute ulceration to 90% of the exposed skin area.

NOTE: It is understood that for the same dose different individuals will experience acute tissue breakdown in different fractions of the exposed skin area. The stipulated fraction is an average over all individuals in the population.

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

Given the specified levels of acute damage, provide your 5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

Assuming supportive medical treatment, for a 24-hour exposure period, provide your 5%, 50%, and 95% values for

- the threshold beta skin dose below which acute epidermal necrosis is not observed,
- the beta skin dose that will result in acute epidermal necrosis to 10% of the exposed skin area,
- the beta skin dose that will result in acute epidermal necrosis to 50% of the exposed skin area,
- the beta skin dose that will result in acute epidermal necrosis to 90% of the exposed skin area.

NOTE: It is understood that for the same dose different individuals will experience acute tissue breakdown in different fractions of the exposed skin area. We are looking for the dose corresponding to the fraction of exposed skin on all individuals.

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

Given the specified levels of acute damage, provide your 5%, 50%, and 95% values for the fraction of the population that would die.

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

Assuming supportive medical treatment, for a 24-hour exposure period, provide your 5%, 50%, and 95% values for

- a) the threshold beta skin dose below which moist desquamation is not observed,
- b) the beta skin dose that will result in moist desquamation to 10% of the exposed skin area,
- c) the beta skin dose that will result in moist desquamation to 50% of the exposed skin area,
- d) the beta skin dose that will result in moist desquamation to 90% of the exposed skin area.

NOTE: It is understood that for the same dose different individuals will experience tissue breakdown in different fractions of the exposed skin area. We are looking for the dose corresponding to the fraction of exposed skin on all individuals.

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

Given the specified levels of moist desquamation, provide your 5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Given the specified levels of moist desquamation, provide your 5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

9.2 Two Distinct Exposure Periods, Decreasing Dose Rates

In Section 9.1, only constant dose rates are considered. This part of the elicitation concerns a simple simulation of dose histories that could result from actual accidents.

After an accident each exposed individual would have a different dose history. If, however, we consider only dose histories that could potentially cause deterministic health effects (dose larger than 1 Gy), some general tendencies can be observed.

There are three time periods that are of main importance:

1. Passing of the cloud:

During this period, the highest dose rate occurs. However, this period is short compared to the others. Therefore, the dose accumulated during cloud passage is smaller than the dose received in the subsequent time periods. (Note that this has only been analyzed for doses larger than 1 Gy.)

2. The rest of the first day:

During the rest of the first day, short lived nuclides decay causing a large dose due to previously inhaled nuclides. Due to the decay of short-lived nuclides inhaled or deposited on the ground during cloud passage, the dose rates are still high, although lower than during cloud passage. Locations where red marrow doses are larger than 1 Gy are usually highly contaminated, resulting in high doses due to groundshine, while people remain there.

3. The period after the first day

After the first day, inhaled nuclides migrate within the body and cause additional doses to various organs.

The situations described in the following questions are similar to those described above in that successive periods marked by substantially different dose rates are postulated.

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

People are exposed to a uniform external source of gamma radiation. As in question 1, this is a whole body exposure.

The total exposure duration is 24 hours, but after cloud passage (the first hour) the dose rate is reduced by approximately a factor 10, so 30% of the total dose is received in the first hour, and 70% during the next 23 hours.

Provide your 5%, 50%, and 95% values for

- a) the threshold 24-hour dose below which early fatalities are not observed.
- b) LD_{10} , the 24-hour dose that will result in fatalities in 10% of exposed individuals.
- c) LD_{50} , the 24-hour dose that will result in fatalities in 50% of exposed individuals.
- d) LD_{90} , the 24-hour dose that will result in fatalities in 90% of exposed individuals.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

Minimal Versus Supportive Treatment: Given that the true LD_{50} with supportive treatment is determined to be above your 50% value, what is the probability that the true LD_{50} with minimal treatment is above your 50% value?

Constant Versus Decreasing Dose Rate: Given that the true LD₅₀ for question 1a at the indicated dose rate is determined to be above your 50% value, what is the probability that the true LD₅₀ for this question is also above your 50% value? Give your response for levels of treatment.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

People are exposed to a volumetrically uniform external source of gamma radiation. As in question 1, this is a whole body exposure.

The total exposure duration is 24 hours, but after cloud passage (the first hour) the dose rate is reduced by approximately a factor 100, so 80% of the total dose is received in the first hour, and 20% during the next 23 hours.

Provide your 5%, 50%, and 95% values for

- the threshold 24-hour dose below which early fatalities are not observed.
- LD₁₀, the 24-hour dose that will result in fatalities in 10% of exposed individuals.
- LD₅₀, the 24-hour dose that will result in fatalities in 50% of exposed individuals.
- LD₉₀, the 24-hour dose that will result in fatalities in 90% of exposed individuals.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Minimal Versus Supportive Treatment: Given that the true LD₅₀ with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ with minimal treatment is above your 50% value?

10:1 Versus 100:1 Dose Rate Decrease: Given that the true LD₅₀ for question 6a is determined to be above your 50% value, what is the probability that the corresponding LD₅₀ for this question is also above your 50% value? Give your response for both levels of treatment.

Minimal Treatment Supportive Treatment

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

People are exposed to a passing radioactive cloud. Aerosols in the cloud contain primarily beta emitters, so doses to organs other than the lung are negligible. The beta energies range from 0 to 2 MeV with an average of 0.6 MeV. The buildup and decay of radionuclides in the lungs is such that the lung dose rate can be approximated as constant during the first day. After the first day the dose rate decreases such that 70% of the total dose is received in the first day, and 30% during the next six days.

Assuming supportive medical treatment, for the indicated lung dose rates, provide your 5%, 50%, and 95% values for

- a) the threshold 7-day lung dose below which early fatalities are not observed.
- b) LD_{10} , the 7-day lung dose that will result in fatalities in 10% of exposed individuals.
- c) LD_{50} , the 7-day lung dose that will result in fatalities in 50% of exposed individuals.
- d) LD_{90} , the 7-day lung dose that will result in fatalities in 90% of exposed individuals.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

Under-40 Versus Over-40: Given that the true LD_{50} with is determined to be above your 50% value for the under 40 age group, what is the probability that the true LD_{50} is also above your 50% value for the over-40 age group?

Constant Versus Decreasing Dose Rate: Given that the true LD_{50} for question 2a at the indicated dose rate is determined to be above your 50% value, what is the probability that the true LD_{50} for this question is also above your 50% value? Give your response for both age groups.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

9.3 Multiple Exposed Organs and Exposure Periods

In this part of the elicitation, exposures that could occur after an accidental release of radioactive material are simulated. All organs are exposed via several pathways to a mixture of different radionuclides. Based on the results of overall dose calculations with COSYMA, two simplified dose histories are given. The only variable in these dose histories is the bone marrow dose D received during the first day. All other doses are specified relative to D .

The ratio of doses to bone marrow, colon and small intestine are rather constant in the relevant dose range - doses larger than 0.1 Gy. The small intestine ratio is about 1. The large intestine dose is approximately 1.5 larger than the bone marrow dose.

The lung dose is about 2 to 10 times larger than the bone marrow dose.

Also, the ratio of lung dose and skin dose is rather constant: the skin dose is approximately 15 times larger than the lung dose.

Combining these ratios with the type of dose histories discussed in Section 9.2, we pose the following questions:

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

The following table gives the organ doses received during the specified time period. The representative dose ' D ' is the bone marrow dose after one day. Skin decontamination is assumed to occur after 24 hours. Exposed skin dose and dose rates are specified at a depth of 7 mg/cm^2 . All exposed individuals have the same fraction of skin exposed.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	$0.3*D$	$0.3*D$	$0.3*D$	$0.4*D$	$1.2*D$
balance of first day	$0.7*D$	$1.2*D$	$0.7*D$	$1.6*D$	$20.1*D$
1 day to 7 days	$1.1*D$	$1.6*D$	$1.1*D$	$0.6*D$	0
Total	$2.1*D$	$3.1*D$	$2.1*D$	$2.6*D$	$21.3*D$

For the indicated fractions of skin exposed, provide your 5%, 50%, and 95% values for

- the threshold one-day bone marrow dose D below which early fatalities are not observed.
- LD_{10} , the one-day bone marrow dose D that will result in fatalities in 10% of exposed individuals.
- LD_{50} , the one-day bone marrow dose D that will result in fatalities in 50% of exposed individuals.
- LD_{90} , the one-day bone marrow dose D that will result in fatalities in 90% of exposed individuals.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Minimal Versus Supportive Treatment: Given that the true LD₅₀ with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ with minimal treatment is above your 50% value?

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

The following table gives the organ doses received during the specified time period. The representative dose 'D' is the bone marrow dose after one day. Skin decontamination is assumed to occur after 24 hours. Exposed skin dose and dose rates are specified at a depth of 7 mg/cm^2 . All individuals have the same fraction of skin exposed.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	$0.3*D$	$0.3*D$	$0.3*D$	$0.0*D$	$1.2*D$
balance of first day	$0.7*D$	$1.2*D$	$0.7*D$	$0.0*D$	$20.1*D$
1 day to 7 days	$1.1*D$	$1.6*D$	$1.1*D$	$0.0*D$	0
Total	$2.1*D$	$3.1*D$	$2.1*D$	$0.0*D$	$21.3*D$

For the indicated fractions of skin exposed, provide your 5%, 50%, and 95% values for

- the threshold one-day bone marrow dose D below which early fatalities are not observed.
- LD_{10} , the one-day bone marrow dose D that will result in fatalities in 10% of exposed individuals.
- LD_{50} , the one-day bone marrow dose D that will result in fatalities in 50% of exposed individuals.
- LD_{90} , the one-day bone marrow dose D that will result in fatalities in 90% of exposed individuals.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Minimal Versus Supportive Treatment: Given that the true LD₅₀ with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ with minimal treatment is above your 50% value?

No skin exposed _____
 20% skin exposed _____
 40% skin exposed _____
 60% skin exposed _____

With Versus Without Lung Dose: Given that the true LD₅₀ with zero lung dose is determined to be above your 50% value, what is the probability that the true LD₅₀ with the lung dose specified in Question 7a1 is above your 50% value?

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

The following table gives the organ doses received during the specified time period. The representative dose 'D' is the bone marrow dose after one day. Skin decontamination is assumed to occur after 24 hours. Exposed skin dose and dose rates are specified at a depth of 7 mg/cm². All individuals have the same fraction of skin exposed.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin ^a
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.7*D	6.3*D
balance of first day	0.7*D	1.2*D	0.7*D	9.3*D	144*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	3.6*D	0
Total	2.1*D	3.1*D	2.1*D	13.6*D	150.3*D

For the indicated fractions of skin exposed, provide your 5%, 50%, and 95% values for

- the threshold one-day bone marrow dose D below which early fatalities are not observed.
- LD_{10} , the one-day bone marrow dose D that will result in fatalities in 10% of exposed individuals.
- LD_{50} , the one-day bone marrow dose D that will result in fatalities in 50% of exposed individuals.
- LD_{90} , the one-day bone marrow dose D that will result in fatalities in 90% of exposed individuals.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD_{10}						
LD_{50}						
LD_{90}						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Minimal Versus Supportive Treatment: Given that the true LD₅₀ with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ with minimal treatment is above your 50% value?

No skin exposed _____
 20% skin exposed _____
 40% skin exposed _____
 60% skin exposed _____

Smaller Versus Larger Lung Dose: Given that the true LD₅₀ for question 7a is determined to be above your 50% value, what is the probability that the true LD₅₀ for this question is also above your 50% value? Give your response for both levels of treatment.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

The following table gives the organ doses received during the specified time period. The representative dose 'D' is the bone marrow dose after one day. Skin decontamination is assumed to occur after 24 hours. Exposed skin dose and dose rates are specified at a depth of 7 mg/cm². All individuals have the same fraction of skin exposed.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin ^a
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.0*D	6.3*D
balance of first day	0.7*D	1.2*D	0.7*D	0.0*D	144*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.0*D	0
Total	2.1*D	3.1*D	2.1*D	0.0*D	150.3*D

For the indicated fractions of skin exposed, provide your 5%, 50%, and 95% values for

- the threshold one-day bone marrow dose D below which early fatalities are not observed.
- LD₁₀, the one-day bone marrow dose D that will result in fatalities in 10% of exposed individuals.
- LD₅₀, the one-day bone marrow dose D that will result in fatalities in 50% of exposed individuals.
- LD₉₀, the one-day bone marrow dose D that will result in fatalities in 90% of exposed individuals.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD ₁₀						
LD ₅₀						
LD ₉₀						

Minimal Versus Supportive Treatment: Given that the true LD₅₀ with supportive treatment is determined to be above your 50% value, what is the probability that the true LD₅₀ with minimal treatment is above your 50% value?

No skin exposed _____
 20% skin exposed _____
 40% skin exposed _____
 60% skin exposed _____

With Versus Without Lung Dose: Given that the true LD₅₀ with zero lung dose is determined to be above your 50% value, what is the probability that the true LD₅₀ with the lung dose specified in Question 7b1 is above your 50% value?

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

EU/USA Population Distribution

Age Group	Male		Female		Total	
	Number	% of Total	Number	% of Total	Number	% of Total
0-1	681992	0.68%	650432	0.65%	1332424	1.33%
1-4	2700831	2.70%	2581197	2.58%	5282028	5.28%
5-9	3370479	3.37%	3222457	3.22%	6592936	6.59%
10-14	3366206	3.37%	3219854	3.22%	6586060	6.59%
15-19	3356643	3.36%	3215718	3.22%	6572361	6.57%
20-24	3338640	3.34%	3209140	3.21%	6547780	6.55%
25-29	3318098	3.32%	3201590	3.20%	6519688	6.52%
30-34	3294784	3.29%	3192353	3.19%	6487137	6.49%
35-40	3266243	3.27%	3179343	3.18%	6445586	6.45%
40-44	3229161	3.23%	3160256	3.16%	6389417	6.39%
45-49	3174736	3.17%	3129625	3.13%	6304361	6.30%
50-54	3091626	3.09%	3081043	3.08%	6172669	6.17%
55-59	2958435	2.96%	3003642	3.00%	5962077	5.96%
60-64	2751877	2.75%	2882456	2.88%	5634333	5.63%
65-69	2452639	2.45%	2560600	2.56%	5013239	5.01%
70-74	2046870	2.05%	2016217	2.02%	4063087	4.06%
75-79	1525728	1.53%	1537841	1.54%	3063569	3.06%
80-84	948695	0.95%	1110530	1.11%	2059225	2.06%
85+	1126316	1.13%	1845704	1.85%	2972020	2.97%
Totals	49999999	50%	49999998	50%	99999997	100%

Question 8 – Seed

The following table gives biological effects that have been observed in persons that were accidentally exposed to external radiation. The measured biological effects are (a) time of first vomiting after the exposure and (b) blood lymphocyte counts for several times after the exposure.

case number	begin of vomiting after exposure hours	H/I	lymphocyte count in ($10^9/\text{litre}$) days after exposure						
			1	1*	2	2*	3	4	5
1	2:00	H	1.6	0.7	0.87	0.66	0.64	0.46	0.63
2	1:00	I	0.57		0.79				
3	3:00	H	0.43				0.74		0.4
4	1:15	I	0.42		0.32		0.24	0.49	0.27
5	1:20	I	0.4		0.3		0.2	0.14	0.16
6	2:00	I	0.34		0.2		0.14	0.2	0.26
7	2:25	I	0.16		0.31		0.16		0.24
8	2:00	H	0		0.18		0.47		
9	2:00	H	0.05	0	0.15		0.06	0.07	0.11
10	0:00	I	0.44	0.61	0.08	0.34	0.09	0.2	0.16

* In these columns counts at a later time in the same day are given.
 ** Homogeneity of the exposure:
 H: homogeneous exposure of RBM
 I: inhomogeneous exposure of RBM

Provide dose estimates of the average dose to the red bone marrow. Provide your 5%, 50%, and 95% values for each case. Assume a large dose rate (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

APPENDIX C

Rationales and Responses of the Expert Panel on Early Health Effects

Note: Tables without data indicate that the expert had no response.

EXPERT A

The range of questions posed to the expert Panel on Early Health Effects was wide-ranging. In reality not all questions could be expected to be within the technical competence of each expert, and thus only limited number of responses have been made by this expert.

Question 1a: Early Fatalities Due to Whole Body Dose.

The question imposes the unlikely situation that individuals will be exposed to uniform doses of external gamma radiation. Most information from exposed groups of individuals is for non-uniform exposure. This includes the most recent series, based on the victims of the Chernobyl nuclear power plant accident. Based on the accumulated data from NUREG/CR - 4214, it would appear that the various dose estimates, for differing whole body dose rates in the range 1 - 100 Gy/hr, would be similar. For exposed individuals receiving minimal treatment there is reasonable agreement as to the likely dose-effect relationship. The greatest uncertainty is on the effects of supportive treatment. This uncertainty relates both to the magnitude of the effects of supportive care and to the influence of the time of its first application. The greatest effect is likely to be at levels of response $\leq LD_{50}$, but without a major effect on the threshold dose. Radiosensitive individuals, who do not respond to treatment, will continue to be the defining factor.

Question 2a: Early Fatalities Due to Beta Lung Doses.

Question 2b: Morbidity Due to Beta Lung Dose.

Estimates of the likely dose-effect relationships associated with this issue have been deduced from studies of the effects of varying dose-rate on both breathing rate and mortality in mice after external irradiation exposure of the whole thorax of mice (1986). Data for human lung is based on cases of severe, radiation-induced pneumonitis in patients receiving upper half body irradiation for malignant disease (Mah and van Dyk, 1988). The ED_{50} for this response was approximately 9 Gy, for patients of a mixed age group. The effects of age on lung mortality/morbidity are uncertain but it seems reasonable to assume that a 20% lower dose is applicable to older individuals. Dose-rate factors of 1.0, 1.15, 2.5, and 4.0 were applied to obtain threshold, LD_{10} , LD_{50} , and LD_{90} values for dose rates of 100 Gy/hr, 10 Gy/hr, 1 Gy/hr, and 0.2 Gy/hr, respectively. What has been loosely termed morbidity was assumed to occur at half the mortality dose.

Question 5: Early Fatalities from Beta Skin Doses.

The exposure of the skin was, as judged by the relative skin depth dose-rate information supplied, was from an intermediate/mixed energy β -emitter. When compared with the relative dose-rate at 16 μm depth (relative dose-rate 1.56) the depth dose distribution was comparable to that of ^{170}Tm (E_{max} 0.97 MeV). The 25% isodose was at approximately 700 μm depth for both sources. This is important since experimental data from pig skin (ICRP 59) can be used to estimate the required parameters for this example of skin contamination. For high dose overexposure, acute ulceration will be the reaction of concern. Acute epithermal necrosis is only a factor for lower energy β -exposure; it is not relevant to this type of skin contamination.

It was noted that the figures for the percentage area of skin exposed given in these questions did not agree with standard charts used to assess the extent of other types of skin burns (Figure 1). For example the skin of the head and neck constituted only 9% of the total skin surface area in adults, not 14-20% quoted as in the questions. Agreement on this point would be essential, since mortality from skin burns is determined by three major parameters: area of damage, depth of damage (deep or superficial), and the age of the patient.

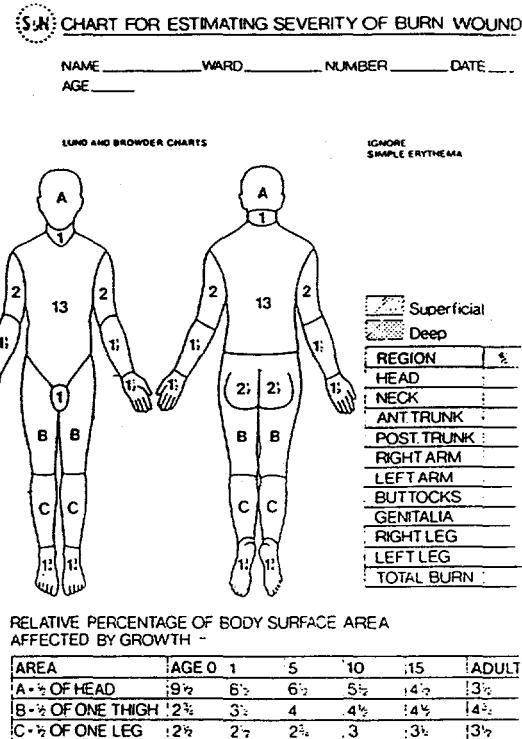


Figure 1. Lund and Browder Chart for more accurate assessment of percentage body surface areas.

Finally, we are asked to provide estimates of dose at a fixed depth in the skin. In reality the incidence of a given event, hence the likely area of involvement, will depend on the depth of relevant tissue targets within the skin. This will be a function of both epidermal and dermal thickness. This varies considerably with body site. For example on the hands, approximately 95% of the surface area of the fingers has an epidermal thickness of $>80 \mu\text{m}$. This is only approximately 50% of surface area on the backs of the hand. On the head and neck less than 15% of the surface area has an epidermal thickness of $>80 \mu\text{m}$ (ICRP-59). None of the variations, although important, were taken into account when assessing the dose to produce a given area of skin breakdown.

Question 5a: Acute Ulceration.

The target cell populations, the death of which is responsible for this reaction, are the endothelial cells and fibroblasts of the superficial dermis (papillary dermis). A nominal depth of $100 \mu\text{m}$ was chosen to enable a comparison to be made between ^{170}Tm and the type of skin contamination proposed in the question.

The early onset of the lesion reflects the nature of cell death in the target cell populations. For small areas of skin exposed to ^{170}Tm , i.e., 0.1 - 2.0 mm diameter sources, no effect was seen that could be related to the area of skin exposed. Based on an understanding of the mechanisms by which damage is expressed, this is understandable, and the results can be extrapolated to larger areas. To provide estimates of the dose to produce acute ulceration for a specified percentage of the area of skin exposed it is assumed that larger areas are made up of multiple small areas. The incidence of ulceration in a small area can then be equated with area of response in a larger area (multiple small areas) assuming no interaction between adjacent areas. When variations in the depth of the papillary dermis are ignored, the doses quoted for each exposure condition will be the same. In reality, doses would be lower as more areas with a thinner epidermis were included.

For adults the percentage of the whole skin area exposed would be (a) 15% skin exposed (6% hands; 9% head and neck), (b) 29% skin exposed, (6% hands; 9% head and neck; 14% arms), (c) 43% of skin exposed, (6% hands; 9% head and neck; 14% arms and lower legs and feet). This is in disagreement with the values of 20%, 40%, and 60% quoted.

The percentage of the total skin area damage with "deep" radiation burns (acute ulceration) would have to be

calculated in relation to the corrected values. Estimates of the probability of mortality would need to be based on percentage of skin surface plus the body area burned, the individual's age, and the depth of the burns. This is of concern to burns units throughout Europe. The topic of disaster management is the subject of a committee of the European Burns Association. This is a very difficult problem, as illustrated by a recent disaster in the UK (Royal Society of Medicine Round Table Series, 1986). It has not been resolved by experts in this specific field. The complexity is illustrated in part by Figure 2. This shows the influence of patient age on the probability of death for burns associated with different percentages of the total skin surface area. For example, a 33-37% burn would result in a $\geq 90\%$ probability of death in the elderly (>70 years) but only 10% in young persons (<20 years). The chart still does not take account of the depth or the site of involvement of the burn on mortality. Deeper burns carry a less favorable prognosis.

Given that there is no real agreement between burns experts, it would not be appropriate for a non-expert, who nevertheless might have a good understanding of radiation reactions of the skin, to speculate on likely mortality rates. This could lead to the development of erroneous conclusions in the models of radiation-induced mortality.

Question 5c: Moist Desquamation.

Exposure of pig skin to β -rays from ^{170}Tm showed that the area of skin exposed was not a factor in determining the dose-related incidence of moist desquamation (ICRP-59). Thus for very large areas the assumption was made that a given incidence of the effect can be extrapolated to the percentage area of the skin involved. While doses are quoted at $70 \mu\text{m}$, depth comparisons between the source of contamination and ^{170}Tm were first made at $700 \mu\text{m}$ depth. Earlier studies, comparing $^{90}\text{Sr}/^{90}\text{Y}$ with ^{170}Tm , have indicated the importance of cells in the hair follicle with respect to the endpoint of moist desquamation (Hopewell, 1991). If variations in skin thickness are not taken into account, then the doses quoted will be the same for the three exposure conditions.

Superficial radiation burns will result in some mortality, even though the duration of moist desquamation is likely to be very short following contamination of the type envisaged. Rapid repopulation of the epidermis is from surviving clonogenic epithelial cells close to the base of hair follicles. Information in the rate of healing of large areas of skin following ^{170}Tm contamination is not available. This, and given uncertainties about mortality from superficial skin

% body area burned	Age (yr)																	
	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	
93+	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
88-92	.9	.9	.9	.9	1	1	1	1	1	1	1	1	1	1	1	1	1	
83-87	.9	.9	.9	.9	.9	1	1	1	1	1	1	1	1	1	1	1	1	
78-82	.8	.8	.8	.8	.9	.9	.9	.9	1	1	1	1	1	1	1	1	1	
73-77	.7	.7	.8	.8	.8	.9	.9	.9	1	1	1	1	1	1	1	1	1	
68-72	.6	.6	.7	.7	.8	.8	.8	.9	.9	.9	1	1	1	1	1	1	1	
63-67	.5	.5	.6	.6	.7	.7	.8	.8	.9	.9	1	1	1	1	1	1	1	
58-62	.4	.4	.4	.5	.5	.6	.6	.7	.7	.8	.9	.9	1	1	1	1	1	
53-57	.3	.3	.3	.4	.4	.5	.5	.6	.7	.7	.8	.9	1	1	1	1	1	
48-52	.2	.2	.3	.3	.3	.4	.5	.6	.6	.7	.8	.9	1	1	1	1	1	
43-47	.2	.2	.2	.2	.3	.3	.4	.4	.5	.5	.6	.7	.8	1	1	1	1	
38-42	.1	.1	.1	.1	.2	.2	.3	.3	.4	.5	.6	.8	.9	1	1	1	1	
33-37	.1	.1	.1	.1	.1	.2	.2	.3	.3	.4	.5	.7	.8	.9	1	1	1	
28-32	0	0	0	0	.1	.1	.1	.2	.2	.3	.4	.6	.7	.9	1	1	1	
23-27	0	0	0	0	0	0	.1	.1	.1	.2	.2	.3	.4	.6	.7	.9	1	
18-22	0	0	0	0	0	0	.1	.1	.1	.1	.2	.3	.4	.6	.8	.9		
13-17	0	0	0	0	0	0	0	0	.1	.1	.1	.2	.3	.5	.6	.7		
8-12	0	0	0	0	0	0	0	0	0	.1	.1	.2	.3	.5	.5	.5		
3-7	0	0	0	0	0	0	0	0	0	0	0	.1	.2	.3	.4			
0-2	0	0	0	0	0	0	0	0	0	0	0	0	.1	.2	.2			

Figure 2. Mortality probability chart (1965-1970).

burns, makes estimates of mortality too speculative to be meaningful. More research work is needed in this important area of radiation accident planning. Cooperation with specialists in thermal burns would be essential if any consensus were to be reached as to the mortality associated with radiation-induced skin burns.

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Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.9	1.0	1.5	1.0	1.5	2.0
LD10	1.0	1.5	2.25	1.5	3.0	4.0
LD50	2.0	3.0	4.0	3.0	4.5	7.0
LD90	4.0	5.0	6.5	4.0	5.5	6.5

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.9	1.0	1.5	1.0	1.5	2.0
LD10	1.0	1.5	2.25	1.5	3.0	4.0
LD50	2.0	3.0	4.0	3.0	4.5	7.0
LD90	4.0	5.0	6.5	4.0	5.5	6.5

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.9	1.0	1.5	1.0	1.5	2.0
LD10	1.0	1.5	2.25	1.5	3.0	4.0
LD50	2.0	3.0	4.0	3.0	4.5	7.0
LD90	4.0	5.0	6.5	4.0	5.5	6.5

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.001	0.01	0.1

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr		
10 Gy/hr	1 Gy/hr		
1 Gy/hr	0.2 Gy/hr		

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD10 _{GI}						
LD50 _{GI}						
LD90 _{GI}						

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD10 _{GI}						
LD50 _{GI}						
LD90 _{GI}						

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD10 _{GI}						
LD50 _{GI}						
LD90 _{GI}						

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD10 _{GI}						
LD50 _{GI}						
LD90 _{GI}						

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr		
10 Gy/hr	1 Gy/hr		
1 Gy/hr	0.2 Gy/hr		

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr		
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	6.5	7.5	9.0	4.5	5.0	5.5
LD10	7.0	9.0	11.0	5.0	7.0	9.0
LD50	8.0	10.0	12.0	6.0	8.0	10.0
LD90	9.0	11.0	13.0	7.0	9.0	11.0

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	7.5	8.5	10.4	5.0	5.8	6.3
LD10	8.0	10.4	12.7	5.8	8.0	10.4
LD50	9.2	11.5	13.8	7.0	9.2	11.5
LD90	10.4	12.7	15.0	8.0	10.4	12.7

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	16.2	18.8	22.5	11.3	12.5	13.8
LD10	17.5	22.5	27.5	12.5	17.5	22.5
LD50	20.0	25.0	30.0	15.0	20.0	25.0
LD90	22.5	27.5	32.5	17.5	22.5	27.5

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	26.0	30.0	36.0	18.0	20.0	22.0
LD10	28.0	36.0	44.0	20.0	28.0	36.0
LD50	32.0	40.0	48.0	24.0	32.0	40.0
LD90	36.0	44.0	52.0	28.0	36.0	44.0

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	0.5
10 Gy/hr	0.5
1 Gy/hr	0.5
0.2 Gy/hr	0.5

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	0.5	0.5
10 Gy/hr	1 Gy/hr	0.5	0.5
1 Gy/hr	0.2 Gy/hr	0.5	0.5

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	3.3	3.8	4.5	2.3	2.5	2.8
ED10	3.5	4.5	5.5	2.5	3.5	4.5
ED50	4.0	5.0	6.0	3.0	4.0	5.0
ED90	4.5	5.5	6.5	3.5	4.5	5.5

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	3.8	4.3	5.2	2.5	2.9	3.2
ED10	4.0	5.2	6.4	2.9	4.0	5.2
ED50	4.6	5.8	6.9	3.5	4.6	5.8
ED90	5.2	6.4	7.5	4.0	5.2	6.4

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	8.2	9.4	11.3	5.7	6.3	6.9
ED10	8.8	11.3	13.8	6.3	8.8	11.3
ED50	10.0	12.5	15.0	7.5	10.0	12.5
ED90	11.3	13.8	16.3	8.8	11.3	13.8

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	13.0	15.0	18.0	9.0	10.0	11.0
ED10	14.0	18.0	22.0	10.0	14.0	18.0
ED50	16.0	20.0	24.0	12.0	16.0	20.0
ED90	15.0	22.0	26.0	14.0	18.0	22.0

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
DR10						
DR50						
DR90						

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 4a – DELETED**Question 4b – DELETED**

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% head and neck)

	5%	50%	95%
Threshold for acute ulceration	40	55	70
Dose for effect in 10% of exposed skin area	70	95	120
Dose causing effect in 50% of exposed skin area	150	200	250
Dose causing effect in 90% of exposed skin area	400	600	800

40% Skin Exposed (6% hands, 20% head and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration	40	55	70
Dose for effect in 10% of exposed skin area	70	95	120
Dose causing effect in 50% of exposed skin area	150	200	250
Dose causing effect in 90% of exposed skin area	400	600	800

60% Skin Exposed (6% hands, 20% head and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration	40	55	70
Dose for effect in 10% of exposed skin area	70	95	120
Dose causing effect in 50% of exposed skin area	150	200	250
Dose causing effect in 90% of exposed skin area	400	600	800

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation	10	12	15
Dose for effect in 10% of exposed skin area	15	30	45
Dose causing effect in 50% of exposed skin area	20	50	70
Dose causing effect in 90% of exposed skin area	45	65	85

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation	10	12	15
Dose for effect in 10% of exposed skin area	15	30	45
Dose causing effect in 50% of exposed skin area	30	50	70
Dose causing effect in 90% of exposed skin area	45	65	85

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation	10	12	15
Dose for effect in 10% of exposed skin area	15	30	45
Dose causing effect in 50% of exposed skin area	30	50	70
Dose causing effect in 90% of exposed skin area	45	65	85

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal
Treatment

Supportive
Treatment

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

threshold	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

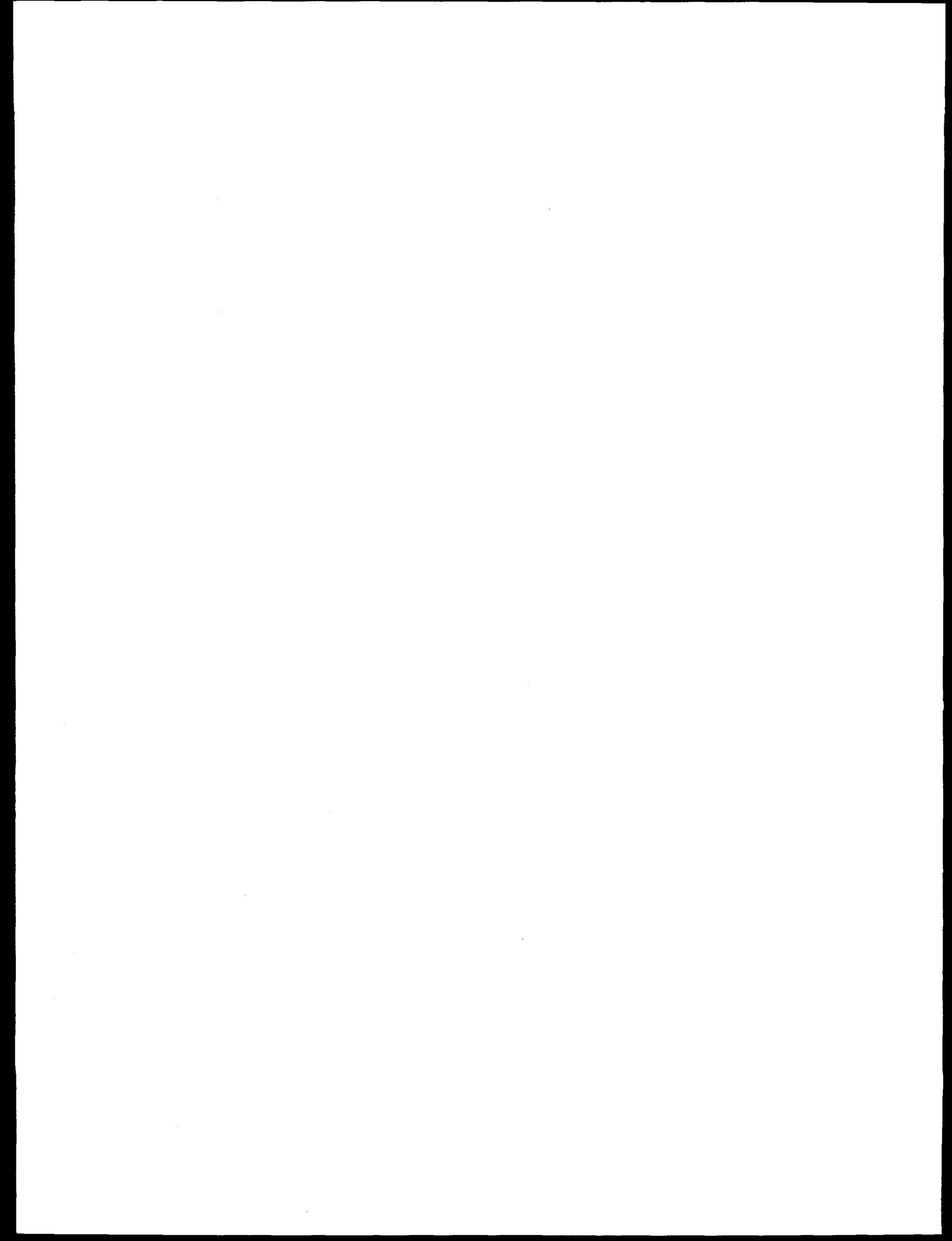
	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			



EXPERT B

Introduction

Unlike the induction of cancer by radiation, deterministic (nonstochastic) radiation effects generally require large doses and therefore occur only when the absorbed dose exceeds a threshold that depends on the effect and individual. Because the deterministic effect either occurs or does not occur in a given irradiated person, such effects are considered quantal. The individual-specific threshold for the quantal deterministic effect is called the tolerance dose in the toxicological literature. In a population, different persons can have different tolerance doses. Sensitive individuals will have lower tolerance doses than resistant individuals. The minimum tolerance dose (smallest individual threshold for the population) is the population threshold that corresponds to what is usually called the threshold in nuclear accident risk assessment. Thus, in responding to elicitation questions, threshold is used to represent the minimum tolerance dose for the deterministic effect and population of interest. Tolerance dose is used to represent the individual-specific threshold radiation dose for a given deterministic effect and member of the population of interest.

If the distribution of tolerance doses over the total population of interest is represented by $f(D')$ for absorbed radiation doses D' , then the integral, $\int f(D')dD'$, evaluated from zero to absorbed dose D , gives the fraction $F(D)$ of the population that would be expected to demonstrate the quantal radiobiological effect of interest after exposure of each member of the population to the same dose D . Other variables in addition to D may also be important (e.g., age, dose rate, etc.), in which case F will also depend on the other variables (covariates), or the other covariates can be fixed [e.g., age- and dose-rate specific risk $F(D)$]. If D is less than the threshold (i.e., minimum tolerance dose), $F(D)$ will be zero.

The function $F(D)$, which represents the dose-dependent risk for a given quantal deterministic effect of irradiation, can be estimated using $F(D)'$, where $F(D)'$ is the fraction of a group (usually small compared to the population of interest), each exposed to a dose D , that demonstrates the effect of interest. A plot of $F(D)'$ vs. D is called a dose-response curve and can be used to estimate the risk $F(D)$ as a function of the dose D for a larger population of interest. To generate risk estimates for any dose of interest, empirical tolerance distribution models such as the probit, logistic, and Weibull can be fitted to dose-response data for $F(D)'$.

For most quantal deterministic effects described by the indicated models, the risk vs. dose relationships are sigmoidal and have characteristic dose percentiles D_{10} , D_{50} , and D_{90} that correspond to doses that would be expected to affect 10%, 50%, and 90% of the population, respectively. For lethality, D_{10} , D_{50} , and D_{90} correspond to dose percentiles LD_{10} , LD_{50} , and LD_{90} , respectively. For morbidity, D_{10} , D_{50} , and D_{90} correspond to effective dose percentiles ED_{10} , ED_{50} , and ED_{90} , respectively.

Like $F(D)$, the D_{10} , D_{50} , and D_{90} doses for a given health effect of irradiation can depend on a number of covariates including dose rate, radiation quality, age at exposure, and in some cases gender. For deterministic effects, dose rate and radiation quality are usually the most important from the indicated set of covariates. Whether age and gender are important enough to be included as covariates when evaluating the risk of a specific deterministic effect depends on the effect considered. For the deterministic effects considered in this elicitation, gender-related susceptibility differences were considered to be of minor importance and accounted for by upper and lower bounds on model parameters (USNRC, 1989a, 1990).

For this elicitation, thresholds (practical), D_{10} , D_{50} , and D_{90} have been generated for different lethality and morbidity effects based on use of a two-parameter, Weibull dose-response model for $F(D)$ (USNRC, 1989a). To account for dose-rate effects, the normalized dose X has been used in place of the absorbed dose D (Scott et al., 1988; USNRC, 1989a). The normalized dose is dimensionless and represents fractions of a D_{50} . For example, $X=0.5$ corresponds to one half of the D_{50} for the quantal effect considered. However, the use of normalized dose requires a model for evaluating D_{50} as a function of dose rate. The empirical model presented in a 1989 NUREG/CR-4214 report (USNRC, 1989a) was used to evaluate D_{50} as a function of dose rate for the endpoints considered in this elicitation.

With the Weibull dose-response model, D_{10} and D_{90} (estimated values) can be calculated as a function of D_{50} and the Weibull model shape parameter V . In addressing elicitation questions, the D_{50} was first estimated, then used along with an estimate of V to obtain estimates of the D_{90} and D_{10} . Errors associated with the D_{50} and V estimates therefore contributed to errors in D_{10} and D_{90} estimates. In most cases (except for elicitation questions related to changing dose rates and multiple organ effects), errors were evaluated by the Monte Carlo method. Also, with the Weibull model, a practical threshold dose can be estimated as a fraction of the D_{50} dose (USNRC, 1989a; USNRC,

1990). For death via the hematopoietic-syndrome, pulmonary-syndrome, or gastrointestinal-syndrome mode, or for respiratory-functional morbidity, a reasonable estimate of the threshold dose is one half of the D_{50} , as was recommended in a 1989 NUREG/CR-4214 report (USNRC, 1989a), based on analyses of extensive data for deterministic effects. Additional rationales for approaches used in addressing elicitation questions are summarized in the sections that follow.

Obtaining 5%, 50%, and 95% Values for Dose Percentiles

To obtain the 5%, 50%, and 95% values requested in the elicitation for a given dose percentile (e.g., LD_{10} , LD_{50} , or LD_{90}), in most cases, a subjective degree-of-belief distribution was constructed for input parameters for models used to generate the dose percentiles. The subjective degree-of-belief distribution was assigned a triangular shape for each parameter. A triangular distribution was selected for the following reasons:

- it requires only lower bound, upper bound and central estimates of parameters;
- the most weight is assigned to the central estimate;
- little weight is usually assigned to values near bounds;
- zero weight is assigned to values outside bounds;
- it provides a reasonable measure of degree of belief.

Because models used in this elicitation process are the same as those presented in USNRC reports (USNRC, 1989a, 1993a) and because lower bound, central, and upper bound estimates of model parameters are mainly provided in the cited reports, use of a triangular degree-of-belief distribution for model parameters was the logical choice. The lower and upper bounds for model parameters were selected in ways judged by a USNRC Early Effects Working Group (USNRC, 1990, 1993a) to account for key uncertainties that include: (1) statistical errors associated with model parameters; (2) possible systematic error associated with use of Weibull-type functions; (3) uncertainty about dose protraction effects; (4) uncertainty associated with cross-species extrapolation; (5) uncertainty about the protection provided by supportive treatment; and (6) uncertainty in threshold dose.

Dose-Response Model Used to Estimate Tolerance Dose Percentiles

The two-parameter Weibull model was used to estimate the threshold, D_{10} , and D_{90} for the quantal deterministic effects considered. The form of the Weibull model is the same as

presented in NUREG/CR-4214 reports (USNRC, 1989a, 1990, 1993a, 1993b) and elsewhere (Scott et al., 1988) and has the structure

$$\text{Risk} = 1 - \exp[-H], \quad (1)$$

$$\text{Cumulative hazard } H = \ln(2)(D/D_{50})^V, \quad (2)$$

where D is absorbed dose and V is shape parameter. The model was selected for the following reasons:

- adequately describes dose-response relationships for numerous deterministic effects (Scott et al., 1988; USNRC, 1989a, 1990, 1993a, 1993b).
- can represent sigmoidal or other dose-response curve shapes.
- can be adapted to accommodate effects of a changing dose rate by replacing D/D_{50} with normalized dose X (which is calculated as $X = \int [d/D_{50}(d)]dt$, for instantaneous dose rate d at time t) (Scott et al., 1988; USNRC, 1989a); the integral is evaluated over the period of exposure (presumed continuous).
- can be adapted to accommodate mixed radiation fields by calculating separate normalized doses for high- and low-LET radiations and adding the normalized doses (Scott et al., 1990; Scott, 1994; USNRC, 1989b, 1993a).
- can be adapted to accommodate non-uniform exposure (Scott, 1995; Scott et al., 1995).
- model uncertainty associated with use of the Weibull model (rather than the unknown true model) can be accommodated by extending the range of uncertainty in model parameters (USNRC, 1990).
- leads to a systematic approach to characterizing risks for deterministic effects (USNRC, 1989a&b, 1990, 1993a&b).

Application of the Weibull model in this elicitation process was achieved by assigning a degree-of-belief distribution for the shape parameter V for each deterministic effect considered. For the pulmonary syndrome mode of death, for internal β or α irradiation, a triangular distribution with parameters (4, 5, 6) was used. For lethal damage from irradiation of bone marrow by external γ rays, a triangular distribution with parameters (4, 6, 8) was used. For lethal damage to the small or large intestine (colon), a triangular

distribution with parameters (8, 10, 12) was used. Parameters for these triangular distributions correspond to lower bound, central, and upper bound estimates provided for V in USNRC reports (USNRC, 1989a, 1993a). For morbidity effects of irradiation of the lung, the same values were used for V as for lethality as recommended in USNRC reports (USNRC, 1989a&b, 1990, 1993a&b).

Dose-Rate Dependent Model Used for D_{50} for Low-LET Effects

An empirical model developed for evaluating dose-rate effects (Scott et al., 1988) and presented in NUREG/CR-4214 reports (USNRC, 1989a, 1990, 1993a&b) was used to obtain the median tolerance dose (D_{50}) for specific deterministic effects of irradiation. The empirical model has the structure

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

where d is used here to represent the dose rate in Gy/h when $D_{50}(d)$ is in Gy. The parameter θ_∞ represents the asymptotic value of D_{50} observed when d becomes very large (e.g., 100 Gy/h). The parameter θ_1 gives the increase in the D_{50} above θ_∞ when $d = 1$ Gy/h. Equation 3 has been demonstrated to adequately represent the LD_{50} for death from the hematopoietic syndrome mode after total-body exposure to photons for different species (humans, mice, rats, dogs, swine, goats, sheep) (Scott et al., 1988; Scott and Dillehay, 1990; USNRC, 1989a). Models recommended by a USNRC Early Effects Working Group for use in evaluating the LD_{50} for death from the pulmonary and hematopoietic syndrome modes after exposure to internal β and/or external γ radiation are based on Equation 3 (USNRC, 1989a). Also, models being developed by the National Radiological Protection Board for characterizing LD_{50} or ED_{50} for a variety of deterministic effects are based on Equation 3 (Stather, personal communication).

For this elicitation, degree-of-belief distributions were assigned to θ_1 and θ_∞ for the hemopoietic and pulmonary syndrome modes of death for exposure to low-LET β and/or γ radiations based on lower bound, central, and upper bound estimates presented in a USNRC report (USNRC, 1989a). For the hematopoietic mode, θ_∞ was assigned a triangular distribution with parameters (2.5 Gy, 3.0 Gy, 3.5 Gy), based on dose to bone marrow; θ_1 was assigned a triangular distribution with parameters (0.06 Gy²/h, 0.072 Gy²/h, 0.084 Gy²/h), based on dose to the bone marrow. For the pulmonary syndrome mode of death, θ_∞ was assigned a triangular distribution with parameters (8 Gy, 10 Gy, 12 Gy), based on dose to the lung; θ_1 was assigned a

triangular distribution with parameters (15 Gy²/h, 30 Gy²/h, 45 Gy²/h), based on dose to the lung.

For the gastrointestinal mode of death, a triangular distribution was used for θ_∞ with parameters (10 Gy, 15 Gy, 20 Gy), based on a 1989 NUREG/CR-4214 report (USNRC, 1989a) and dose to the small intestine or colon (the largest dose for the two sites was used). The cited report did not provide an estimate of the parameter θ_1 for the gastrointestinal syndrome mode of death. However, using data for the gastrointestinal mode of death after gavage feeding of ¹⁰⁶Ru-¹⁰⁶Rh to Wistar rats (Sullivan et al., 1988) along with lower bound, central, and upper bound estimates of θ_∞ , θ_1 was assigned a triangular distribution with parameters (2 Gy²/h, 4 Gy²/h, 6 Gy²/h). For this elicitation, where total doses to the colon were higher than total doses to the small intestines, risk calculations were based on doses to the colon. Otherwise, the risks were based on doses to the small intestine.

Based on Equation 3, the dose rate at which the D_{50} is twice as large [doubling dose rate (DDR)] as the high-dose-rate, asymptotic value θ_∞ , is given by $DDR = \theta_1/\theta_\infty$. Thus, uncertainty in parameters θ_1 , and θ_∞ contribute to uncertainty in the DDR. This uncertainty was evaluated by the Monte Carlo Method.

Dose-Rate Dependent Model Used for D_{50} for High-LET Effects

High linear-energy-transfer (LET) α -radiation effects in the lung were accounted for through use of an relative biological effectiveness (RBE) factor (often used approach) here indicated as RBE_α . The factor RBE_α can be used to convert the D_{50} for β/γ -induced effects into the corresponding value for α irradiation. For low-LET β and/or γ irradiation, D_{50} is represented here as:

$$D_{50\beta\gamma} = (\theta_1, \beta\gamma/d\beta\gamma) + \theta_\infty, \beta\gamma \quad (4)$$

The variable $d\beta\gamma$ is the low-LET dose rate (either constant or averaged over a preferably short exposure period). For high-LET α radiation, the corresponding equation can be obtained by first replacing $d\beta\gamma$ in Equation 4 with the corresponding adjusted alpha radiation dose rate (USNRC, 1993a) $(RBE_\alpha)d_\alpha$ which equals $d\beta\gamma$ (where d_α is the α dose rate to the target tissue) and dividing the resultant equation by RBE_α to convert to corresponding Grays of α radiation. This leads to the following equation for evaluating the D_{50} for a specified deterministic effect for α irradiation

$$D_{50\alpha} = (\theta_1, \beta\gamma/(RBE_\alpha^2 d_\alpha)) + (\theta_\infty, \beta\gamma/RBE_\alpha) \\ = (\theta_1, \alpha/d_\alpha) + \theta_\infty, \alpha \quad (5)$$

where

$$\theta_1, \alpha = \theta_1, \beta\gamma/RBE_\alpha^2, \text{ in units of Gy}^2/h, \\ \theta_\infty, \alpha = \theta_\infty, \beta\gamma/RBE_\alpha, \text{ in units of Gy.}$$

Equations 4 and 5 apply to fixed dose rates or to changing dose rates averaged over relatively short time intervals. For application of Equation 5 in the present elicitation, a degree-of-belief distribution was needed for RBE_α . A triangular distribution with parameters (5, 7, 10) was initially selected for RBE_α with the lower bound, central, and upper bound estimates being the same as recommended in a USNRC report (USNRC, 1993a). However, because the RBE_α can increase as dose rate decreases (ICRP, 1990) and because very low dose rates apply to the elicitation question related to α irradiation of the lung, a wider range of uncertainty was subsequently judged to be needed for RBE_α . Thus, the triangular distribution of (5, 12, 20) was used instead of the triangular distribution (5, 7, 10). The central value of 12 was selected because it generated results similar to those observed in studies in beagle dogs exposed via inhalation to the α -emitting aerosol $^{239}\text{PuO}_2$, when followed for 3 years (period of interest for this elicitation for α irradiation) (Scott et al., 1986).

The upper bound for RBE_α corresponds to the judgmental maximum at low dose rates (same as the current central estimate for stochastic effects) (USNRC, 1993a). A wide range of uncertainty in RBE_α for deterministic effects in the lung was therefore used for this elicitation to account for a larger uncertainty at the very low dose rates considered. Different distributions of uncertainty in RBE_α would likely apply for different exposure scenarios (e.g., for different nuclear accidents involving different α radiation dose rates to the lung). However, new research is needed related to evaluating RBE_α (and its uncertainty) for deterministic effects as a function of dose rate to the lung. Preliminary results of studies of workers at the MAYAK Production Association (PA) in Russia (Okladnikova, 1996) that were exposed over a number of years (presumably at low dose rates) to α radiation from inhaled ^{239}Pu , suggest that RBE_α for deterministic effects in the lung may be higher than the upper bound of 10 recommended in a USNRC publication (USNRC, 1993a).

Accounting for Protection Provided by Supportive Treatment

To account for the influence of supportive or other treatment provided to irradiated persons, a protection factor (PF) was used to modify (multiply) the D_{50} for death via the hematopoietic syndrome mode. This is the same approach as recommended in NUREG/CR-4214 reports (USNRC 1989a). Multiplying the D_{50} for death via the hematopoietic syndrome mode by PF shifts the dose-response curve for lethality along the dose axis (to the right) by the factor PF. For this elicitation, a triangular degree-of-belief distribution was used for PF for protection against lethal injury to the hematopoietic system for the supportive treatment category. Parameters of the triangular distribution were (1.3, 1.5, 2). The lower bound estimate of PF=1.3 is based on data reported in an USNRC report for dogs exposed to fission neutrons (USNRC, 1989a). The central estimate of PF=1.5 is the value recommended for humans in the cited USNRC report based on animal studies with low-LET radiation. The upper bound estimate of PF=2 is based on data for Chernobyl accident victims presented in Figure 2.4 of the cited USNRC report.

For exposure at very low dose rates, large radiation doses may be required to induce death via the hematopoietic mode. In such circumstances, it is unclear whether supportive treatment will be necessary after protracted doses of a few Gy. Supportive treatment was not found necessary for workers chronically exposed at very low dose rates to such doses of external γ rays for several years while working at the MAYAK PA in Russia (Okladnikova, personal communication).

Protection factors afforded by supportive treatment for deterministic effects in the lung or gastrointestinal tract have not been reported.

Accounting for Age-Related Sensitivity Differences

Published data have suggested that for the induction of radiation pneumonitis, persons under age 21 y appear more resistant than persons over age 21 y (Weiner et al., 1986). Using these data and the Weibull dose-response model, it was deduced that persons under age 21 y would require doses about 1.2 times larger than persons over age 21 y for inducing radiation pneumonitis. This age-related susceptibility factor (SF) of 1.2 is much less important than was implied by the recommended SF of 2 in a 1989 NUREG/CR-4214 report (USNRC 1989a) for persons over age 40 (relative to persons under age 40). The SF of 2 was based on extrapolation from animal data. Because the age-

related susceptibility factor of 1.2 is based on humans and is small in comparison to changes related to dose rate and radiation quality (RBE), age-related changes in susceptibility for the induction of death via the pulmonary syndrome mode were considered not important enough for inclusion in this elicitation response. However, for respiratory-functional morbidity, an SF of 2 was used for persons over age 50 (relative to those under age 50) for obtaining the lower 5% value for the threshold, ED₁₀, ED₅₀, and ED₉₀ percentiles. Use of a SF of 2 for deriving the 5% values for these dose percentiles is presumed to account for uncertainty about age-related changes in susceptibility for the induction of respiratory-functional morbidity, as defined in this elicitation.

Age-related changes in susceptibility were considered negligible for lethal injury to the gastrointestinal tract or bone marrow which is consistent with the approach used in NUREG/CR-4214 reports. As in a 1989 NUREG/CR-4214 report (USNRC 1989a), bounds on model parameters were presumed to account for key uncertainties.

Dealing with Competing Modes of Death

For competing modes of death, separate lethality hazard (cumulative hazards) were calculated for each mode of death, and the different lethality hazards were added to obtain the total lethality hazard. This method of accounting for competing risk is identical to that used in NUREG/CR-4214 reports (USNRC, 1989a, 1993a&b). However, the use of this approach has two implied assumptions: (1) synergistic effect between organs is negligible; and (2) radiosensitivity of different organs is not correlated. The indicated method was not applied in this elicitation process to exposure scenarios where large areas of the skin are severely damaged by β radiation in combination with large radiation doses to internal organs such as bone marrow.

Generating Distributions for Elicited Variables

In most cases, distributions (e.g., 5%, 50%, 95% values) were generated using the Monte Carlo approach based on triangular degree-of-belief distributions for model input parameters. For each Monte Carlo run, 5000 trials were used to obtain degree-of-belief distributions for the outcome variable. Crystal Ball software was used to carry out the Monte Carlo calculations (Decisioneering, 1993).

For evaluating effects of changing dose rates or evaluating competing modes of death, no analytical solution could be obtained for the LD₁₀, LD₅₀, and LD₉₀; thus, Monte Carlo calculation of uncertainty-related distributions was not

carried out. Instead, the key input variables (e.g., initial dose rate) were systematically changed (with model parameters fixed at central estimates) until the desired level of risk was achieved. The 5% and 95% values were in most cases estimated using combinations of upper and lower bounds on model parameters. In a few instances where this approach led to unsatisfactory results (e.g., too narrow a spread in uncertainty), simple scaling based on estimates of ratios (5% value)/(50% value) and (95% value)/(50% value) from other related elicitation questions were used to obtain the 5% and/or 95% value from the 50% value. Thresholds were estimated as 50% of the D₅₀.

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Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.4	1.5	1.6	2.1	2.3	2.8
LD10	1.9	2.2	2.4	3.0	3.3	4.1
LD50	2.7	3.0	3.3	4.1	4.5	5.6
LD90	3.3	3.7	4.0	5.0	5.5	6.9

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.4	1.5	1.6	2.1	2.3	2.8
LD10	1.9	2.2	2.4	3.0	3.3	4.1
LD50	2.7	3.0	3.3	4.1	4.5	5.6
LD90	3.3	3.7	4.0	5.0	5.5	6.9

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.4	1.5	1.7	2.1	2.3	2.9
LD10	2.0	2.2	2.4	3.0	3.4	4.2
LD50	2.8	3.1	3.4	4.2	4.6	5.7
LD90	3.4	3.8	4.1	5.2	5.6	7.0

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.6	1.7	1.8	2.3	2.5	3.1
LD10	2.2	2.5	2.7	3.4	3.7	4.6
LD50	3.1	3.4	3.7	4.7	5.0	6.2
LD90	3.8	4.1	4.5	5.7	6.2	7.7

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.02	0.024	0.03

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	>0.5
10 Gy/hr	>0.5
1 Gy/hr	>0.5
0.2 Gy/hr	>0.5

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	1	1
10 Gy/hr	1 Gy/hr	1	1
1 Gy/hr	0.2 Gy/hr	1	1

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	6.2	7.5	8.9	>6.2	>7.5	>8.9
LD10 _{GI}	10.0	13.0	15.0	>10.0	>13.0	>15.0
LD50 _{GI}	12.0	15.0	18.0	>12.0	>15.0	>18.0
LD90 _{GI}	14.0	17.0	20.0	>14.0	>17.0	>20.0

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	6.4	7.7	9.1	>6.4	>7.7	>9.1
LD10 _{GI}	11.0	13.0	15.0	>11.0	>13.0	>15.0
LD50 _{GI}	13.0	15.0	18.0	>13.0	>15.0	>18.0
LD90 _{GI}	14.0	17.0	21.0	>14.0	>17.0	>21.0

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	8.1	9.5	11.0	>8.1	>9.5	>11.0
LD10 _{GI}	13.0	16.0	18.0	>13.0	>16.0	>18.0
LD50 _{GI}	16.0	19.0	22.0	>16.0	>19.0	>22.0
LD90 _{GI}	18.0	21.0	25.0	>18.0	>21.0	>25.0

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	15.0	18.0	21.0	>15.0	>18.0	>21.0
LD10 _{GI}	24.0	29.0	34.0	>24.0	>29.0	>34.0
LD50 _{GI}	29.0	35.0	41.0	>29.0	>35.0	>41.0
LD90 _{GI}	33.0	40.0	46.0	>33.0	>40.0	>46.0

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.2	0.27	0.4

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	_____
10 Gy/hr	_____
1 Gy/hr	_____
0.2 Gy/hr	_____

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	1	1
10 Gy/hr	1 Gy/hr	1	1
1 Gy/hr	0.2 Gy/hr	1	1

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	0.5	0.5
10 Gy/hr	0.5	0.5
1 Gy/hr	0.5	0.5
0.2 Gy/hr	0.5	0.5

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	4.5	5.2	5.9	4.5	5.2	5.9
LD10	6.1	7.1	8.1	6.1	7.1	8.1
LD50	8.9	10.0	12.0	8.9	10.0	12.0
LD90	11.0	13.0	15.0	11.0	13.0	15.0

Lung dose rate of 10 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	5.7	6.5	7.3	5.7	6.5	7.3
LD10	7.7	8.9	10.0	7.7	8.9	10.0
LD50	11.0	13.0	15.0	11.0	13.0	15.0
LD90	14.0	17.0	19.0	14.0	17.0	19.0

Lung dose rate of 1 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	15	20	25	15	20	25
LD10	20	27	35	20	27	35
LD50	30	40	51	30	40	51
LD90	38	51	64	38	51	64

Lung dose rate of 0.2 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	55	80	106	55	80	106
LD10	75	110	146	75	110	146
LD50	109	160	212	109	160	212
LD90	139	203	271	139	203	271

For persons over 50 years of age, can also use results for persons 18-50 years old.

Dependencies

Age Groups: Probability that the true LD50 for individuals 18-50 years old is above the 50% value.

100 Gy/hr	1
10 Gy/hr	1
1 Gy/hr	1
0.2 Gy/hr	1

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 18	18-50	Over 50
100 Gy/hr	10 Gy/hr	1	1	1
10 Gy/hr	1 Gy/hr	1	1	1
1 Gy/hr	0.2 Gy/hr	1	1	1

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 18	18-50	Over 50
100 Gy/hr	0.5	0.5	0.5
10 Gy/hr	0.5	0.5	0.5
1 Gy/hr	0.5	0.5	0.5
0.2 Gy/hr	0.5	0.5	0.5

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	2.7	3.4	4.6	2.7	3.4	4.6
ED10	3.6	4.7	6.3	3.6	4.7	6.3
ED50	5.3	6.9	9.1	5.3	6.9	9.1
ED90	6.8	8.7	12.0	6.8	8.7	12.0

Lung dose rate of 10 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	3.4	4.3	5.8	3.4	4.3	5.8
ED10	4.6	6.0	7.9	4.6	6.0	7.9
ED50	6.8	8.7	12.0	6.8	8.7	12.0
ED90	8.6	11.0	15.0	8.6	11.0	15.0

Lung dose rate of 1 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	9.4	13.0	19.0	9.4	13.0	19.0
ED10	13.0	18.0	26.0	13.0	18.0	26.0
ED50	19.0	27.0	37.0	19.0	27.0	37.0
ED90	24.0	34.0	47.0	24.0	34.0	47.0

Lung dose rate of 0.2 Gy/hr

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	31	53	77	31	53	77
ED10	48	73	106	48	73	106
ED50	70	107	154	70	107	154
ED90	90	136	197	90	136	197

For persons over 50 years of age, can also use results for persons 18-50, for 50% and 95% values. However the indicated 5% values should be reduced by a factor of 2 for the over 50 age group.

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 18 Years Old			Individuals 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	0.00092	0.0014	0.0023	0.00092	0.0014	0.0023
DR10	0.0012	0.0019	0.0032	0.0012	0.0019	0.0032
DR50	0.0018	0.0028	0.0047	0.0018	0.0028	0.0047
DR90	0.0023	0.0036	0.006	0.0023	0.0036	0.006

Under-18 Versus 18-50: Probability that the true LD50 for individuals 18-50 years old is above the 50% value.

100 Gy/hr	1
10 Gy/hr	1
1 Gy/hr	1
0.2 Gy/hr	1

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 18	18-50	Over 50
100 Gy/hr	1	1	1
10 Gy/hr	1	1	1
1 Gy/hr	1	1	1
0.2 Gy/hr	1	1	1

Question 4a – DELETED

Question 4b – DELETED

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.5	1.8	2.0	2.0	2.7	4.0
LD10	2.2	2.6	2.9	2.9	3.9	5.8
LD50	3.0	3.5	4	3.9	5.3	8
LD90	3.6	4.2	4.9	4.7	6.3	9.8

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	1	1
1 Gy/hr	1	1
0.2 Gy/hr	1	1

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.4	1.7	1.9	1.8	2.5	3.8
LD10	2.0	2.5	2.8	2.6	3.6	5.6
LD50	2.8	3.3	3.8	3.6	5.0	7.6
LD90	3.4	4.0	4.7	4.4	6.2	9.4

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

1

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Treatment Supportive Treatment

1

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 18 Years Old			Persons 18-50 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	6.1	8.1	9.8	6.1	8.1	9.8
LD10	9.0	12.0	14.0	9.0	12.0	14.0
LD50	12.0	16.0	20.0	12.0	16.0	20.0
LD90	15.0	20.0	25.0	15.0	20.0	25.0

Under-18 Versus 18-40: Probability that the true LD50 is above the 50% value for the 18-50 age group.

1

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 18	18-50	Over 50
10 Gy/hr	1	1	1
1 Gy/hr	1	1	1
0.2 Gy/hr	1	1	1

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.1	1.2	1.3	1.4	1.8	2.6
LD10	1.6	1.9	2.0	2.1	2.8	4.1
LD50	2.1	2.3	2.6	2.8	3.5	5.1
LD90	2.5	2.7	3.2	3.2	4.1	6.3

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

threshold	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.1	1.2	1.3	1.4	1.8	2.6
LD10	1.6	1.9	2	2.1	2.8	4.1
LD50	2.1	2.3	2.6	2.8	3.5	5.1
LD90	2.5	2.7	3.2	3.2	4.1	6.3

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.1	1.2	1.3	1.4	1.8	2.6
LD10	1.6	1.9	2.0	2.1	2.8	4.1
LD50	2.1	2.3	2.6	2.8	3.5	5.1
LD90	2.5	2.7	3.2	3.2	4.1	6.3

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.1	1.2	1.3	1.4	1.8	2.6
LD10	1.6	1.9	2.0	2.1	2.8	4.1
LD50	2.1	2.3	2.6	2.8	3.5	5.1
LD90	2.5	2.7	3.2	3.2	4.1	6.3

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1	>0.5	2.5	>3.0
2	>0.5	>2.4	>2.4
3	>0.5	2.5	>3.0
4	>2.5	>4.5	>6.0
5	>4.5	>5.5	>6.5
6	>3.5	>6.0	>8.0
7	>3.5	>5.5	>6.0
8	3.0	6.0	9.0
9	5.0	8.0	10.0
10	>4.5	>7.0	>12.0

EXPERT C

1. Models

Dose-incidence data for acute effects have been analysed in the literature using a variety of models. Many of these are empirical in nature, using statistical probability distributions (e.g., probit, logistic, Weibull). Others have a radiobiological basis, related to the depletion of tissue-rescuing units, tissue functional sub-units, or tissue target cells by irradiation according to exponential or modified-exponential dose response functions.

A Weibull-type risk function has been used (NUREG, 1985).

$$\text{Risk} = 1 - \exp(-H)$$

The cumulative hazard function

$$H = \ln 2 \left(\frac{D^V}{D_{50}} \right)$$

where V is a shape parameter describing the slope of the dose-response curve. Hence

$$\text{Risk} = 1 - \exp \left[-\ln 2 \left(\frac{D^V}{D_{50}} \right) \right]$$

An alternative radiobiological approach is based on the following:

$$\text{Risk} = \exp \left[-k \cdot \exp \left(\frac{-D}{D_0} \right) \right]$$

where k is the number of tissue-rescuing units at risk, of which one surviving unit will rescue the tissue or organ from failure (Thames and Hendry, 1987). D_0 is the mean lethal dose for the units, often taken to be the same as that for the target cells responsible for renewing the damaged units. This correspondence is probably more appropriate in the case of early-reacting tissues, e.g., marrow or lung, rather than late-reacting tissues where tissue structure plays an increasingly important role, e.g., CNS or kidney. The D_0 can be replaced by $1/(\alpha + 2\beta D)$ to take account of the

steepness increasing more than exponentially with increasing dose. Hence

$$\text{Risk} = \exp \left[\ln 0.5 \exp \left(\frac{LD_{50} - D}{D_0} \right) \right]$$

or

$$\exp \left[\ln 0.5 \exp \{ (LD_{50} - D) \cdot (\alpha + 2\beta D) \} \right]$$

A comparison of the two approaches is shown in Figure 1. The example chosen is where $LD_{50} = 3.4$ Gy and $V = 10$. This is intermediate between probit curves with coefficients of variation 10% and 20% for mortality 0–50%. For mortality levels of 50–100%, $V = 10$ corresponds better to $CV = 10\%$ on a probit plot. $V = 6$ corresponds to $CV = 20\%$ at low levels of mortality. The radiobiological function based on $D_0 = 0.8$ Gy fits the curve for $CV = 20\%$ fairly well for 1–50% mortality, but it curves off less rapidly than the probit or V functions at high levels of mortality. Good agreement between the curves for $V = 10$ and say $D_0 = 0.56$ Gy can be achieved over the mortality range 3–50% but the curves deviate at higher levels of mortality. Allowing for a lowering of D_0 with increasing dose by using $\alpha/\beta = 15$ Gy, mortality increases at high doses (the arrow at 5 Gy) to values near those predicted using the $CV = 20\%$ probit curve. Hence the empirical probit curve and this radiobiologically-based curve can be brought into good agreement over the range of mortality under consideration. To re-iterate, the Weibull curve is convex compared to probit with mortality increasing more with increasing dose. In contrast, the radiobiological model is concave compared to probit; mortality increases less with increasing dose. However, the linear-quadratic version of the radiobiological model is close to probit.

Other features of the Weibull approach are (a) the convex shape may be appropriate when there are competing risks of mortality, and a second target tissue comes into play at higher doses so steepening the curve, and (b) the product of risks from two or more irradiated organ systems can be simply accommodated, with the caveat that any synergism is not taken into account.

2. Data

Reliance has been placed heavily on data sources referenced in NUREG (1985) and UNSCEAR (Annex G, 1988).

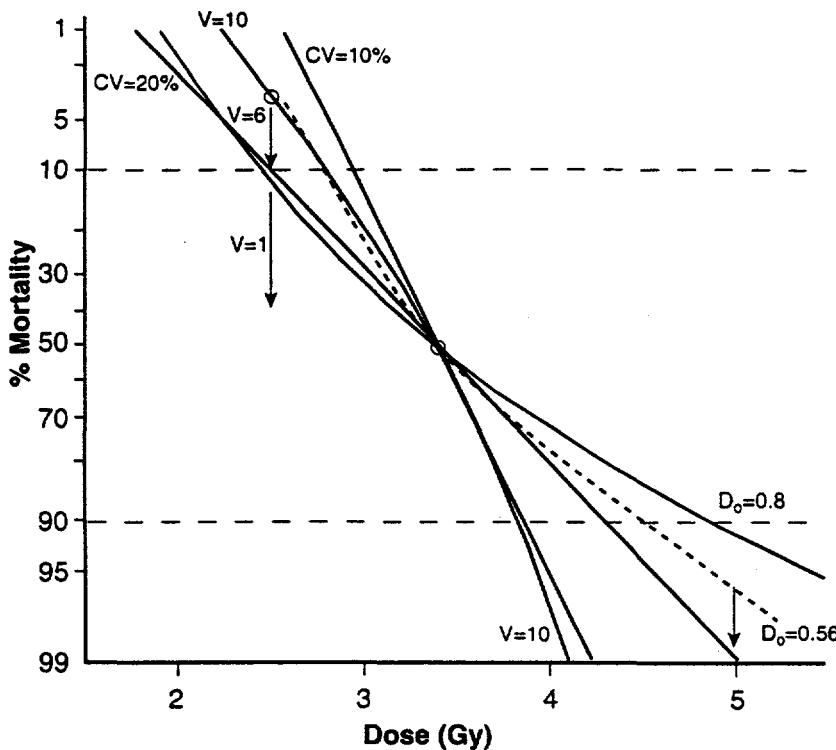


Figure 1. Comparison of model functions for describing the incidence of mortality versus dose, taking $LD_{50} = 3.4$ Gy as an example. These comprise probit curves with coefficients of variation (CV) of 10% and 20%, Weibull functions using $V = 10$ (the effect of choosing $V = 6$ or $V = 1$ is shown by the vertical arrows), and double-log functions assuming $D_0 = 0.8$ Gy or 0.56 Gy to coincide with the curve for $V = 10$ at 2.5 Gy.

2.1 Bone Marrow

2.1.1 High dose-rate

Data for man comprise (a) Two series of cancer patients given whole-body irradiation together with chemotherapy for the treatment of disseminated disease (Langham, 1967; Lushbaugh et al., 1966), (b) a series of patients given whole-body irradiation for immune suppression prior to organ transplantation (Mathé et al., 1964), (c) some accident cases and a small series of relatively-fit adolescents with osteosarcoma given whole-body irradiation for metastatic disease (Mole, 1984; 1985; Mathé et al., 1964), and (d) various groups of Japanese irradiated by the A-bombs in World War II (Fujita et al., 1987).

The above data suggest that the $LD_{50/60}$ is about 3 Gy marrow dose (2.7 Gy mid-line dose) for the Japanese with minimal medical support, and for the cancer patients (Figure 2). The slopes of the dose-response curves are fairly flat. However, it is unlikely that the back extrapolation of these curves can be true using any model, because they predict up to 10% mortality at doses up to 1 Gy. It is more likely that this slope flattening is due to heterogeneity peculiar to these populations, in terms of dosimetry

(Japanese) or health status (cancer patients). For control populations it is likely that the curves are steeper, corresponding to a CV of 20–25% (as for other large animals), and with an $LD_{50/60}$ of possibly 3–3.5 Gy. The slope would correspond to a shape parameter $V = 6-7$ (Figure 1). This would give on a probit plot $LD_{10} = 2.2$ Gy, and $LD_{90} = 4.3$ Gy.

What is a threshold dose? A threshold level of 0.005, i.e., 1/200, seems a reasonable definition (NUREG, 1985), if several hundred people are exposed to high doses in a reactor accident. On a probit plot, this threshold would be about 1.2 Gy. If several thousand people are exposed, 0.001 is probably a more appropriate level with a threshold dose of around 1 Gy. Taking 95% confidence limits to exclude “unlikely” values, it is unlikely that the LD_{50} is less than 2.5 Gy, nor greater than say 4.5 Gy. It is unlikely that anyone would die from doses less than 1 Gy, the upper bound here being 2.0 Gy. The proportion of individuals in the general population with genetic syndromes resulting in increased sensitivity by two- or three-fold is unlikely to be greater than 1 in 10^4 . Hence, the dose corresponding to a threshold level of 1 in 10^3 reflects the heterogeneity in response of the population due to a combination of individual variability in genetic constitution together with

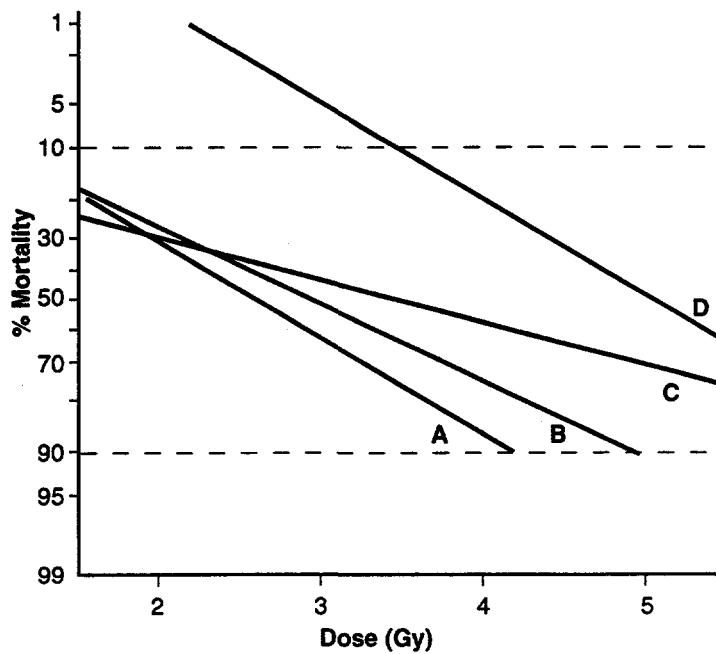


Figure 2. Dose-mortality curves for hemopoietic failure in man derived from data for ill cancer patients receiving radiotherapy (curves A and B), transplantation patients receiving whole-body irradiation (TBI) for immunosuppression (curve E), and relatively fit adolescents with osteosarcoma receiving TBI for metastatic deposits (curve D).

the stochastic variability in surviving target cell number. LD₉₀ is unlikely to be less than 2.5 Gy, nor greater than 6 Gy.

Supportive treatment will increase the LD_{50/60}. The human data pertain to several accident cases and the cancer patients. Intensive treatment with growth factors in dogs and in monkeys has been shown to increase the LD_{50/30} by at least 1.5 Gy (reviewed by MacVittie and Farese, 1995). The human data are consistent with this. Here it has been assumed that the slope remains the same; there is little evidence to suggest otherwise. Radiobiologically, one would expect an increase in steepness at tolerable higher doses, but treatment may be more efficacious at higher doses, thus reversing the trend. On balance the same slope has been assumed, and the "confidence" values have been increased by 1 Gy.

2.1.2 Low dose-rates

There are few reliable human data regarding LD_{50/60} for protracted irradiation. There are a few accidents, fall-out irradiation from A-bomb tests, and radiotherapy patients receiving low-dose-rate or fractionated irradiation. Models have been devised to calculate dose-rate effects; these are either empirical and too simple to be used with any

confidence, or biologically-based and too complex with many unknown parameter values. Here the judgement has been based on radiobiological modeling of mouse data, scaled to the human acute equivalent doses. "Confidence" values cannot really be made with confidence.

Three comprehensive mouse datasets have been analysed together using the Millar et al. (1993) model. These comprise data for a range of doses and dose-rates, with an LD_{50/30} endpoint. The model is based on a Poisson approach, with parameters α , β , TRU number, and repair half time. The fitted dose-mortality curves are shown in Figure 3 for the different chosen dose-rates. The high dose-rate LD₅₀ was 8.3 Gy, i.e., two to three times the value for man. On the radiobiological basis that the sparing effect of dose-rate is dose-dependent, the human values have been scaled by *half* the increase in dose in mice at the various low dose-rates. Confidence intervals and values for supportive treatment have been similarly scaled.

For the dose-rate at which LD₅₀ doubles, data in UNSCEAR, Annex G, Table 19 (1988) have been used. Probably 6 Gy (i.e., 2 \times LD₅₀ at high dose rate) delivered over 15 days would be close, giving a dose-rate of 0.017 Gy/hour rounded to 0.02 Gy/hour.

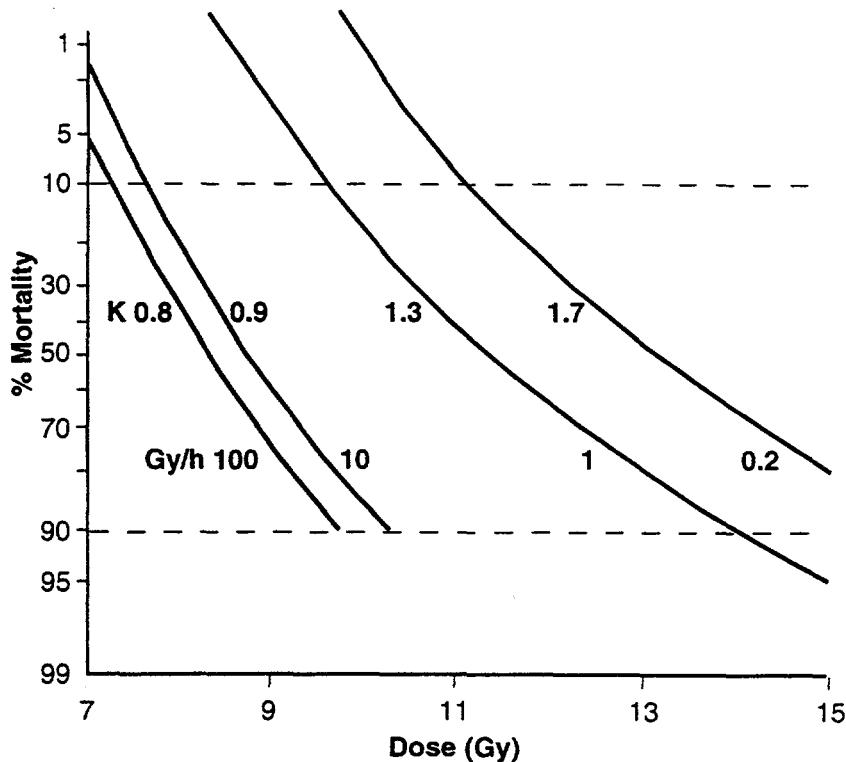


Figure 3. Calculated dose-mortality curves for hemopoietic failure in mice using a double-log model incorporating biphasic repair. Dose-rates of 100, 10, 1, and 0.2 Gy/hour. Approximate corresponding probit widths (PW) indicated on curves.

2.1.3 Dependencies

In view of the uncertainties in the LD_{50} both with and without support, the probabilities are given as 50%. Dose-rate effects are more sound, although they are scaled on the basis of mouse values. For both minimal and supportive treatment 75% dependency is stated, i.e., halfway between zero (50%) and the full amount (100%).

3.1 Intestine

3.1.1 High dose-rate

There are no good dose-incidence data for the GI syndrome in man. Probably the best group is 8 deaths out of 21 people in the Hiroshima Bankers Club at the time of the A-bombing (Oughterson et al., 1955), but the dose is not accurately known. Otherwise, there are the radiotherapy patients noting signs of GI injury (but not death) at doses ≥ 12 Gy delivered at 0.05 Gy/minute (Deeg, 1983). For conventionally-housed mice the $LD_{50/7}$ is about 11 Gy at high dose-rate. NUREG (1985) used 15 Gy for man, based on exteriorized exposures of rat intestines and the human (transplant) doses of 10 Gy (at 0.05 Gy/minute) not causing

acute deaths. Humans are generally *less* tolerant than rodents. Hence the $LD_{50/7}$ or 10 is put at around 10 Gy (1.7 Gy/minute). This corresponds to around 17 Gy at 0.05 Gy/minute. The slope is problematic. NUREG (1985) chose $V = 10$ (as for the marrow). For $LD_{50} = 10$ Gy, $V = 10$ corresponds to a probit width of about 1.3 Gy and a D_0 of 1.0 Gy. The latter is less than the D_0 of 1.3 Gy deduced from mouse mortality data, which itself is consistent also with intestinal colony data (Hendry et al., 1983). Also, other heterogeneity factors are likely to decrease V . $V = 8$ has been chosen, which corresponds to a probit width of 1.6 Gy and a D_0 of 1.3 Gy (as above). The true curve for man, however, is likely to be less steep than this. An attempt has been made here to match up (a) the lack of deaths in the radiotherapy patients at 12 Gy (0.05 Gy/minute) and (b) the factor of 1.7 between the mouse LD_{50} at 0.05 and >1.0 Gy/min (Thames and Hendry, 1987). Reasonable agreement is achieved for $LD_{50} = 10$ Gy (1.7 Gy/min), $V = 8$, and $LD_{50} = 17$ Gy (0.05 Gy/min) (Figure 4). For the different dose-rates requested, I have just scaled all values at high dose-rate by factors 1.4 (0.17 Gy/min), 1.9 (0.017 Gy/min), and 2.2 (0.0033 Gy/min). Confidence intervals on all these values are really conjectural.

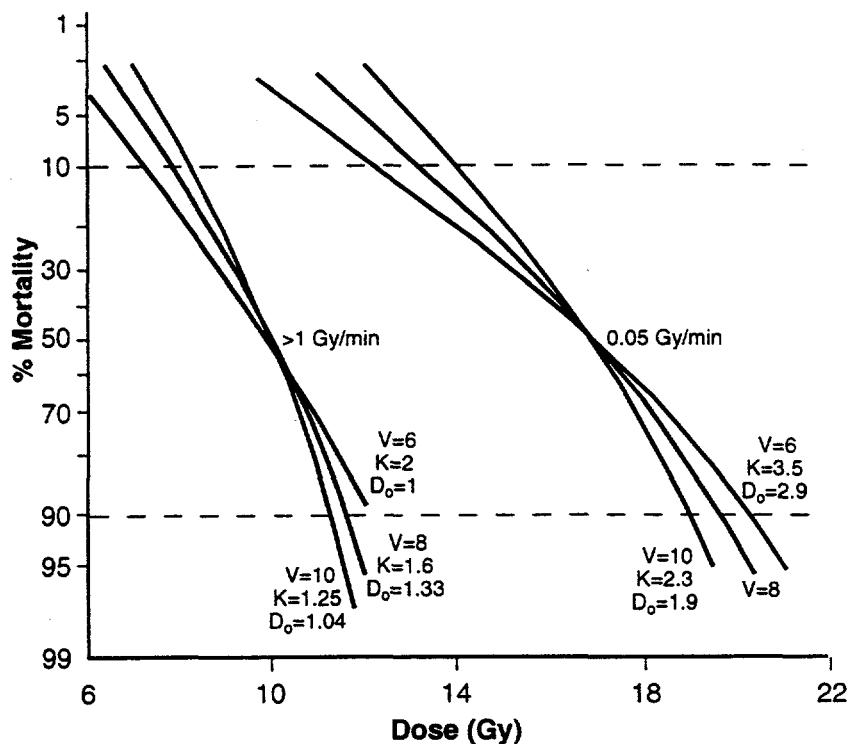


Figure 4. Estimated dose-mortality curves for intestinal failure in man, based on $LD_{50} = 10$ Gy and $V = 6, 8$ or 10 Gy, at high dose-rate (>1 Gy/min.) or low dose-rate (0.05 Gy/min.). Corresponding approximate values of probit width (K) and D_0 shown on curves.

The values applicable with supportive treatment are also conjectural. There are no data for man, and very little for experimental animals. For mice, the LD_{50} can be increased by around 1 Gy (i.e., 10%) with antibiotic treatments (Hendry et al., 1983) and for rats by 40% using salt solutions as well as antibiotics (Taketa, 1962). A value of 40% has been used for the present purpose, at all LD values. At even higher LD values, e.g., LD_{100} , there would be no effect of support because all individuals would have zero clonogens surviving anyway. However, this does not apply in the present case because even at LD_{90} 10% of individuals survived and others could be rescued with a reasonably good content of clonogens. At very high doses, latency times to death may be increased using supportive treatment, but not the eventual outcome.

3.1.2 Dependencies

There probably is some positive dependence for support at the high dose-rate (70%). However, the uncertainty in the dose-rate effect suggests a reduction in this to zero (i.e., 50%) at the lower dose-rates. Similarly, for dose-rate, any dependence probably declines to zero (50%) at the lower dose rates. The LD_{50} (marrow) and LD_{50} (GI) are well-separated in dose, particularly at the lower dose-rates. A

very small amount of dependence has been assumed, and more with supportive treatment e.g., it is likely that antibiotics would affect both syndromes to some (but different) extents.

3.2 The Lungs

It is stated that following the exposure period the dose-rate drops rapidly to zero. This is unlikely to be the case in practice with many long-lived and retained radionuclides. ^{80}Y is probably the nearest isotope to this scenario. For these high dose-rates and short exposure periods I have used data from van Dyk (1981; 1989), regarding morbidity/mortality after lung irradiation of cancer patients (Figures 5 and 6). Some of these patients died, and hence their data have been taken as reflecting mortality, although the measurements were basically lung-function tests and hence also related to morbidity. The differences in effect resulting in morbidity or mortality are not very clear. NUREG (1985) used dog data to indicate that morbidity doses were 50% of mortality doses. Intuitively this difference seems too large.

[After this document was prepared, an article was found reporting dose-response data for lung density, perfusion, and ventilation (Boersma et al., 1994). The ED_{50} based on

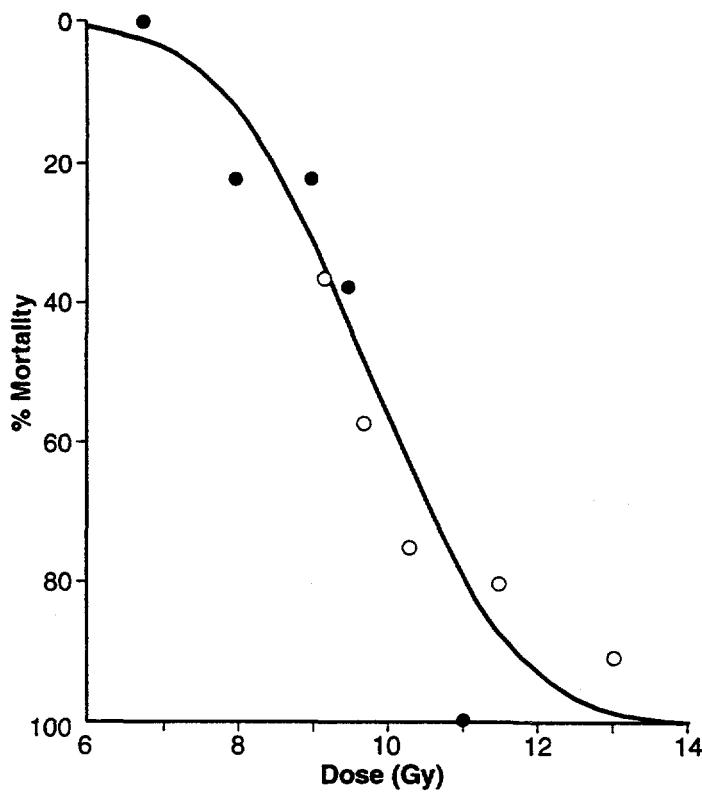


Figure 5. Sigmoid (linear) survival curves for pneumonitis in man, taking data from van Dyk et al. (1981; 1989). Larger symbols indicate data from the first series of patients.

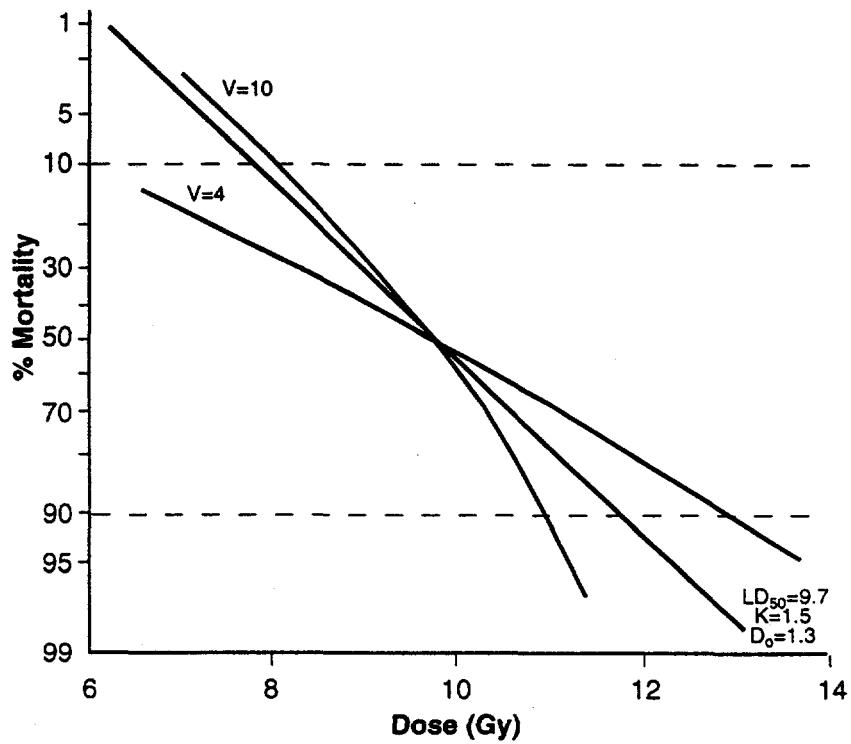


Figure 6. Estimated dose-mortality curves for radiation-induced mortality, deduced from the van Dyk data in Figure 5. $LD_{50} = 9.7$ Gy, probit width = 1.5 Gy, or $D_0 = 1.3$ Gy. Curves are also shown for $V = 4$ or $V = 10$.

lung density was higher than reported by van Dyk et al., with the ED₅₀s for the other endpoints being intermediate. Also the slopes of the dose-response curves were lower than in van Dyk's study, by a factor of about two].

For dose-rate effects, the human values have been scaled by factors derived from mouse data, calculated from data in the literature. In practice, these scaling factors are very similar to those for the intestine.

This writer does not know any good data for effects in young versus adult individuals. Hence the same values have been assumed for both age groups. This also applies to the dependencies regarding age. Again, reliance is placed on the mouse data for the dependency on dose-rate, and no interaction is assumed between lung and marrow endpoints.

Question 3 refers to a 3-year endpoint. The only known relevant data here are for dogs (rats do not live long enough). Even then, in NUREG (1988), in the group of dogs given Pu only (n=10) only one dog survived 428 days, accumulating 48.7 Gy total dose from α rays. Hence there is insufficient information available to make a judgement about LD values for exposures to 3 years.

3.3 The Skin

Question 5 relates to 24 hour skin exposures from beta emitters with average energies such as those from iodine, and uniform deposition on the skin surface. Acute ulceration has been observed after high dose irradiation of 1-2 mm diameter plaques on pig skin (ICRP-59, p. 35). This was attributed to death of fibroblasts and endothelial cells in the dermis, aggravating the epidermal denudation in these small areas. There was a marked field-size effect going from 1 mm to 2 mm with ⁹⁰Sr/⁹⁰Y but not for the less penetrating ¹⁷⁰Tm. An average of all the data for both radiation types and field sizes has been assumed giving an average "surface" ED₅₀ of 270 Gy, ED₁₀ = 120 Gy, threshold = 75 Gy, ED₉₀ = 420 Gy. Assuming no field size effect for this endpoint, a dose-rate factor of 2.5 going from acute to 24-hour exposures, and a reduction in dose at 70 μ m versus 16 μ m by a factor 1.6, gives new dose values respectively of 420, 190, 120, and 660 Gy. The factor 1.6 is not actually the appropriate factor for these calculations. In the experiments conducted, it is calculated that the dose at 70 μ m is not the depth of the endothelial cells and fibroblasts responsible for this particular endpoint of acute ulceration. Hence it is not known at what depth the target cells are in order to specify the dose there, and then to recalculate the dose to a 70 μ m depth. In any case, the target cells may be a combination of stromal/epithelial cells,

making these arguments more speculative still. Hence the original factor of 1.6 has been used from the depth/dose table provided. Any fine adjustments would be well within the overall uncertainties. These are all extrapolated and speculative values. Confidence intervals have been taken as being 50% either way.

Regarding acute epidermal necrosis, Hopewell's data quoted in ICRP-59 has been used, for ¹⁴⁷Pm using 2-15-mm diameter plaques. For the largest field area of 15-mm diameter, dose values were 500 Gy (ED₅₀), 300 Gy (ED₁₀) and 200 Gy (threshold dose) quoted at 16 μ m depth. Hence using a dose-rate factor of 2.5 (24-hour versus acute exposures) and a depth factor of 1.6 (Table 1 of questionnaire), these doses become 780, 470, and 310 Gy respectively. Uncertainties are probably at least 50% either way on these values.

There are no reliable human data where known beta skin doses caused moist desquamation (Question 5c). Moritz and Henriques (1952) using ¹³⁷Cs and pig skin, gave 17 Gy as the relevant dose at 90 μ m. This equals 19.4 Gy at 70 μ m depth using the appropriate depth-dose factor in the table provided. This is about the same as the 20 Gy for ED₁₀ using small field sizes on pig skin with ⁹⁰Sr (Hopewell), and also the 20 Gy tolerance single doses for human skin for (6 \times 4) cm² fields sizes. Doses of 17 Gy (threshold), 20 Gy (ED₁₀), 30 Gy (ED₅₀), and 40 Gy (ED₉₀) therefore have been used for acute surface irradiations using β emitters. For exposures over 24 hours a dose-rate effect has to be allowed for. Two approaches have been used here. One is the simple dose-rate equation applicable to early skin damage in mice and humans. $T = A.R^b$ where T is exposure time, A and b are constants (b = -1.35 for mouse and human skin) and R is the dose-rate (Wilkinson et al., 1980). The Hopewell data for plaques on pig skin were for high dose-rates. He quotes 3.4 Gy/min. for the larger strontium plaques. The above ED values as applicable for 100 Gy/hour (1.7 Gy/min.) have thus been used. In this case, the ED₅₀ for a 24-hour exposure would be 93.4 Gy, i.e., increased by three times. It has also been assumed here that there is no field-size effect for large areas with lightly penetrating radiations, as Hopewell has shown by comparing ¹⁴⁷Pm with ⁹⁰Sr. Hence, for this discussion, the values for different percentages of the body surface exposed are considered to be about the same. The other approach using 24-hour exposures is to use a more elaborate model. The use of one of these models gives 18 Gy (ED₅), 23 Gy (ED₁₀), 29 Gy (ED₅₀), and 36 Gy (ED₉₀) for 100 Gy/hour low LET irradiation, respectively 23, 31, 40, and 52 Gy at 10 Gy/hour, and 37, 53, 96, and 111 Gy at 1 Gy/hour. For the ED₅₀ values, values of b ($T = A.R^b$) are -1.15

(100 \rightarrow 10 Gy/h), -1.38 (10 \rightarrow 1 Gy/h), or overall -1.26 (100 \rightarrow 1 Gy/h). Using the latter gives a two and a half rather than a three fold increase in ED₅₀ for a 24-hour exposure versus an acute exposure. This value has been used to scale the above ED values. The uncertainty in the dose-rate effect has been incorporated into the uncertainties in the various ED values for 24-hour exposures.

6. Decrease in dose-rate

6a.

If the LD₅₀ for a 1-hour exposure is about 3 Gy and about 4 Gy for a 20-hour exposure (response to Question 1), then for 30% of the dose in 1 hour and 70% in 23 hours 25% has been added to the 3 Gy dose and all the other doses. More sophisticated calculations can be done, but these are probably not warranted, considering the uncertainties in the initial starting values.

6b.

With 80% of the dose in the first hour, and 20% in the next 23 hours at a 100 fold lower dose-rate, 10% has been added to all high-dose-rate estimates.

6c.

For the lung, the LD₅₀ was estimated to be 20 Gy at 1 Gy/hour, i.e., delivered in 20 hours. For a 24-hour exposure it might be slightly higher, say 21 Gy, but for simplicity and realizing the uncertainties involved 20 Gy has been used. At 0.2 Gy/hour the LD₅₀ was given as 31.3 Gy, i.e., delivered over 155 hours (6 1/2 days). Hence for 70% of the dose in the first day, and 30% over the next six days, the sum has been taken of 0.7 of the LD₅₀ (1 Gy/hr) and 0.3 of the LD₅₀ (0.2 Gy/hour). This has been done similarly for all other levels of effect.

7. Multiple organs

There is little evidence regarding synergy between damage in lung, skin, and marrow. Potentially, there may be synergy between damage in marrow and intestine regarding the influence of endogenous and exogenous infections in exacerbating injury in both organs, but there is little evidence about this in particular for large animals. It has been considered here that there is little evidence for synergy, and on this basis the COSYMA codes can be used to calculate the combination of effects directly.

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Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	2.0	1.5	2.0	3.0
LD10	1.0	2.0	3.0	2.0	3.0	4.0
LD50	2.5	3.0	4.5	3.5	4.0	5.5
LD90	3.0	4.0	6.0	4.0	5.0	7.0

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	2.0	1.5	2.0	3.0
LD10	1.0	2.0	3.0	2.0	3.0	4.0
LD50	2.5	3.0	4.5	3.5	4.0	5.5
LD90	3.0	4.0	6.0	4.0	5.0	7.0

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.57	1.1	2.2	1.7	2.2	3.4
LD10	1.2	2.3	3.5	2.3	3.5	4.6
LD50	3.0	3.5	5.3	4.1	4.7	6.5
LD90	3.7	4.9	7.3	4.9	6.1	8.5

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.62	1.2	2.5	1.8	2.5	3.7
LD10	1.3	2.5	3.8	2.5	3.8	5.0
LD50	3.3	3.9	5.9	4.6	5.2	7.2
LD90	4.1	5.4	8.1	5.4	6.8	9.5

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
.015	0.02	.03

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	50%
10 Gy/hr	50%
1 Gy/hr	50%
0.2 Gy/hr	50%

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	75%	75%
10 Gy/hr	1 Gy/hr	75%	75%
1 Gy/hr	0.2 Gy/hr	75%	75%

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	3	5	7	4	7	10
LD10 _{GI}	6	8	10	8	11	14
LD50 _{GI}	8	10	12	11	14	17
LD90 _{GI}	10	12	14	14	17	20

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5	7	9	7	10	13
LD10 _{GI}	9	11	13	13	16	19
LD50 _{GI}	12	14	16	17	20	22
LD90 _{GI}	15	17	19	21	24	26

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	8	10	12	11	14	17
LD10 _{GI}	13	15	17	18	21	24
LD50 _{GI}	17	19	21	24	27	30
LD90 _{GI}	21	23	25	30	32	35

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	9	11	13	13	15	17
LD10 _{GI}	16	18	20	22	25	28
LD50 _{GI}	20	22	24	28	31	34
LD90 _{GI}	24	26	28	34	36	39

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.2	0.6	2

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	70%
10 Gy/hr	70%
1 Gy/hr	50%
0.2 Gy/hr	50%

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	70%	70%
10 Gy/hr	1 Gy/hr	60%	60%
1 Gy/hr	0.2 Gy/hr	50%	50%

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	55%	60%
10 Gy/hr	55%	60%
1 Gy/hr	55%	60%
0.2 Gy/hr	55%	60%

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	5	6	7	5	6	7
LD10	7	8	9	7	8	9
LD50	8.7	9.7	10.7	8.7	9.7	10.7
LD90	10.5	11.5	12.5	10.5	11.5	12.5

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	6.5	7.7	9.0	6.5	7.7	9.0
LD10	9.0	10.3	11.6	9.0	10.3	11.6
LD50	11.2	12.5	13.8	11.2	12.5	13.8
LD90	13.5	14.8	16.1	13.5	14.8	16.1

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	10.1	12.1	14.1	10.1	12.1	14.1
LD10	14.1	16.2	18.2	14.1	16.2	18.2
LD50	17.6	19.6	21.6	17.6	19.6	21.6
LD90	21.2	23.2	25.3	21.2	23.2	25.3

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	16.2	19.4	22.6	16.2	19.4	22.6
LD10	22.6	25.8	29.1	22.6	25.8	29.1
LD50	28.1	31.3	34.6	28.1	31.3	34.6
LD90	33.9	37.1	40.4	33.9	37.1	40.4

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	100%
10 Gy/hr	100%
1 Gy/hr	100%
0.2 Gy/hr	100%

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	75%	75%
10 Gy/hr	1 Gy/hr	75%	75%
1 Gy/hr	0.2 Gy/hr	75%	75%

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	50%	50%
10 Gy/hr	50%	50%
1 Gy/hr	50%	50%
0.2 Gy/hr	50%	50%

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
DR10						
DR50						
DR90						

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 4a – DELETED**Question 4b – DELETED**

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration	80	120	180
Dose for effect in 10% of exposed skin area	130	190	285
Dose causing effect in 50% of exposed skin area	280	420	630
Dose causing effect in 90% of exposed skin area	440	660	990

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration	80	120	180
Dose for effect in 10% of exposed skin area	130	190	285
Dose causing effect in 50% of exposed skin area	280	420	630
Dose causing effect in 90% of exposed skin area	440	660	990

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration	80	120	180
Dose for effect in 10% of exposed skin area	130	190	285
Dose causing effect in 50% of exposed skin area	280	420	630
Dose causing effect in 90% of exposed skin area	440	660	990

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis	210	310	470
Dose for effect in 10% of exposed skin area	310	470	700
Dose causing effect in 50% of exposed skin area	530	780	1200
Dose causing effect in 90% of exposed skin area	730	1090	1600

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis	210	310	470
Dose for effect in 10% of exposed skin area	310	470	700
Dose causing effect in 50% of exposed skin area	530	780	1200
Dose causing effect in 90% of exposed skin area	730	1090	1600

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis	210	310	470
Dose for effect in 10% of exposed skin area	310	470	700
Dose causing effect in 50% of exposed skin area	530	780	1200
Dose causing effect in 90% of exposed skin area	730	1090	1600

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation	33	43	53
Dose for effect in 10% of exposed skin area	35	50	65
Dose causing effect in 50% of exposed skin area	55	75	95
Dose causing effect in 90% of exposed skin area	80	100	120

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation	33	43	55
Dose for effect in 10% of exposed skin area	35	50	65
Dose causing effect in 50% of exposed skin area	55	75	95
Dose causing effect in 90% of exposed skin area	80	100	120

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation	33	43	53
Dose for effect in 10% of exposed skin area	35	50	65
Dose causing effect in 50% of exposed skin area	55	75	95
Dose causing effect in 90% of exposed skin area	80	100	120

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0%	10%	25%
	Moist Desquamation in 50% of Exposed Skin	25%	50%	75%
	Moist Desquamation in 90% of Exposed Skin	50%	90%	100%
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0%	10%	25%
	Moist Desquamation in 50% of Exposed Skin	25%	50%	75%
	Moist Desquamation in 90% of Exposed Skin	50%	90%	100%
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0%	10%	25%
	Moist Desquamation in 50% of Exposed Skin	25%	50%	75%
	Moist Desquamation in 90% of Exposed Skin	50%	90%	100%

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.63	1.3	2.5	1.9	2.5	3.8
LD10	1.3	2.5	3.8	2.5	3.8	5
LD50	3.1	3.8	5.6	4.4	5	6.9
LD90	3.8	5	7.5	5	6.3	8.8

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

50%

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	50%	50%
1 Gy/hr	50%	50%
0.2 Gy/hr	50%	50%

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.55	1.1	2.2	1.7	2.2	3.3
LD10	1.1	2.2	3.3	2.2	3.3	4.4
LD50	2.8	3.3	5.0	3.9	4.4	6.1
LD90	3.3	4.4	6.6	4.4	5.5	7.7

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

50%

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Treatment Supportive Treatment

75% 75%

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	11.9	14.3	16.7	11.9	14.3	16.7
LD10	16.7	19.1	27.8	16.7	19.1	27.8
LD50	20.8	23.1	25.5	20.8	23.1	25.5
LD90	25.0	27.4	29.8	25.0	27.4	29.8

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

100%

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr	75%	75%
1 Gy/hr	75%	75%
0.2 Gy/hr	75%	75%

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

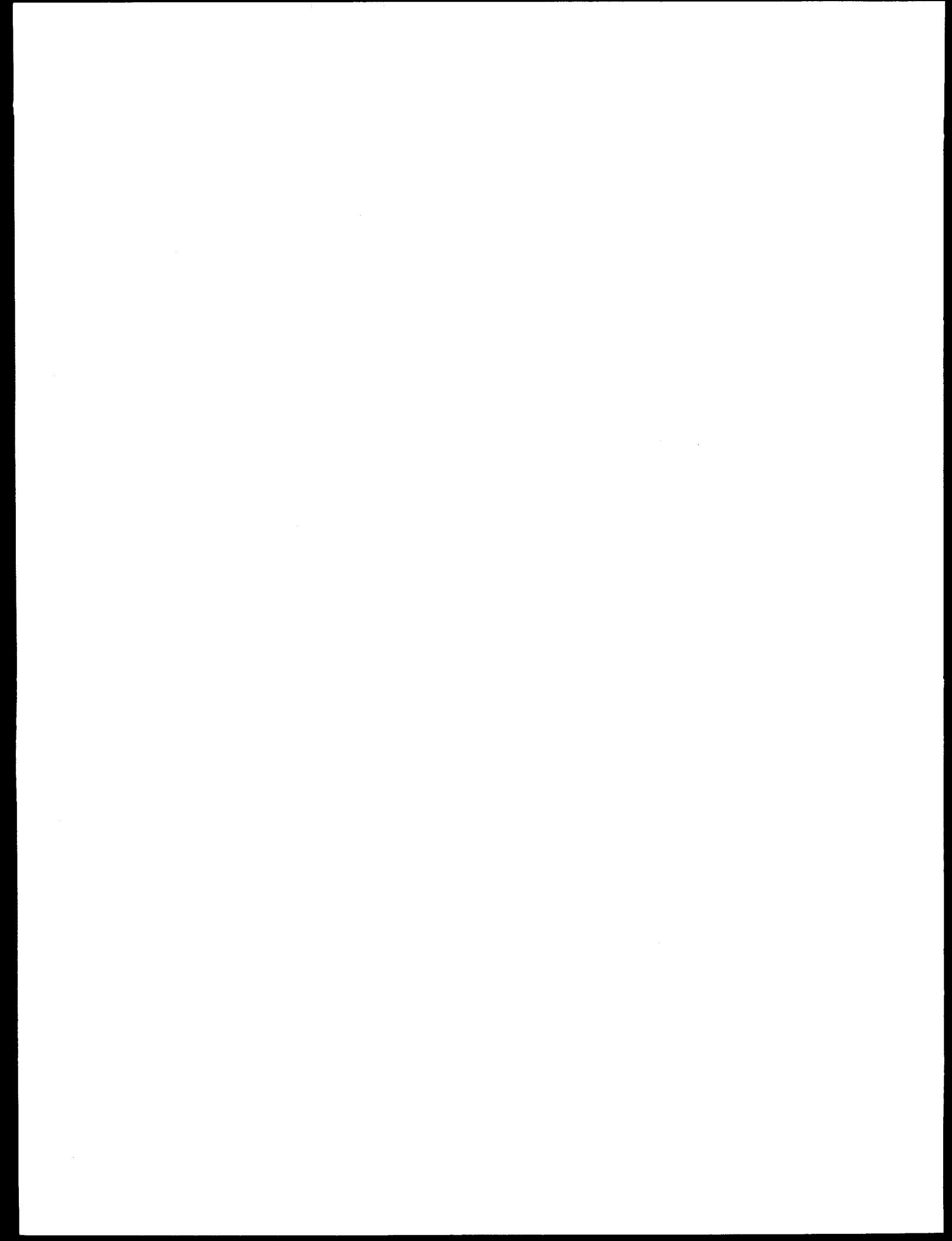
	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			



EXPERT D

Arguments and Statements forwarded in order to decide on values of parameters required for describing deterministic effects.

Arguments and statements are organized according to number of each specific question and/or page of the questionnaire. Calculations substantiating arguments are provided in the appendices. A separate list of references has been included.

Except for skin, values for LD₅₀ have been taken from human data in the literature. Whenever possible, confidence limits for LD values have been derived from appropriate human data. Otherwise, confidence limits have been estimated based on animal data describing corresponding tissue responses.

All of the specified LD values relate to *Standard Man*. Factors which might influence these values are listed in Appendix VI. However, no attempt has been made to account for such variations because of scarce relevant information available from the literature.

The threshold dose has been taken to be the dose at the 5% incidence level of morbidity (or cause) of death(-rate). Different threshold levels of less than 5% can be adopted, and corresponding values can be calculated by probit analysis. However, for practical epidemiological purposes, a 5% threshold level has been favored, according to ICRP recommendations for deterministic effects (ICRP-41, 1984). This is in agreement with the notion that "...no individuals would be expected to die at doses below about 1 Gy" (ICRP-60, 1991b, B.3.3, p. 104). We are unaware of practical arguments for choosing threshold levels of less than 5%, e.g., 0.1%.

Furthermore, several biological and circumstantial factors are likely to severely restrict selection of a threshold as low as 0.1%. Large variations in threshold dose are to be expected regardless of the high precision governed by statistical models. Factors we assume to influence the slopes of dose-response relationships for deterministic effects and, consequently, all of the specified LD values including threshold doses, are given in Appendix VI.

Question 1a: Early Fatalities Due to Whole Body Dose.

It is assumed that the fatalities result from the bone marrow syndrome (BM) and that victims of BM will die within 30 to 35 days after exposure.

Whole body dose rate of 100 Gy • h⁻¹.

1. Data on LD have been derived from data presented in UNSCEAR (1988) report, p. 567, Figure XXI.
2. The dose survival curves in this report represent lethality of Japanese A-bomb victims who were in poor health at the time before and after the explosion. Therefore, for a healthy population, the LD₅₀ value provided for *Minimal Treatment*, has been taken to be 0.5 Gy larger than the LD₅₀ = 3.0 Gy of curve A, Figure XXI, UNSCEAR (1988), and subsequently all other LD values for *Minimal Treatment* are larger by 0.5 Gy.
3. All LD values specified for *Supportive Treatment* have been taken to be a factor of 1.8 larger than the corresponding values specified for *Minimal Treatment*. This factor reflects the effect of supportive care on survival as shown by reconstitution of bone marrow after total body irradiation in rhesus monkeys employing treatment with autologous bone marrow, thrombocyte transfusion, erythrocyte transfusion, selective decontamination, parental fluid and systemic antibiotics (Wagemaker, 1995; Wielenga, 1990, p. 112, Figure 4.4).

Whole body dose rate of 10 Gy • h⁻¹.

1. Neither repair nor repopulation will substantially affect the shape of the survival curve when the dose rate changes from 100 Gy • h⁻¹ to 10 Gy • h⁻¹. Accordingly, in this case no differences in values of LD from those derived for a dose rate of 100 Gy • h⁻¹ are expected.
2. This argument applies to both *Minimal Treatment* and *Supportive Treatment*.

Whole body dose rate of 1 Gy • h⁻¹.

1. Experimental data obtained after TBI X-irradiation of F1(CBA/Rij × C57BL/Rij) mice, employing different dose rates show an increase by a factor of 1.25 in LD_{50/30} when changing the dose rate from 5 Gy • h⁻¹ to 1 Gy • h⁻¹ (Broerse, 1966, Table XXVI, p. 118).

2. This factor has been adopted for calculating LD doses for both *Minimal Treatment* and *Supportive Treatment* from corresponding data derived for exposures at a whole body dose rate of $10 \text{ Gy} \cdot \text{h}^{-1}$.

Whole body dose rate of $0.2 \text{ Gy} \cdot \text{h}^{-1}$.

1. At low dose rates, i.e., exposure times in the order of one day or longer, repopulation of bone marrow stem cells partially compensates for cell kill. The acute dose at high dose rate required for compensating repopulation in tumors is about $0.6 \text{ Gy} \cdot \text{d}^{-1}$ but may be $0.4 \text{ Gy} \cdot \text{d}^{-1}$ for bone marrow stem cells (Wielenga, 1990, Figure 3.5, p. 87:ln2 repopulation in 2.3 d; Figure 4.9, p. 124:ln2 cell kill requiring 0.75 Gy).
2. At low dose rate, the daily dose required for compensating repopulation is estimated to be about $1.0 \text{ Gy} \cdot \text{d}^{-1}$. Accordingly, all of the LD doses specified for exposure at $0.2 \text{ Gy} \cdot \text{h}^{-1}$ are larger by 1.0 Gy as compared with corresponding LD doses specified for exposure at $1 \text{ Gy} \cdot \text{h}^{-1}$.

Dose rate at which LD_{50} doubles.

1. From values of LD_{50} specified for a whole body dose rate of $100 \text{ Gy} \cdot \text{h}^{-1}$, dose rates corresponding to twice these LD values have been calculated by employing the Linear-Quadratic formalism (Barendsen, 1982).
2. For details of these calculations see Appendix I.

Question 1b: Early Fatalities Due to Gastrointestinal Syndrome.

Whole body dose rates of $100 \text{ Gy} \cdot \text{h}^{-1}$ and $10 \text{ Gy} \cdot \text{h}^{-1}$.

1. First answer whole body dose rate of $10 \text{ Gy} \cdot \text{h}^{-1}$ from UNSCEAR (1988 – acute exposure: p. 554; protracted irradiation: p. 583); Broerse (1966, p. 118, Table XXVI); HAL-73; Broerse and MacVittie (1984 – supportive care: p. 210-211) data.
2. Assuming less repair at a higher dose rate, the LD values specified for the dose rate of $10 \text{ Gy} \cdot \text{h}^{-1}$ have all been reduced by 0.5 Gy.

Whole body dose rate of $1 \text{ Gy} \cdot \text{h}^{-1}$.

According to experimental data on gastrointestinal effects after TBI X-irradiation of F1(CBA/Rij \times C57BL/Rij) mice, employing different dose rates, LD values for whole body dose rate of $1 \text{ Gy} \cdot \text{h}^{-1}$ have been calculated to be larger by a factor of 1.6 compared to those specified for $10 \text{ Gy} \cdot \text{h}^{-1}$. (Broerse, 1966, p. 118, Table XXVI).

Whole body dose rate of $0.2 \text{ Gy} \cdot \text{h}^{-1}$.

At this low dose rate compensating doses for repopulation are assumed to be required at each level of lethal doses specified for a dose rate of $1 \text{ Gy} \cdot \text{h}^{-1}$ as follows:

- + 3.0 Gy at threshold level and for the LD_{10} ,
- + 2.5 Gy for the LD_{50} , and,
- + 2.0 Gy for the LD_{90} .

Dose rate at which LD_{50GI} doubles.

1. By comparing LD_{50} values specified for dose rates of $100 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$, the latter dose rate is expected to be close to the dose rate at which $LD_{50GI} = 9.5 \text{ Gy}$ doubles to $LD_{50GI} = 19.0 \text{ Gy}$.
2. By similar reasoning as described for Question 1a a dose rate of $0.82 \text{ Gy} \cdot \text{h}^{-1}$ has been calculated to correspond to an $LD_{50GI} = 19.0 \text{ Gy}$. Calculations assuming values of $a/b = 20 \text{ Gy}$; $a = 0.1 \text{ Gy}^{-1}$; and $Tp = 24 \text{ h}$, are detailed in Appendix II.
3. Values intermediate between 0.2 and $0.8 \text{ Gy} \cdot \text{h}^{-1}$ have been specified.

Question 2a: Early Fatalities Due to Beta Lung Dose.

Lung dose rate of $100 \text{ Gy} \cdot \text{h}^{-1}$.

1. In our opinion, the distinction between effects on persons exposed younger than 40 y or 40 y and older will not yield meaningful information. If lung-function is supposed to be of important influence on radiation effects, a better distinction would be made by grouping persons according to ages between 0 - 18 y, 19 - 40 y, and over 40 y old. LD-values are specified only for persons older than 40 y.
2. Values of LD for a dose rate of $100 \text{ Gy} \cdot \text{h}^{-1}$ have been estimated to be $0.75x$ the values specified for LD values at $10 \text{ Gy} \cdot \text{h}^{-1}$ (Steel, 1993, p. 123, Figure 15.5).

Lung dose rate of $10 \text{ Gy} \cdot \text{h}^{-1}$.

LD-values have been derived from data on the dose response relationship for human pneumonitis (van Dyke et al., 1981).

Lung dose rate of $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$.

1. From values of LD₅₀ specified for 40 y old persons exposed to irradiation at a dose-rate of $10 \text{ Gy} \cdot \text{h}^{-1}$ LD values have been calculated for dose rates of $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$ by employing the linear-quadratic formalism (Barendsen, 1982). Values for parameters involved have been derived from data on radiation effects in rat lung (van Rongen, 1989).
2. Calculations are detailed in Appendix III and Appendix IV.

Dependencies.

To our knowledge no data are available comparing radiation effects on lung tissue in young and adult persons. Therefore this question has not been answered.

Question 2b: Morbidity Due to Beta Lung Dose.

Lung dose rates of $10 \text{ Gy} \cdot \text{h}^{-1}$ and $1 \text{ Gy} \cdot \text{h}^{-1}$.

Based on data reported by van Dyke (1981) which include both morbidity and mortality from pneumonitis, LD values for morbidity were estimated to be 10% lower than those specified for mortality at corresponding dose rates.

Lung dose rates of $0.2 \text{ Gy} \cdot \text{h}^{-1}$.

By similar reasoning LD values for morbidity were estimated to be smaller than the corresponding LD values specified for mortality at this dose rate. However, in this case LD values were calculated to be 3 Gy less at each level assuming parallel dose response curves for morbidity and mortality.

Question 5a: Acute Breakdown of the Skin.

20% Skin exposed.

1. Calculations have been performed assuming skin irradiation with an energy of an isotope equivalent to that of ^{90}Sr .

2. The assumption was made that the dose per unit area required for producing ulceration in skin of the face is most critical. Exposure of larger body area is assumed to contribute little more to the overall detrimental effect.
3. A value of 2 m^2 for skin surface of *Standard Man* was adopted.
4. Variation in biological effect, i.e., acute ulceration as a function of dose was derived from data reported in ICRP (1991a), p. 35, Table 5.
5. Specified values of LD have been calculated for acute ulceration occurring in a 4000 cm^2 area.
6. Values of LD specified for each level have been calculated to be in proportion to those presented in ICRP (1991a), p. 34, Figure 17 and with data on LD₅₀ and LD₁₀ presented in ICRP (1991a), p. 35, Table 5.

40% Skin exposed; 60% Skin exposed.

As explained before, it is assumed that exposure of skin areas from arms and legs in addition to that of the face will not significantly increase the overall detrimental radiation effect. This could be different if the skin of the trunk (back and abdomen) were exposed.

Fraction of the population that would die from acute skin ulceration.

It should be noted that ulceration of the face after exposure of head and neck is life threatening if more than 20% of the skin of the face is involved. Skin transplantation of irradiated areas has a notoriously bad prognosis.

Question 5b: Acute Epidermal Necrosis of the Skin.

20% Skin exposed.

1. It is assumed that epidermal necrosis, i.e., epidermolysis, is the sole lesion imposed on the skin. This implies that the energy of the β -particle is deposited in the superficial layer of the skin ($< 300 \mu\text{m}$ from the skin surface).
2. Accordingly, calculations have been performed assuming skin irradiation with an isotope of an energy equivalent to that of promethium, ^{147}Pm , emitting β radiation of 0.22 MeV. Data on skin effects for this element are reported in ICRP (1991a), p. 35, Table 5.

The energy of ^{147}Pm is close to that of 0.39 MeV of ^{103}Ru which has been detected in radioactive fallout.

3. Basically, similar starting conditions have been considered as described for acute ulceration.
4. Variation in biological effect, i.e., epidermolysis as a function of dose was derived from data reported in ICRP (1991a), p. 35, Table 5.
5. Specified values of LD have been calculated for epidermolysis occurring in a 4000 cm^2 area.
6. Values of LD specified for each level have been calculated to be in proportion to those presented in ICRP (1991a), p. 36, Figure 18-19 and with data on LD_{50} and LD_{10} presented in ICRP (1991a), p. 35, Table 5.

40% Skin exposed; 60% Skin exposed.

It is assumed that exposure of skin areas from arms and legs in addition to that of the face will not significantly increase the overall detrimental radiation effect. This could be different if the skin of the trunk (back and abdomen) were exposed.

Fraction of the Population that Would Die from Epidermolysis.

It is assumed that the amount of lethal skin damage is comparable to that of 2nd-degree skin burns leading to death.

Question 5c: Early Fatalities by Lesions of Moist Desquamation.

20% Skin exposed; 40% Skin exposed.

1. Basically, similar starting conditions have been considered as described for acute ulceration.
2. Variation in biological effect, i.e., moist desquamation as a function of dose was derived from data reported for ^{90}Sr in ICRP (1991a), p. 35, Table 5.
3. Specified values of LD have been calculated for moist desquamation occurring in 4000 cm^2 and 8000 cm^2 areas (i.e., 20 and 40% skin exposed, respectively).
4. Values of LD specified for each level have been calculated to be in proportion to those presented in

ICRP (1991a), p. 36, Figure 18-19 and with data on LD_{50} and LD_{10} presented in ICRP (1991a), p. 35, Table 5.

60% Skin exposed.

1. In addition to the considerations for 20 and 40% skin exposed, toxic compounds released from skin destruction (proteins) as well as from bacteria contaminating the damaged skin (infection, fever, shock) may contribute to the detrimental effect.
2. Also, reduced resistance due to decreased number of immune-associated Langerhans cells (ICRP, 1991a, p. 47) may influence LD values. It was assumed that large skin areas could sustain relatively lesser doses than small areas if the number of Langerhans cells per mm^2 was reduced to less than one-third of that in normal individuals, i.e., at doses in excess of 16 Gy (see ICRP, 1991a, p. 48, Figure 26).

Development of Secondary Ulceration from Moist Desquamation.

It is assumed that the development of secondary ulcerations is due mainly to impairment of irradiated cutaneous and subcutaneous capillaries and that poor hygienic conditions or pre-existing cutaneous infections do not act as complicating factors.

Fraction of the Population that Would Die from Moist Desquamation.

As specified before, it has been assumed that exposure of the skin of the face and, therefore, the dose per unit area required for producing secondary ulceration in skin of the face is most critical. Exposure of a larger body area, except that of the trunk, will contribute little more to the overall detrimental effect caused by secondary ulceration.

Question 6a: Early Fatalities Due to Whole Body Dose: Decrease in Dose Rate 10:1.

1. The effects to be expected should be in the range of those specified for dose rates between $1\text{ Gy} \cdot \text{h}^{-1}$ and $0.2\text{ Gy} \cdot \text{h}^{-1}$, implying that LD values should be in the order of those specified.
2. As for the LD_{50} (minimal treatment), 30% of that dose should be equivalent to 30% of $\text{LD}_{50} = 4.5\text{ Gy}$, i.e., about 1.5 Gy. Similarly, the complementary dose required should be 70% of $\text{LD}_{50} = 5.5\text{ Gy}$, i.e., about

3.5 Gy. The combined total LD₅₀ should be 1.5 + 3.5 = 5.0 Gy.

3. From this result it was concluded that all of the LD values at 10:1 decreased dose rate should be 0.5 Gy larger than those specified for LD values specified at a dose rate of 1 Gy • h⁻¹.
4. The effect of supportive care should result in a similar shift in LD values as might be expected for cases given minimal treatment. Values specified for the LD₉₅ dose are relatively larger because it takes longer exposure time during which repopulation will be more effective.

Question 6b: Early Fatalities Due to Whole Body Dose: Decrease in Dose Rate 100:1.

1. In principle, the same reasoning as described above led to calculation of the specified LD values. However, LD values relating to minimal treatment did not differ significantly from those calculated for corresponding values at a 10:1 decreased dose rate.
2. Because, in this case, the fractions of the LD values contributed by the low dose rate exposure are small compared to those of the case before, repopulation will be smaller and so the compensating doses.

Question 6c: Early Fatalities Due to Lung Dose: Decrease in Dose Rate 14:1.

1. From LD₅₀ = 10 Gy, specified for whole body dose rate of 10 Gy • h⁻¹, a value for LD₅₀ has been calculated by employing the linear-quadratic formalism (Barendsen, 1982).
2. For details of these calculations see Appendix V.
3. From the result it can be concluded that the LD₅₀ value at the present decreased dose rate is 16.5 Gy larger than that specified for the dose rate at 10 Gy • h⁻¹. Values of LD for different levels of effect have been calculated to be in proportion to this larger LD₅₀ value.

Question 7a1: First 24 h Lung Dose 2x larger than First 24 h Bone Marrow Dose.

No Skin exposed.

1. First, calculate the LD₅₀ relating to the dose D₁ administered within 1 day plus the dose D₂₋₇ administered between days 2 through 7.

- a. Set the bone marrow dose D = 5.5 Gy, being equal to the highest LD₅₀ value as specified for the bone marrow syndrome.

- b. The dose resulting from exposure between days 2 through 7 would then be equal to:

$$D_{2-7} = D_{(\text{total, over 7 d})} - D_{(\text{over first 24 h})} = 2.1 \times D - 1.0 \times D = 1.1 \times D$$

Accordingly, the dose D₂₋₇ = 1.1 × 5.5 Gy = 6.05 Gy and the corresponding dose rate would be 6.05/(6 × 24) = 0.04 Gy • h⁻¹.

- c. From the results of Question 1a, it follows that the LD₅₀ corresponding to a dose rate of 0.04 Gy • h⁻¹, would be double the LD₅₀ at a dose rate of 100 Gy • h⁻¹, or, LD_{50(protracted)} = 2 × LD_{50(acute)}.

This implies that a dose to be given at a dose rate of 0.04 Gy • h⁻¹ should be equal to 2 × D_x in order to cause the same effect as a dose D_x given at 100 Gy • h⁻¹. Conversely, a given dose D_x administered at 0.04 Gy • h⁻¹ will be half as effective due to protraction, so that D_{x-protracted} is equivalent to 0.5 × D_{x-acute}.

- d. Since the ratio of D_{x-acute} to D_{x-protracted} is given to be 1.0 to 1.1 an acute equivalent 50% dose, AED₅₀, can be defined to be:

$$AED_{50} = 1.0 \times D_{x-\text{acute}} + 1.1 \times D_{x-\text{protracted}} = 1.0 \times D_{x-\text{acute}} + 1.1 \times 0.5 \times D_{x-\text{acute}} = 1.0 \times D + 1.1 \times 0.5 \times D = 1.55 \times D.$$

2. The dose D can be selected as follows:

D (Gy)	1.0 × D _{x-acute} (Gy)	1.1 × D _{x-protracted} (Gy)	AED ₅₀ = LD ₅₀ (Gy)
2.5	2.5	3.375	3.875
3.5*	3.5*	4.125*	5.425*
4.5	4.5	5.225	6.975

* Preference matching LD₅₀ at 0.2 Gy • h⁻¹

3. The average dose rate corresponding to 1 × D = 3.5 Gy within the first 24 h equals 3.5/24 = 0.15 Gy • h⁻¹. Consequently, the argument to select LD₅₀ = 5.425 Gy matching LD₅₀ at 0.2 Gy • h⁻¹ is valid.

4. The selected dose $D = 3.5$ Gy corresponds to the LD_{50} dose of 3.5 Gy specified for lethality at a dose rate of $100 \text{ Gy} \cdot \text{h}^{-1}$. Assuming equally steep slopes of the dose response curves for dose rates of $100 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$, all of the other LD values specified for the present question are taken to be in agreement with those specified for a dose rate of $100 \text{ Gy} \cdot \text{h}^{-1}$.

20% of total Skin Area exposed.

1. According to the conditions specified, the total dose to the skin is $10x$ the total dose D to the bone marrow ($21.3 \times D$ and $2.1 \times D$, respectively). Since for skin ulceration the $LD_{50} = 35$ Gy, the dose D should be no larger than $D = 35/21.3 = 1.5$ Gy.
2. All of the other LD values specified, i.e., both for *Minimal Treatment* and *Supportive Treatment* as well as those for situations in which 40 and 60% of the skin are exposed, have been calculated to be in proportion with LD values specified for no skin exposure and minimal treatment. It is assumed that supportive treatment ameliorating ulceration of the skin is not effective and, therefore, LD values with or without supportive treatment are not expected to be different.

Question 7a2:

Zero Lung dose, otherwise Same as Question 7a1.

Answers to be given are not different from those given before (see Question 7a1).

Question 7b1:

Acute dose to the Lung Dose 10x Acute dose to the Bone Marrow.

No Skin Exposed.

1. According to the conditions specified, the acute dose to the lung is $10x$ that to the bone marrow ($10.0 \times D$ and $1.0 \times D$, respectively) and the total lung dose is $13.6 \times D$. Since for lung mortality the highest $LD_{50} = 33$ Gy, the dose D should be no larger than $D = 33/13.6 = 2.4$ Gy.
2. Whereas the doses to the bone marrow and to the lungs during the first 24 h are equal to $1 \times D$ and $10 \times D$, respectively, the corresponding dose rates are equal to $2.4/24 = 0.1 \text{ Gy} \cdot \text{h}^{-1}$ and $24/24 = 1.0 \text{ Gy} \cdot \text{h}^{-1}$. This would imply that the LD_{50} dose to the lung instead of

being 33 Gy, as assumed before, should be smaller; i.e., $LD_{50} = 21.0$ Gy. As a consequence the dose $D = 21/13.6 = 1.5$ Gy.

3. All of the other LD values specified, i.e., both for minimal treatment and supportive treatment have been calculated to be in proportion with LD values specified for lung doses at a dose rate of $1 \text{ Gy} \cdot \text{h}^{-1}$. It is assumed that supportive treatment ameliorating lung damage is not effective and will not influence LD values given for minimal treatment.

20% of total Skin Area exposed.

1. According to the conditions specified, the acute dose to the skin is close to $150x$ the acute dose D to the bone marrow, whereas the acute dose to lung is $10x D$, or, $D_{\text{skin}} = 150.3 \times D$; $D_{\text{lung}} = 10 \times D$; and, $D_{\text{BM}} = 1.0 \times D$. The total lung dose (acute + protracted) is $13.6 \times D$.
2. Three potentially critical doses should be considered:
 - $LD_{50} = 21$ or 33 Gy for lung damage (depending on dose rate);
 - $LD_{50} = 35$ Gy for skin ulceration, possibly leading to lethality at 30 Gy;
 - $LD_{50} = 18$ Gy for moist desquamation of the skin.
3. Considering the dose D , the following conclusions can be drawn:
 - as discussed before, with respect to lung damage, $D = 1.5$ or 2.4 Gy at dose rates of $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$, respectively;
 - with respect to ulceration, $D = 35/150.3 = 0.23$ Gy and lethality $D = 30/150.3 = 0.20$ Gy;
 - with respect to moist desquamation, $D = 18/150.3 = 0.12$ Gy.
4. If it is assumed that moist desquamation does not lead to fatalities but ulceration does, the value of $D = 0.21$ Gy has been adopted to be the critical dose (i.e., intermediate between 0.20 and 0.23 Gy).
5. All of the other LD values specified, i.e., both for *Minimal Treatment* and *Supportive Treatment*, have been calculated to be in proportion with LD values specified for doses to the skin of Question 5a. It is

assumed that supportive treatment ameliorating ulceration will not be effective and will not influence LD values adopted for minimal treatment.

40 and 60% of total Skin Area exposed.

Same values of LD apply based on the same arguments as described before.

Question 7b2:

Zero lung dose, otherwise same as Question 7b1.

Same answers apply as those given to Question 7a1.

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Appendix I

LQ calculations for dose rates at which LD₅₀ doubles

1. The original value of LD₅₀ = 3.5 Gy at a dose rate of 100 Gy • h⁻¹ should attain a value of LD₅₀ = 7.0 Gy by changing this dose rate;

2. For bone marrow an a/b ratio equal to 15 Gy has been selected:

- for acute reacting tissue the literature reports a/b = 10 Gy
- from data by Broerse, 1966, a/b = 20 can be derived as follows:

$$\text{for } T = 8 \text{ h, } D = 11.8 \text{ Gy the dose rate is } r = 11.8/8 = 1.5 \text{ Gy} \cdot \text{h}^{-1}$$

$$\text{for } T = 2 \text{ h, } D = 9.4 \text{ Gy the dose rate is } r = 9.4/2 = 4.7 \text{ Gy} \cdot \text{h}^{-1}$$

According to Barendsen (1982), an Extrapolated Tolerance Dose (ETD) for protracted irradiation can be calculated from ETD = D[1 + 2r(a/b)⁻¹] Gy.

$$\begin{aligned} \text{ETD} &= 11.8 \times [1 + 2 \times 1.5 \times (a/b)^{-1}] \\ &= 9.4 \times [1 + 2 \times 4.7 \times (a/b)^{-1}] \text{ Gy.} \end{aligned}$$

Solving this equation, a value for (a/b) = 22 Gy has been obtained.

Also, according to Barendsen (1982), an ETD for acute irradiation without repopulation can be calculated for 1. and 2. described above:

$$\text{ETD} = D \times [1 + D(a/b)^{-1}] = 3.5 \times [1 + 3.5/15] = 4.3 \text{ Gy.}$$

Note:

a. For exposure times of less than 10 h, a parameter μ should be applied (Awwad, 1990, p. 579), implying that ETD is equal to:

$$\text{ETD} = D[1 + 2r/[\mu(a/b) \times (1 - \{1 - \exp(-\mu \times T)\})/(\mu \times T)]] \text{ Gy.}$$

A value of (a/b) = 15 Gy, according to Awwad (1990), p. 165, is a reasonable estimate.

b. An ETD which accounts for repopulation can be calculated according to:

$$\text{ETD} = D \times [1 + 2r(a/b)^{-1}] - 0.693 \times T/(a \times T_p) \text{ Gy,}$$

T_p(h) being the potential doubling time for repopulation and T(h) being the over-all radiation time (h) (Awwad, 1990, p. 165).

3. Assuming a = 0.88 Gy⁻¹, T_p = 48 h, and using the simplified relationship for ETD (Barendsen, 1982), the dose rate r can be calculated as follows:

$$\begin{aligned} \text{ETD} &= D \times [1 + 2r(a/b)^{-1}] - 0.693 \times T/(a \times T_p) \\ 0.3 &= 7 \times [1 + 2r/15] - 0.693 \times T/(0.88 \times 48) = \\ 7 + 14r/15 &- 0.0164 \times T \end{aligned}$$

or:

$$r = (0.0164 \times T - 2.7) \times (15/14)$$

where T should be at least T = 165 h in order that r be positive. By increasing T, a proper value can be obtained:

$$T = 165 \text{ h (6.88 d) gives } r = 0.00 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 0.00 \text{ Gy}$$

$$T = 166 \text{ h (6.92 d) gives } r = 0.02 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 3.32 \text{ Gy}$$

$$T = 167 \text{ h (6.96 d) gives } r = 0.04 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 6.68 \text{ Gy*}$$

$$T = 168 \text{ h (7.00 d) gives } r = 0.06 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 10.1 \text{ Gy}$$

* Preference, matching LD₅₀

Appendix II

LQ calculations for dose rates at which LD₅₀ doubles

1. According to Barendsen (1982), an ETD for acute irradiation without repopulation can be calculated to be:

$$ETD = D \times [1 + D(a/b)^{-1}] = 9.5 \times [1 + 9.5/20] = 14 \text{ Gy.}$$

2. Assuming $a = 0.1 \text{ Gy}^{-1}$, $T_p = 24 \text{ h}$, and using the simplified relationship for ETD (Barendsen, 1982), the dose rate r can be calculated as follows:

$$ETD = D \times [1 + 2r(a/b)^{-1}] - 0.693 \times T/(a \times T_p)$$

$$14 = 19 \times [1 + 2r/20] - 0.693 \times T/(0.1 \times 24) = 19 + 1.9r - 0.29 \times T$$

or:

$$r = (0.29 \times T - 5)/1.9$$

where T should be at least $T = 17.5 \text{ h}$ in order that r be positive. By increasing T , a proper value can be obtained:

$$T = 17.5 \text{ h (0.73 d)} \text{ gives } r = 0.00 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 0.00 \text{ Gy}$$

$$T = 18.0 \text{ h (0.75 d)} \text{ gives } r = 0.07 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 1.26 \text{ Gy}$$

$$T = 20.0 \text{ h (0.83 d)} \text{ gives } r = 0.37 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 7.40 \text{ Gy}$$

$$T = 22.0 \text{ h (0.92 d)} \text{ gives } r = 0.67 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 14.74 \text{ Gy}$$

$$T = 23.0 \text{ h (0.82 d)} \text{ gives } r = 0.82 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 18.86 \text{ Gy*}$$

$$T = 24.0 \text{ h (1.00 d)} \text{ gives } r = 0.97 \text{ Gy} \cdot \text{h}^{-1}; D_{\text{tot}} = 23.28 \text{ Gy}$$

* Preference

Appendix III

LQ calculations for Acute Lung Effects (threshold-, LD₁₀, LD₅₀ and LD₉₀ doses)

1. Calculations of LD doses for lung tissue exposed to $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$ have been performed by employing the linear-quadratic formalism as follows:
 - a. $\text{ETD} = D \times [1 + D(a/b)^{-1}]$ for acute irradiation ($10 \text{ Gy} \cdot \text{h}^{-1}$)
 - b. $\text{ETD} = D \times [1 + 2r(a/b)^{-1}]$ for protracted irradiation ($0.2-1.0 \text{ Gy} \cdot \text{h}^{-1}$)
 - c. Meaning and values of parameters (van Rongen, 1989):
3. Procedure for calculating above listed LD doses specified for lung exposure at dose rates of $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$, employing $a/b = 3.5 \text{ Gy}$ for acute effects:
 - a. $r = 1.0$; $\text{ETD} = D_x \times [1 + 2 \times 1/(0.693 \times 3.5)] = D_x \times \text{RE}_1$;
 $\text{RE}_1 = 1.8245$, $\text{LD}_{50} = \text{ETD}_{50} / \text{RE}_1$
 - b. $r = 0.2$; $\text{ETD} = D_x \times [1 + 2 \times 0.2/(0.693 \times 3.5)] = D_x \times \text{RE}_{0.2}$;
 $\text{RE}_{0.2} = 1.165$, $\text{LD}_{50} = \text{ETD}_{50} / \text{RE}_{0.2}$

r = dose rate; expression b. (above) is valid if T for irradiation is $> 10 \text{ h}$;

Data selected for acute radiation effects and irradiation at $10 \text{ Gy} \cdot \text{h}^{-1}$:

$$a/b = 3.5 \text{ Gy}$$

$$T_{1/2} = 1.0 \text{ h and } \mu = (\ln 2)/T_{1/2} = 0.693 \text{ h}^{-1}$$

Data selected for late radiation effects and irradiation at $0.2 \text{ Gy} \cdot \text{h}^{-1}$:

$$a/b = 2.3 \text{ Gy}$$

$$T_{1/2} = 1.1 \text{ h and } \mu = (\ln 2)/T_{1/2} = 0.630 \text{ h}^{-1}$$

2. At a dose rate of $10 \text{ Gy} \cdot \text{h}^{-1}$ the specified LD values vary between 7 and 12 Gy. Values calculated for ETD vary between 21 - 53.1 Gy.

Acute dose D_x (Gy)	Extrapolated dose ETD (Gy)	Corresponding LD (Gy) $r = 1 \text{ Gy} \cdot \text{h}^{-1}$	$r = 0.2 \text{ Gy} \cdot \text{h}^{-1}$
--------------------------	--	---	--

7.0	21.0	11.5	18.0
8.0	26.3	14.4	22.6
8.5	29.1	16.0	25.0
9.0	32.1	17.6	27.6
9.5	35.3	19.3	30.3
10.0*	38.6	21.1	33.1
11.0	45.6	25.0	39.1
12.0	53.1	29.1	45.6

* Selected

Appendix IV

LQ calculations for Late Lung Effects (threshold-, LD₁₀, LD₅₀ and LD₉₀ doses)

1. Calculations of LD doses for lung tissue exposed to $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$ have been performed by employing the linear-quadratic formalism as follows:

- a. $\text{ETD} = D \times [1 + D(a/b)^{-1}]$ for acute irradiation ($10 \text{ Gy} \cdot \text{h}^{-1}$)
- b. $\text{ETD} = D \times [1 + 2r(a/b)^{-1}]$ for protracted irradiation ($0.2-1.0 \text{ Gy} \cdot \text{h}^{-1}$)
- c. Meaning and values of parameters (van Rongen, 1989):

r = dose rate; expression b. (above) is valid if T for irradiation is $> 10 \text{ h}$;

Data selected for acute radiation effects and irradiation at $10 \text{ Gy} \cdot \text{h}^{-1}$:

$$a/b = 3.5 \text{ Gy}$$

$$T_{1/2} = 1.0 \text{ h and } \mu = (\ln 2)/T_{1/2} = 0.693 \text{ h}^{-1}$$

Data selected for late radiation effects and irradiation at $0.2 \text{ Gy} \cdot \text{h}^{-1}$:

$$a/b = 2.3 \text{ Gy}$$

$$T_{1/2} = 1.1 \text{ h and } \mu = (\ln 2)/T_{1/2} = 0.630 \text{ h}^{-1}$$

2. At a dose rate of $10 \text{ Gy} \cdot \text{h}^{-1}$ the specified LD values vary between 5 and 11 Gy. Values calculated for ETD vary between 15.87 - 63.61 Gy. The corresponding LD₅₀ values are larger than those shown in Appendix III. Therefore, the LD₅₀ values selected to answer the questions on p. 15 (see questionnaire) are the lowest lethal LD₅₀ values calculated, which are presented in Appendix III.

Acute dose D _x (Gy)	Extrapolated dose ETD (Gy)	Corresponding LD (Gy) $r = 1 \text{ Gy} \cdot \text{h}^{-1}$	Corresponding LD (Gy) $r = 0.2 \text{ Gy} \cdot \text{h}^{-1}$
5.0	15.87	6.66	12.40
6.0	21.65	9.10	16.97
6.5	24.87	10.45	19.50
8.0	35.83	15.05	28.10
9.0	44.22	18.60	34.65
10.0*	53.48	22.50	41.90
11.0	63.61	26.70	49.85

* Compared

3. Procedure for calculating above listed LD doses specified for lung exposure at dose rates of $1 \text{ Gy} \cdot \text{h}^{-1}$ and $0.2 \text{ Gy} \cdot \text{h}^{-1}$, employing $a/b = 2.3 \text{ Gy}$ for late effects:

- a. $r = 1.0 \text{ ETD} = D_x \times [1 + 2 \times 1/(0.63 \times 2.3)] = D_x \times RE_1$;
 $RE_1 = 2.380$, $LD_{50} = ETD_{50} / RE_1$
- b. $r = 0.2 \text{ ETD} = D_x \times [1 + 2 \times 0.2/(0.63 \times 2.3)] = D_x \times RE_{0.2}$;
 $RE_{0.2} = 1.276$, $LD_{50} = ETD_{50} / RE_{0.2}$

Appendix V

LQ calculations for Combined Acute and Low Dose Rate Effects (threshold-, LD₁₀, LD₅₀ and LD₉₀ doses)

1. For acute irradiation ($10 \text{ Gy} \cdot \text{h}^{-1}$) the LD₅₀ = 10 Gy

The corresponding ETD = 38.6 Gy (see: Appendix III, point 2., selected: $D_x = 10 \text{ Gy}$).

2. Calculate $\text{ETD}_{\text{tot}} = \text{ETD}_1 + \text{ETD}_{(2-7)}$

ETD_{tot} = extrapolated dose corresponding to total irradiation time (7 d);

ETD_1 = extrapolated dose corresponding to irradiation during day 1;

$\text{ETD}_{(2-7)}$ = extrapolated dose corresponding to irradiation during days 2-7.

3. If the dose rate during days 2-7 equals $r \text{ Gy} \cdot \text{h}^{-1}$, then the dose rate at day 1 equals $14 \times r \text{ Gy} \cdot \text{h}^{-1}$.

4. Accordingly:

the total dose for day 1 is $D_1 = 24 \times 14 \times r \text{ Gy}$

the total dose for days 2-7 is $D_{2-7} = 144 \times r \text{ Gy}$

5. $\text{ETD}_1 = 4 \times 14 \times r[1 + 2 \times 14 \times r/(0.693 \times 3.5)] = 336 \times r \times (1 + 11.5 \times r) \text{ Gy}$

$\text{ETD}_{(2-7)} = 144 \times r[1 + 2 \times r/(0.693 \times 3.5)] = 144 \times r \times (1 + 0.82 \times r) \text{ Gy}$

6. $\text{ETD}_{(\text{tot})} = [336 \times r(1 + 11.5 \times r)] + [144 \times r(1 + 0.82 \times r)] \text{ Gy}$

$$\text{ETD}_{(\text{tot})} = 3982 \times r^2 + 480 \times r = 38.6 \text{ Gy}$$

7. Solving r from:

$$a \times r^2 + b \times r + c = 0, \text{ where: } a = 3982; b = 480; \text{ and, } c = -38.6$$

$$\begin{aligned} r &= [-b \pm \sqrt{b^2 - 4 \times a \times c}]/2 \times a \\ &= [-480 \pm \sqrt{(-480)^2 - 4 \times 3982(-38.6)}]/2 \times 3982 \\ &= [-480 \pm \sqrt{230400 + 614821}]/7964 \\ &= 0.055 \text{ Gy} \cdot \text{h}^{-1} \text{ (the positive root only)} \end{aligned}$$

8. Total dose for LD₅₀:

$$\begin{aligned} \text{LD}_{50} &= 24 \times 14 \times 0.055 + 144 \times 0.055 \\ &= 18.5 + 7.9 \\ &= 26.5 \text{ Gy} \end{aligned}$$

Appendix VI

Factors which may Influence Specified LD-values

1. Variations in cellular reactions:
 - 1.1 variation in intrinsic radiosensitivity associated with cell type.
 - 1.2 variation in intrinsic radiosensitivity within a given cell type.
 - 1.3 variation in repair capacity.
 - 1.4 variation in repopulation capacity.
2. Variations in tissue reactions:
 - 2.1 variation in number of stem-cells.
 - 2.2 variation in ratio of parenchyma to stroma.
 - 2.3 variation in number of tissue units governing structural repair of damage.
 - 2.4 age related variation.
 - 2.5 sex related variation.
 - 2.6 racial differences.
3. Circumstantial factors:
 - 3.1 the number of persons exposed.
 - 3.2 health conditions, including nutritional conditions of persons exposed.
 - 3.3 intercurrent diseases.
 - 3.4 complicating injuries.
 - 3.5 capacity and quality of supportive care.

Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	3.0	4.0
LD10	1.0	2.5	4.0	4.0	5.5	7.0
LD50	2.5	3.5	4.5	5.0	6.5	8.0
LD90	3.0	4.5	6.0	6.0	7.5	9.0

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	3.0	4.0
LD10	1.0	2.5	4.0	4.0	5.5	7.0
LD50	2.5	3.5	4.5	5.0	6.5	8.0
LD90	3.0	4.5	6.0	6.0	7.5	9.0

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	2.0	4.0	6.0
LD10	1.5	3.0	4.5	5.0	7.0	9.0
LD50	3.0	4.5	6.0	6.0	8.0	10.0
LD90	4.5	6.0	7.5	7.0	9.0	11.0

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.5	2.0	2.5	3.0	5.0	7.0
LD10	2.5	4.0	5.5	6.0	8.0	10.0
LD50	4.0	5.5	7.0	7.0	9.0	11.0
LD90	5.5	7.0	8.5	8.0	10.0	12.0

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.02	0.04	0.06

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	90%
10 Gy/hr	90%
1 Gy/hr	50%
0.2 Gy/hr	50%

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	95%	50%
10 Gy/hr	1 Gy/hr	75%	50%
1 Gy/hr	0.2 Gy/hr	50%	50%

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	2.0	4.0	6.0	3.0	5.0	7.0
LD10 _{GI}	5.5	7.5	9.5	6.5	8.5	10.5
LD50 _{GI}	7.5	9.5	11.5	8.5	10.5	12.5
LD90 _{GI}	9.5	11.5	13.5	10.5	12.5	14.5

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	2.5	4.5	6.5	3.5	5.5	7.5
LD10 _{GI}	6.0	8.0	10.0	7.0	9.0	11.0
LD50 _{GI}	8.0	10.0	12.0	9.0	11.0	13.0
LD90 _{GI}	10.0	12.0	14.0	11.0	13.0	15.0

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	4.0	7.0	10.0	6.0	9.0	12.0
LD10 _{GI}	10.0	13.0	16.0	11.5	14.5	17.5
LD50 _{GI}	13.0	16.0	19.0	14.5	17.5	20.5
LD90 _{GI}	16.0	19.0	22.0	17.5	20.5	23.5

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	7.0	10.0	13.0	9.0	12.0	15.0
LD10 _{GI}	13.0	16.0	19.0	14.5	17.5	20.5
LD50 _{GI}	15.5	18.5	21.5	17.0	20.0	23.0
LD90 _{GI}	18.0	20.0	24.0	19.5	22.5	25.5

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.2	0.4	0.6

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	90%
10 Gy/hr	90%
1 Gy/hr	70%
0.2 Gy/hr	50%

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	95%	50%
10 Gy/hr	1 Gy/hr	75%	50%
1 Gy/hr	0.2 Gy/hr	50%	50%

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	50%	50%
10 Gy/hr	50%	50%
1 Gy/hr	50%	50%
0.2 Gy/hr	50%	50%

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				5.0	6.0	7.0
LD10				6.0	7.0	8.0
LD50				7.0	8.0	9.0
LD90				8.0	9.0	10.0

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				7.0	8.0	9.0
LD10				8.0	9.0	10.0
LD50				9.0	10.0	11.0
LD90				10.0	11.0	12.0

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				8.0	12.0	16.0
LD10				13.0	17.0	21.0
LD50				18.0	21.0	24.0
LD90				21.0	25.0	29.0

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				10.0	17.0	24.0
LD10				20.0	27.0	34.0
LD50				28.0	33.0	38.0
LD90				32.0	39.0	46.0

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	_____
10 Gy/hr	_____
1 Gy/hr	_____
0.2 Gy/hr	_____

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	_____	75%
10 Gy/hr	1 Gy/hr	_____	75%
1 Gy/hr	0.2 Gy/hr	_____	75%

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	50%
10 Gy/hr	_____	50%
1 Gy/hr	_____	50%
0.2 Gy/hr	_____	50%

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				2.5	3.0	3.5
ED10				3.0	3.5	4.0
ED50				3.5	4.0	4.5
ED90				4.0	4.5	5.0

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				4.5	6.5	8.5
ED10				6.0	8.0	10.0
ED50				8.0	9.0	10.0
ED90				8.0	10.0	12.0

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				4.0	10.0	16.0
ED10				9.0	15.5	22.0
ED50				15.5	19.0	22.5
ED90				16.0	22.5	29.0

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				7.0	14.0	21.0
ED10				17.0	24.0	31.0
ED50				25.0	30.0	35.0
ED90				29.0	36.0	43.0

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
DR10						
DR50						
DR90						

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 4a – DELETED**Question 4b – DELETED**

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration	20	25	30
Dose for effect in 10% of exposed skin area	25	30	35
Dose causing effect in 50% of exposed skin area	30	35	40
Dose causing effect in 90% of exposed skin area	35	40	45

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration	20	25	30
Dose for effect in 10% of exposed skin area	25	30	35
Dose causing effect in 50% of exposed skin area	30	35	40
Dose causing effect in 90% of exposed skin area	35	40	45

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration	20	25	30
Dose for effect in 10% of exposed skin area	25	30	35
Dose causing effect in 50% of exposed skin area	30	35	40
Dose causing effect in 90% of exposed skin area	35	40	45

5%, 50%, and 95% values for the fraction of the population

	Fraction that die			
	5%	50%	95%	
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin	0.05	0.002	0.001
	Acute Ulceration in 90% of Exposed Skin	0.9	0.8	0.7
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin	0.9	0.8	0.7
	Acute Ulceration in 90% of Exposed Skin	1.0	1.0	1.0
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin	1.0	1.0	1.0
	Acute Ulceration in 90% of Exposed Skin	1.0	1.0	1.0

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis	100	150	200
Dose for effect in 10% of exposed skin area	200	250	300
Dose causing effect in 50% of exposed skin area	250	300	350
Dose causing effect in 90% of exposed skin area	300	350	400

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis	100	150	200
Dose for effect in 10% of exposed skin area	200	250	300
Dose causing effect in 50% of exposed skin area	250	300	350
Dose causing effect in 90% of exposed skin area	300	350	400

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis	100	150	200
Dose for effect in 10% of exposed skin area	200	250	300
Dose causing effect in 50% of exposed skin area	250	300	350
Dose causing effect in 90% of exposed skin area	300	350	400

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin	0.05	0	0
	Acute Epidermal Necrosis in 90% of Exposed Skin	0.05	0	0
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin	0.05	0	0
	Acute Epidermal Necrosis in 90% of Exposed Skin	0.10	0.05	0
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin	0.10	0.05	0
	Acute Epidermal Necrosis in 90% of Exposed Skin	0.80	0.20	0.05

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation	6.0	11.0	16.0
Dose for effect in 10% of exposed skin area	7.5	15.0	22.5
Dose causing effect in 50% of exposed skin area	9.0	18.0	27.0
Dose causing effect in 90% of exposed skin area	11.0	21.0	31.0

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation	6.0	11.0	16.0
Dose for effect in 10% of exposed skin area	7.5	15.0	22.5
Dose causing effect in 50% of exposed skin area	9.0	18.0	27.0
Dose causing effect in 90% of exposed skin area	11.0	21.0	31.0

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation	4.0	9.0	14.0
Dose for effect in 10% of exposed skin area	6.0	13.0	20.0
Dose causing effect in 50% of exposed skin area	7.0	16.0	25.0
Dose causing effect in 90% of exposed skin area	9.0	19.0	29.0

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0	0	0
	Moist Desquamation in 50% of Exposed Skin	0	0	0
	Moist Desquamation in 90% of Exposed Skin	0.3	0.2	0.1
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0	0	0
	Moist Desquamation in 50% of Exposed Skin	0.3	0.2	0.1
	Moist Desquamation in 90% of Exposed Skin	0.35	0.25	0.15
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0	0	0
	Moist Desquamation in 50% of Exposed Skin	0.35	0.25	0.15
	Moist Desquamation in 90% of Exposed Skin	0.75	0.50	0.25

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin	0	0	0
	Moist Desquamation in 90% of Exposed Skin	0.25	0.20	0.15
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin	0.25	0.20	0.15
	Moist Desquamation in 90% of Exposed Skin	0.30	0.25	0.20
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin	0.30	0.25	0.20
	Moist Desquamation in 90% of Exposed Skin	0.70	0.50	0.25

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.0	1.5	2.0	2.5	4.5	6.5
LD10	2.0	3.5	5.0	5.5	7.5	9.5
LD50	3.5	5.0	6.5	7.5	9.0	10.5
LD90	5.0	6.5	8.0	9.0	11.0	13.0

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	90%	90%
1 Gy/hr	90%	90%
0.2 Gy/hr	90%	90%

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.0	1.5	2.0	1.5	2.5	3.5
LD10	3.0	4.0	5.0	6.0	7.0	8.0
LD50	3.5	5.0	6.5	7.5	8.5	9.5
LD90	5.0	6.5	8.0	8.5	10.0	11.5

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Treatment	Supportive Treatment
90%	90%

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				14.0	18.0	22.0
LD10				16.0	21.0	26.0
LD50				22.5	26.5	30.5
LD90				27.0	32.0	37.0

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		90%
1 Gy/hr		90%
0.2 Gy/hr		90%

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	3.0	4.0
LD10	1.0	2.5	4.0	4.0	5.5	7.0
LD50	2.5	3.5	4.5	5.0	6.5	8.0
LD90	3.0	4.5	6.0	6.0	7.5	9.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.9	1.2	0.6	0.9	1.2
LD10	0.9	1.2	1.5	0.9	1.2	1.5
LD50	1.2	1.5	1.8	1.2	1.5	1.8
LD90	1.5	1.8	2.1	1.5	1.8	2.1

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.9	1.2	0.6	0.9	1.2
LD10	0.9	1.2	1.5	0.9	1.2	1.5
LD50	1.2	1.5	1.8	1.2	1.5	1.8
LD90	1.5	1.8	2.1	1.5	1.8	2.1

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.9	1.2	0.6	0.9	1.2
LD10	0.9	1.2	1.5	0.9	1.2	1.5
LD50	1.2	1.5	1.8	1.2	1.5	1.8
LD90	1.5	1.8	2.1	1.5	1.8	2.1

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	50%
20% skin exposed	50%
40% skin exposed	50%
60% skin exposed	50%

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	3.0	4.0
LD10	1.0	2.5	4.0	4.0	5.5	7.0
LD50	2.5	3.5	4.5	5.0	6.5	8.0
LD90	3.0	4.5	6.0	6.0	7.5	9.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.9	1.2	0.6	0.9	1.2
LD10	0.9	1.2	1.5	0.9	1.2	1.5
LD50	1.2	1.5	1.8	1.2	1.5	1.8
LD90	1.5	1.8	2.1	1.5	1.8	2.1

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.9	1.2	0.6	0.9	1.2
LD10	0.9	1.2	1.5	0.9	1.2	1.5
LD50	1.2	1.5	1.8	1.2	1.5	1.8
LD90	1.5	1.8	2.1	1.5	1.8	2.1

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.9	1.2	0.6	0.9	1.2
LD10	0.9	1.2	1.5	0.9	1.2	1.5
LD50	1.2	1.5	1.8	1.2	1.5	1.8
LD90	1.5	1.8	2.1	1.5	1.8	2.1

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	50%
20% skin exposed	50%
40% skin exposed	50%
60% skin exposed	50%

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.4	0.8	1.2	0.4	0.8	1.2
LD10	0.9	1.3	1.6	0.9	1.3	1.6
LD50	1.3	1.5	1.7	1.3	1.5	1.7
LD90	1.5	1.8	2.1	1.5	1.8	2.1

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.13	0.17	0.20	0.13	0.17	0.20
LD10	0.17	0.20	0.23	0.17	0.20	0.23
LD50	0.18	0.21	0.24	0.18	0.21	0.24
LD90	0.19	0.22	0.25	0.19	0.22	0.25

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.13	0.17	0.20	0.13	0.17	0.20
LD10	0.17	0.20	0.23	0.17	0.20	0.23
LD50	0.18	0.21	0.24	0.18	0.21	0.24
LD90	0.19	0.22	0.25	0.19	0.22	0.25

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.13	0.17	0.20	0.13	0.17	0.20
LD10	0.17	0.20	0.23	0.17	0.20	0.23
LD50	0.18	0.21	0.24	0.18	0.21	0.24
LD90	0.19	0.22	0.25	0.19	0.22	0.25

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	50%
20% skin exposed	50%
40% skin exposed	50%
60% skin exposed	50%

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal_____ Supportive_____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	3.0	4.0
LD10	1.0	2.5	4.0	4.0	5.5	7.0
LD50	2.5	3.5	4.5	5.0	6.5	8.0
LD90	3.0	4.5	6.0	6.0	7.5	9.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.4	0.7	1.0	0.4	0.7	1.0
LD10	0.7	1.0	1.3	0.7	1.0	1.3
LD50	1.0	1.3	1.6	1.0	1.3	1.6
LD90	1.3	1.6	1.9	1.3	1.6	1.9

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.3	0.6	0.9	0.3	0.6	0.9
LD10	0.6	0.9	1.2	0.6	0.9	1.2
LD50	0.9	1.2	1.5	0.9	1.2	1.5
LD90	1.2	1.5	1.8	1.2	1.5	1.8

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.2	0.5	0.8	0.2	0.5	0.8
LD10	0.5	0.8	1.1	0.5	0.8	1.1
LD50	0.8	1.1	1.4	0.8	1.1	1.4
LD90	1.1	1.4	1.7	1.1	1.4	1.7

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	50
20% skin exposed	50
40% skin exposed	40
60% skin exposed	30

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

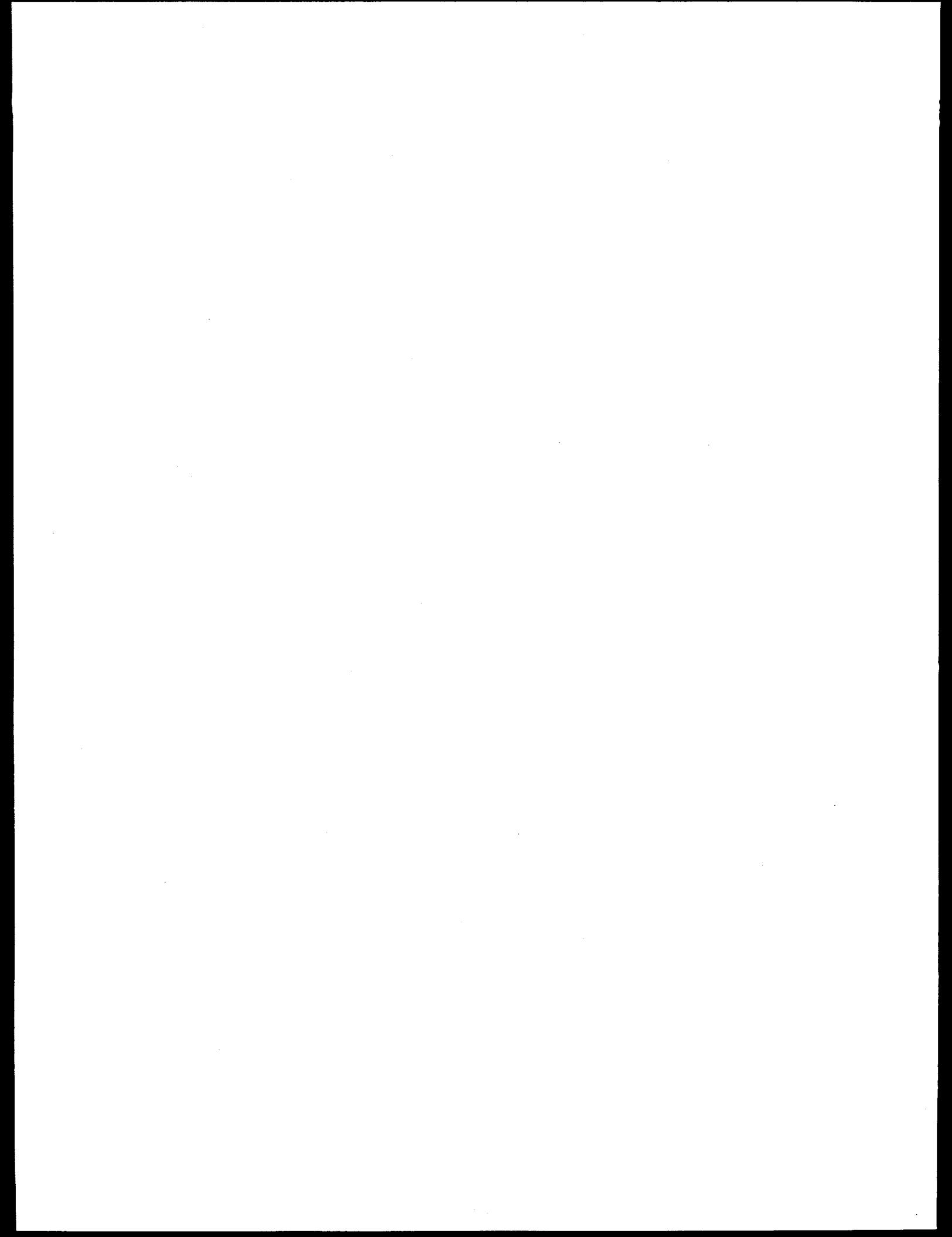
	Minimal Treatment	Supportive Treatment
No Skin Exposed	50	50
20% of Skin Exposed	<50	50
40% of Skin Exposed	<50	50
60% of Skin Exposed	<50	50

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1	2.5	3.5	4.5
2	7.5	9.0	11.5
3	3.5	4.5	5.5
4	4.5	5.5	6.5
5	4.5	5.5	6.5
6	4.0	5.0	6.0
7	4.0	5.0	6.0
8	5.0	6.5	8.0
9	4.0	5.0	6.0
10	8.0	9.0	10.0



EXPERT E

Early Fatalities Due to Whole-Body Dose

Introduction

The prediction of early fatalities from radiation exposure has been a crucial concern in radiobiology for many years. However, estimation of radiation mortality has remained difficult because there is little data which accurately define both the dose and the response for humans, despite the large number of early fatalities which resulted from the atomic bomb detonations in Japan. The difficulty in interpreting these data arises primarily from the uncertainty in radiation doses, all of which are reconstructions. Additionally, it is uncertain what type of trauma actually caused death in most cases. Subsequent radiation accidents, including Chernobyl, suffer from the same difficulty in interpretation. Because of this situation, the first two truly credible dose-response curves from Japan have just been published in the last decade (Fujita et al., 1989; Levin et al., 1992). Even when human dose response curves are generated, they are hard pressed to define the median lethal dose, and have large uncertainties at the high and low incidence ends of the curve. When the dose is protracted, human data are even more sparse. Because of these difficulties, the radiation research community has conducted many animal experiments designed to define the dose-response space. These studies have contributed substantially to our understanding of the effects of radiation on biological beings, but these efforts have neither mapped the entire area of concern to planners nor entirely solved the problem of extrapolation from other animals to man. Biologically- and mathematically-based models have endeavored to make prediction of the dose response more complete, but these tools have their constraints as well, and are extremely difficult to validate. Recently, the combination of more complete understanding of the effects of radiation on cell kinetics and the new mathematical approaches in a single model (Marrow-Cell Kinetic Model) has expanded our ability to predict mortality for a wide range of protracted doses with greater confidence. The Marrow-Cell Kinetic Model, which was used for the current calculations, provides the widest range of flexibility in predicting the hematopoietic effects of radiation and the most complete benchmarking of any model available today.

Assumptions

In order to ensure a common frame of reference, doses to tissue relative to exposure field have to match the specified

spectrum of interest. Historically, inattention to this has contributed substantially to the apparent variation reported in the human LD₅₀. Accordingly, doses are reported as both whole-body free-in-air exposures and as bone-marrow doses (which are $0.71 \times$ FIA dose), referenced to ⁶⁰Co. Four assumptions were made in the construction of the Marrow-Cell Kinetic Model. First, the probit model can fit mortality data from prompt exposure. Second, the species-specific radiosensitivity of a particular cell lineage is proportional to its nuclear DNA. Third, the potency of different X and gamma photons depends on linear energy transfer above 3.5 keV/ μ m. Forth, the probability of death depends on a minimum number of a "critical" lineage of cells whose radiosensitivity is described mathematically in terms of sublethal injury, repair of sublethal injury, lethal injury from additional irradiation of sublethal sites, direct lethal injury of phenotypically normal cells, and compensatory repopulation. Given the LD₅₀ and its standard deviation for the probit model of equivalent prompt-dose mortality, mortality curves for protracted exposures can be determined by indexing the protracted dose effects to the equivalent prompt dose, even when the individuals are exposed to different radiation sources, dose rates, or variations in dose protraction patterns.

Human Mortality Prediction

There is currently fairly broad agreement that the human LD₅₀ for high-dose-rate penetrating-gamma radiation is a dose of approximately three Gy to the bone marrow. The only human dose-response evaluation reported for a single cohort of well documented individuals with good dose information was estimated to have an LD₅₀ of 2.9 Gy (Levin et al., 1992). Estimates of the LD₁₀ and LD₉₀ are considerably less certain. Human dose response functions for highly fractionated dose rates do not exist. This gap in our knowledge has been filled largely by point estimate extrapolations from higher dose rate data or animal data. However, the recent maturation of the Bone-Marrow Cell-Kinetic Model (Jones et al., 1991; Jones et al., 1993a&b; Morris et al., 1991; Morris et al., 1993) provides a new, more comprehensive, and well benchmarked model to predict mortality under a wide range of radiation conditions.

Protracted Dose Model

All estimates for threshold, LD₁₀, LD₅₀, and LD₉₀ reported in this analysis were obtained from the MarCell (Version 4.1), which is the highly automated PC computer implementation of the Marrow-Cell Kinetic Model developed by T.D. Jones, M.D. Morris, and J.S. Hasan at Oak Ridge National Laboratory. The model of bone-

marrow cell-kinetic used in this code has been reported and discussed extensively in the literature. The Bone-Marrow Cell-Kinetics Model was developed by applying maximum likelihood principles to evaluate the data from 105 animal mortality experiments using a set of compartmental differential equations. Level dose rate and continuous uninterrupted exposure experiments from 13 species of test animal were used to establish the kinetic rate constants employed in the model. Proof-of-principle for the cell-kinetic model employed 7 experiments, 380 dose groups and more than 7,600 animals irradiated to 250 kVp X rays. The low-linear-energy-transfer cell-kinetic model was developed using data from 27 experiments comprised of six species, 851 dose groups and 18,940 test animals. The neutron model employed seven experiments for six different investigators, 146 dose groups, and more than 4,000 animals in neutron- and photon-induced acute-mortality experiment which were conducted in parallel experimental designs. Cell survival curves for 74 lineages of human leukemia and lymphoma cells were used to estimate rate constants for four reference malignant cells.

Data from differing radiation sources were used to make the model applicable to tritium beta, 100 kVp X, 22 MV X, 250 kVp X, ^{60}Co , ^{137}Cs , 2 MeV e-, Triga Reactor neutron, D-T neutrons, and blends of mixed field fission radiations. The model was adapted for humans using consensus principles and available human data. Marrow cell kinetics are modeled in terms of sublethal injury, repair, one-hit killing, killing of cells having transitory unrepaired sublethal injury, and compensatory repopulation. Kinetic rate constants have been determined for both radiosensitive hematopoietic bone marrow stem cells (CFU-S) and radioresistant bone marrow stromal cells (CFU-F). A total of 303 different LD₅₀ experiments served to independently validate the kinetics model.

Supportive Treatment

Supportive treatment is estimated to give approximately a two-fold increase in the LD₅₀ when currently-available cytokines are administered with the other supportive therapy specified in the elicitation protocol. Supportive therapy, without cytokines, was scaled to reflect the state-of-the-art in the therapy specified in the elicitation, and agrees reasonably well with the increase in LD₅₀ seen for the victims who received treatment after the Chernobyl accident. The 5% confidence value was taken to be approximately 1.3x the untreated LD₅₀. This was taken as a conservative lower bound from the most recent animal work

using contemporary therapy. The upper bound is limited in some cases either by the limitations of other radiation injuries or the ability of current medical practice to save the irradiated individual.

10 Gy/hr

Estimates are reported for the whole body dose rate of 10 Gy/hr, despite the small, and probably insignificant, differences in the minimal treatment group. There is essentially no difference at the lower incidences of mortality, but a difference begins to appear at LD₉₀ due to the effect of dose rate on time for repair. This effect is quite noticeable at LD₉₀ under conditions of supportive treatment where treatment and additional time for repair begin to combine to raise the value.

Confidence Values

Given that the dose estimates for the effects requested in this elicitation are derived values, the confidence limits assigned to them are quite subjective and can be derived in a number of ways. My approach to this was to take the derived human values, where they exist, and extend them to other parts of the problem where appropriate. This is a conservative approach because most calculated values are quite broad and encompass all of the published point estimates for the parameters evaluated here.

The 5% and 95% confidence values were taken from the calculated values for the LD₅₀ for the Nagasaki cohort (Levin et al., 1992). These values include all published credible values for the high dose rate LD₅₀. The 5% confidence value for the LD₁₀ was taken as the LD₁₀ calculated for the Nagasaki cohort. Similarly, the 95% confidence value for the LD₉₀ was taken as the LD₉₀ calculated for the Nagasaki cohort, thus providing a anchoring set of overall confidence bounds from which extrapolations can be made. The ratio of the LD₉₀/LD₁₀ for this set of human data is 6.2, a value highly likely to include the real value because the LD₉₀/LD₁₀ ratio for animal studies rarely exceeds a value of three, and is more commonly two. The complementary 10% confidence value for the LD₉₀ and the 95% confidence for the LD₁₀ were calculated to yield symmetrical values. The 95% confidence value for the threshold value was calculated to be the most likely value seen for zero deaths in animal studies (.54/LD₅₀). The 5% confidence level was calculated to be symmetrical.

Dose Rate at Which LD₅₀ Doubles

The dose rate at which the median lethal dose doubles is calculated from the bone-marrow cell-kinetic model to be .0492 Gy/hr. The 5% and 95% values were estimated to contain approximately 35% of the values on either side of the LD₅₀.

Minimal Versus Supportive Treatment

Given that the values for minimal treatment are derived from the cell-kinetics model, based on data which did not involve treatment of the irradiated individuals, there is little, if any dependence of the minimal treatment value on the supportive treatment value. The supportive treatment values were derived from both animal studies and human experience, especially Chernobyl. They are roughly a factor of 2 higher than the minimal treatment at the LD₅₀ point.

Dose Rate Effects

The dose rate effects dependency was assigned a probability of .8 to reflect the fact that the values are all anchored to the same LD₅₀ for high dose rate radiation. Similarly, the same cell kinetics determine the values for all dose rates. While each calculation at each dose rate is independent, they are all dependent on the same kinetics, algorithm, and anchor values.

Early Fatalities Due to Gastrointestinal Syndrome

Data on radiation-induced gastrointestinal (GI) mortality, both human and animal, are sparse. Further, except in laboratory animal experiments, it is difficult to clearly differentiate the GI mortality from other concomitant causes of radiation-induced mortality. Because GI mortality occurs at doses which are supralethal due to hematopoietic and lung injury, calculation of the threshold, LD₁₀, LD₅₀ and LD₉₀ for GI mortality must be determined by some metric other than the number of deaths. Consequently, estimates of GI mortality are mathematical extrapolations of animal data using some form of best fit solution. In an effort to move beyond this and provide a more generalized model of radiation-induced GI injury and death, a group of mathematical modelers, radiobiologists, statisticians, and computer math specialists have generated a Gut Injury Model (GIM) (Anno et al., 1991).

The GIM integrates the effects of radiation on both the anatomy and the physiology of the intestinal mucosa. GIM calculates GI injury and mortality using three nested

models: the lethal potentially lethal model (Curtis, 1986) which calculates cell survival after irradiation; the PSRC PAIR Model (Anno et al., 1991) which calculates cell proliferation and intracellular repair; and PSRC Gut Functional Model (Anno et al., 1991) which integrates a compartmental description and hierarchical structure model of the intestinal epithelium. The GIM has been benchmarked against Withers' crypt cell survival data from mouse jejunum (Anno et al., 1991) and Krebs and Leong's protracted dose mouse LD₅₀ data (Krebs and Leong, 1970).

GI Modeling Assumptions

Given that all doses associated with the GI syndrome will be fatal, the threshold, LD₁₀, LD₅₀, and LD₉₀ values have been determined from time to death. Based on Oughterson and Warren's observation of a six- to nine-day survival for persons dying of gastrointestinal injury in Hiroshima and Nagasaki (Oughterson and Warren, 1956), and Lushbaugh's (1989) estimate of seven to fourteen days as the survival time of radiation accident victims who have died from primarily GI injury, seven to fourteen days was taken as the time interval for death due to GI injury in this analysis. Following the protocol used by Dutreix et al. (1979) and Travis et al. (1985) for laboratory animal evaluations of GI death, a ten-day survival dose was taken as the LD₅₀. Confidence values for all LD values were taken as survival time either one day more or one day less than the LD value. Specifically, the 5% confidence value for the LD₅₀ was taken as the dose producing death in eleven days, whereas the 95% confidence value was taken as the dose producing death in nine days. The LD₁₀ was assumed to be the fourteen-day survival dose bracketed by the thirteen and fifteen day survival. The LD₉₀ was taken to be the seven-day survival dose bracketed by the six and eight-day survival doses. Twenty-day survival was taken as the threshold dose for the GI syndrome because this is the point where bone marrow death clearly begins to be the dominant mechanism responsible for mortality. Medical experience with radiation injury indicates that there is a point at which radiation injury to multiple organ systems overcomes the ability of medical intervention to affect survival. Based on this observation, fifteen Gy was taken as the upper limit for medical benefit.

10:1 and 100:1 Exposure Scenarios

These values were calculated using MarCell 4.1 using two constant gamma dose rates in the specified ratio, using the same assumptions as were used to determine the whole-body effects previously discussed for a single dose.

Multiple Exposed Organs and Exposure Periods

Assumptions

This scenario was assumed to be substantially similar to the exposure profile in Chernobyl, which allows that experience to be used as guidance for the response of patients who receive supportive medical treatment. From Chernobyl we know that radiation burns which cover 60% or more of the body are fatal; radiation burns to 30-60% of the body are severely life threatening; and burns to less than 30% of the body are not life-threatening (Guskova et al., 1988). The Nagasaki lethality analysis (Levin et al., 1992) indicates that the overall LD₅₀ is reduced by 20% for untreated persons who have both radiation and burn injuries. However, no one survived who was burned over more than one third of their body and received a whole-body radiation dose of more than four Gy. Generally, experts in the treatment of burns indicate that patients with greater than 30% body burns will die if they are not treated aggressively in a barrier burn facility. Thus, anyone in a minimal treatment group who had 40% or 60% of their bodies burned were assumed to be fatalities for any radiation dose above threshold. Overall, with the exception of burns to a substantial portion of the face, body surface burned was considered to be the major factor in determining the effects of burns on mortality.

Approach

The effects of the radiation dose scenario were calculated for bone marrow dose using MarCell 4.1 for three constant dose-rate gamma exposures, referenced to ⁶⁰Co, at the exposure ratio indicated. For burns, the Chernobyl experience was used to estimate the limits for supportive treatment. The effects of the radiation scenario alone were scaled for level of burn and type of treatment using the assumptions listed above. Forty percent burn with minimal treatment conditions was assumed to be equivalent to the Nagasaki experience, and thus was calculated to be 80% of the LD₅₀ for the no burn condition with minimal treatment.

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Question 1a – Early Fatalities Due To Whole Body Dose

(Note: Data are with growth factors; data without growth factors are shown in parentheses.)

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.61	.98	1.57	1.1 (1.3)	1.6 (2.0)	2.0 (2.4)
LD10	1.2	1.94	2.59	2.1 (2.5)	3.0 (4.0)	4.0 (5.0)
LD50	1.8	2.91	3.9	4.2 (5.5)	4.8 (6.0)	5.7 (6.5)
LD90	3.42	3.88	7.40	5.7 (6.5)	6.2 (7.8)	7.5 (9.0)

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.62	.99	1.59	1.1 (1.3)	1.6 (2.0)	2.0 (2.4)
LD10	1.24	2.0	2.67	2.1 (2.5)	3.0 (4.0)	4.0 (5.0)
LD50	1.86	3.0	4.02	5.0 (5.5)	5.2 (6.5)	6.5 (7.0)
LD90	3.57	4.05	7.72	7.5 (8.5)	8.0 (10.0)	9.5 (12.0)

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.64	1.03	1.65	1.3 (1.5)	1.9 (2.1)	2.3 (2.5)
LD10	1.39	2.25	3.0	3.0 (3.2)	4.1 (4.6)	4.5 (5.0)
LD50	2.24	3.63	4.86	5.0 (5.5)	6.6 (7.4)	7.4 (8.0)
LD90	4.54	5.15	9.82	8.0 (9.5)	9.5 (10.5)	10.5 (12.0)

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.71	1.15	1.84	1.4 (1.5)	2.1 (2.3)	3.0 (3.2)
LD10	1.61	2.6	3.47	3.5 (4.0)	4.8 (5.3)	5.5 (6.0)
LD50	2.69	4.35	5.83	6.0 (6.5)	8.0 (9.0)	9.0 (10.0)
LD90	5.6	6.35	12.11	10.0 (11.0)	12.0 (13.0)	13.0 (15.0)

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
.021	.05	.21

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	.9
10 Gy/hr	.9
1 Gy/hr	.9
0.2 Gy/hr	.9

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	.8	.8
10 Gy/hr	1 Gy/hr	.8	.8
1 Gy/hr	0.2 Gy/hr	.8	.8

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	3.9	4.2	5.4	4.7	5.4	6.7
LD10 _{GI}	6.5	7.2	8	7.4	8	8.7
LD50 _{GI}	9.1	10.2	12.2	10.1	12.1	13.4
LD90 _{GI}	14.4	16.8	20.0	14.4	16.8	20.0

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	3.9	4.4	5.4	4.7	5.4	6.7
LD10 _{GI}	7.4	8.2	9.25	7.4	9.1	10.1
LD50 _{GI}	10.6	12.2	14.4	10.6	12.2	14.4
LD90 _{GI}	17.1	20.8	26.1	17.1	20.8	26.1

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5.4	6.0	7.4	5.4	6.7	8.0
LD10 _{GI}	11.3	12.9	15.0	11.3	12.9	15.0
LD50 _{GI}	17.8	22.1	28.8	17.8	22.1	28.8
LD90 _{GI}	35.9	47.6	65.7	35.9	47.6	65.7

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5.4	10.1	11.4	6.12	11.56	13.6
LD10 _{GI}	13.0	14.9	17.6	13.0	14.9	17.6
LD50 _{GI}	21.2	26.9	35.6	21.2	26.9	35.6
LD90 _{GI}	45.2	61.0	87.1	45.2	61.0	87.1

Dose Rate Where LD₅₀_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD₅₀_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
1.0	1.5	2

Dependencies

Minimal and Supportive Treatment: Probability that the true LD₅₀_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	.8
10 Gy/hr	.85
1 Gy/hr	.9
0.2 Gy/hr	.9

Dose Rate Effects: Probability that the true LD₅₀_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	.85	.85
10 Gy/hr	1 Gy/hr	.85	.90
1 Gy/hr	0.2 Gy/hr	.85	.95

LD₅₀_{GI} Versus LD₅₀: Probability that the true LD₅₀ for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	.8	.8
10 Gy/hr	.8	.8
1 Gy/hr	.8	.8
0.2 Gy/hr	.8	.8

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	_____
10 Gy/hr	_____
1 Gy/hr	_____
0.2 Gy/hr	_____

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	_____	_____
10 Gy/hr	1 Gy/hr	_____	_____
1 Gy/hr	0.2 Gy/hr	_____	_____

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

		Under 40	Over 40
100 Gy/hr	_____	_____	_____
10 Gy/hr	_____	_____	_____
1 Gy/hr	_____	_____	_____
0.2 Gy/hr	_____	_____	_____

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
ED10						
ED50						
ED90						

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
DR10						
DR50						
DR90						

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	_____
10 Gy/hr	_____	_____
1 Gy/hr	_____	_____
0.2 Gy/hr	_____	_____

Question 4a – DELETED

Question 4b – DELETED

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

	Fraction that die		
	5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.77	1.25	2.0	1.79	2.77	3.6
LD10	1.72	2.77	3.7	3.87	5.98	7.78
LD50	2.69	4.36	5.84	6.03	9.34	12.15
LD90	5.27	5.98	11.4	8.1	12.5	16.32

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

.1

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	.9	.9
1 Gy/hr	.9	.9
0.2 Gy/hr	.9	.9

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	.73	1.19	1.9	1.59	2.46	3.2
LD10	1.52	2.46	3.28	3.26	5.03	6.54
LD50	2.31	3.74	5.01	4.88	7.56	9.83
LD90	4.44	5.03	9.59	6.48	10.0	13.04

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

.1

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Treatment Supportive Treatment

.9 .9

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	2.1	3.4	2.5	4.0	6.0
LD10	3.0	4.9	6.5	5.5	9.0	11.0
LD50	4.6	7.5	10.1	9.5	10.5	12.5
LD90	9.0	10.3	15.0	10.5	12.0	14.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.1	1.8	3.0	2.2	3.6	5.4
LD10	2.4	4.0	5.0	5.0	8.0	10.0
LD50	4.0	6.5	8.8	8.6	9.5	11.3
LD90	7.0	8.5	12.0	9.5	10.8	15.0

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.9	1.5	2.4	2.0	3.3	4.7
LD10	2.4	4.0	5.3	3.5	5.0	6.0
LD50	3.6	6.0	8.1	5.0	7.0	8.0
LD90	7.0	8.0	10.0	7.5	9.0	12.0

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.7	1.2	2.0	1.5	2.5	4.0
LD10	1.5	2.0	3.0	3.0	4.0	4.5
LD50	2.5	3.0	3.5	4.5	5.0	6.0
LD90	3.5	4.0	5.0	6.0	6.5	7.5

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	0.6
20% skin exposed	0.6
40% skin exposed	0.6
60% skin exposed	0.6

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	2.1	3.4	2.5	4.0	6.0
LD10	3.0	4.9	6.5	5.5	9.0	11.0
LD50	4.6	7.5	10.1	9.5	10.5	12.5
LD90	9.0	10.3	15.0	10.5	12.0	14.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.0	1.7	2.7	2.0	3.2	4.8
LD10	2.4	3.9	5.2	5.5	7.2	8.8
LD50	3.7	6.0	8.1	7.6	8.4	10.0
LD90	7.2	8.2	12.0	8.4	9.6	11.2

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

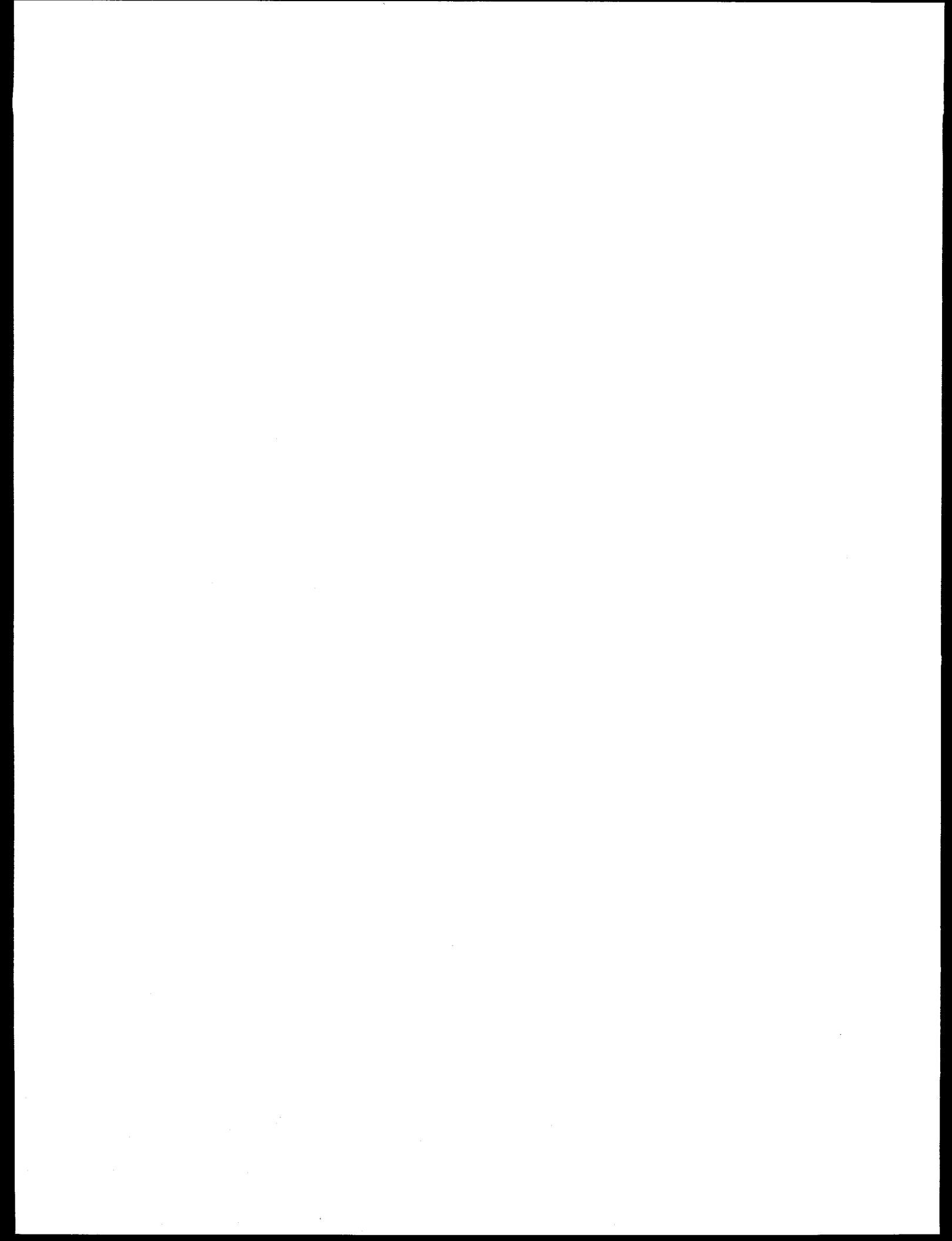
	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1	1	1.8	2.5
2	3	7	8
3	1.5	2	3
4	3	5.5	8.5
5	4.5	6	9
6	3.5	4.5	9
7	3.5	6.5	9
8	3.4	4	9
9	5.3	6.5	10
10	4.5	9.0	12



EXPERT F

The materials given below represent the summary of data of different authors (see attached reference list) concerning viewpoints on human radiation injury caused by major radiation accidents. The model was considered to be similar to Chernobyl accident (1986, USSR).

The principles to treat acute radiation disease (ARD) have been discussed at several international conferences, symposia, and meetings since 1962 and have also been documented in some publications (1954-1988) (1-4). The experience has accumulated slowly and gradually, and scientists all over the world have joined in efforts to increase our knowledge.

This gradual, slow progress has been due to the fact that many scientists in different countries had access to only single cases of ARD which were available during peace as a result of various types of accidents. The war acts in Japan 1945 still remains the only and unique event presenting the manifest form of ARD without treatment. Thus the total number of fatal cases reported after 1945 was 69 (5). Single countries (USSR, China) have presented data on 20-30 cases, but usually the results were documented (France, USA, England, Yugoslavia, USSR) to avoid similar syndromes in future groups of patients in the broad radiation dose range. Accidental incidents were primarily cases of uneven body irradiation, with its peculiarities (6, 7).

The other source of information concerning ARD treatment has been obtained from the last two decades by observation of patients receiving whole body irradiation before bone marrow transplantation. Despite the theoretical advantages obtained from these observations, many aspects of treatment regimes can be considered as rather specific, and the conclusions from such results are not always in agreement with the results obtained during different accidental circumstances outside the hospitals.

The Chernobyl accident gave scientists in the USSR experience diagnosing and treating a number of patients who simultaneously had been exposed to a comparatively evenly distributed dose of penetrating radiation. This population had ARD experience resulting in substantial numbers of severe injury and mortality. This report is devoted to the analysis of how this experience contributed to our knowledge of ARD therapies.

The physicians in charge had great responsibility for the outcome of the patients, and they therefore initially

followed earlier regimes, when this group was treated. The now recommended regimes are based on the physicians' personal and international experience, and no substantial modifications have been introduced.

Acute Radiation Disease

Our main principles in treatment of ARD are as follows:

- Grouping of patients was performed repeatedly according to definitions based on progress, severeness, and evaluation of possible radiation dose. This made it possible for us to define optimal time for treatment and prophylactic precautions.
- Careful evaluation of direct evidences of acute radiation syndromes and their complications was made in order to apply proved and effective schemes of treatment.
- The adopted schemes for ARD therapy were individualized in relation to prognosis and identified syndromes on the basis of specific features in the clinical signs of each individual patient, signs which were registered by careful observations at various time intervals after the radiation exposure.

Thus the treatment procedures were individualized and repeatedly evaluated. Procedures contained both general recommendations for the group of hospitalized patients and specific recommendations for single patients. This made possible the following generalized grouping of patients with ARD of varying degrees, groupings which are now in accordance with the classification system used in the USSR, i.e., bone marrow syndrome (BMS) degrees I to IV, intestinal syndrome (IS), oropharyngeal syndrome (OPS), local radiation skin injuries (LRSI), and radiation burns (RB) (6, 7).

Skin Radiation Injuries

The complications caused by skin radiation injuries in relation to the general clinical syndrome ARD were evaluated not only by the broadness of the process, but also by the degree of pathological changes and also by the progressive development of specific pathological conditions with their peculiar relapses. Late secondary erythemas sometimes disappeared within two weeks with only local therapy. But in the most severe cases it was necessary to use additional resources i.e., prescription of glucocorticoids, which quickly made both generalized and local clinical appearance of the dermatitis disappear.

Following appearance of secondary erythemas on more than 40% of the body surface 10-14 days after the radiation

exposure, the fever-toxemia syndrome developed in these patients, with signs of kidney-liver insufficiency and finally encephalopathic coma, with edema of the brain causing death 14-18 days after irradiation. The genetic linkage of fatal kidney-liver insufficiency and encephalopathic coma with skin injuries is proven by the fact that related syndromes appear in patients without heavy BMS or intestinal syndromes (IS). But in the majority of cases fatal burns were combined with BMS of higher degrees and with intense acute enteritis, i.e., the radiation intestinal syndrome (10, 12).

The treatment of radiation burns and other non-bone marrow syndromes and their complications generated a complex pattern of problems (13, 14). One of these was the severe syndromes of toxemia. In order to reduce such effects in the period from the 2nd to the 13th day, patients with the most severe skin injuries were subjected to 15 hemoperfusions by use of cell sorbents. Three patients with received doses of radiation of 2-4.6 Gy survived. They had a single hemoperfusion on the 5-8th days, which is much later than is recommended to cure ARD. This treatment did not influence the patients' survival and did not change substantially the dynamics of blood parameters.

It can be concluded that during the process of hemoperfusion, especially toward the end of the treatment period, patients showed short-term (several hours per day) improvement in their health condition, with less pronounced or disappearing pains in injured extremities and also a decrease of tissue edema. It is impossible to exclude such effects due to the simultaneous medical treatment.

Plasmapheresis was used in several cases (17 patients) in order to avoid development of kidney-liver insufficiency and fatal encephalopathic coma. Indications for such conditions were heavy (30-40% or more of the body surface) burns from gamma-radiation. Plasmapheresis was used between the 18th and 37th day. Some patients were treated that way daily up to six times. The positive result of repeated plasmapheresis was noticed as decreasing bilirubinemia, transaminasemia, and lowered levels of nitrogen compounds due to the kidney-liver insufficiency caused by the burns.

Radiation Pulmonitis

Radiation pulmonitis was observed in seven patients having ARD of degrees II-IV. A characteristic sign was rapidly developing dyspnea; during 2-3 days respiratory insufficiency developed fast. A lethal outcome due to

hypoxic coma on the 14-30th day after irradiation was observed. At autopsy large blue lungs were found with clear interstitial edema without signs of destruction of the mucous membranes of trachea or bronchi of all sizes. Interstitial pulmonitis usually developed several days before the death from a combination of extremely severe injuries of the skin and intestines. Respiratory complications occurred in 13 men and were clinically especially significant for seven of them.

In the treatment of that group of patients, in conjunction with usual regimes for therapy, hyperbaric oxygenation was administered in special chambers under specified conditions: 1.2-1.5 ATA for about 40 min to 1 hour.

There were no obvious therapeutic effects.

Survival and Death

As discussed earlier at the expert IAEA meeting in August 1986, the evaluation of effectiveness used the criteria of new definitions introduced for LD₅₀ for 30 and 60 days. Despite that, our American colleagues illustrated such methods using our data.

We lost one of 53 patients having ARD stage II, with the radiation dose of 4.1 Gy, in spite of almost complete recovery from ARD. This was because of disturbances in the blood circulation of the brain from relapsing burn erythemas.

Out of 21 patients with ARD stage III (dose range from 4.0 to 6.0 Gy) 14 survived. All the patients with ARD of stage IV doses from 6.0 to 16.0 Gy died with only one exception. But it has become clear from the analyses of the pathological-anatomical data that their deaths were the results of combinations of several different clinical syndromes, primarily combinations of intestinal and bone marrow syndromes with total or subtotal simultaneous skin injuries.

Deaths with combined thermoradiation injuries occurred the 16th to the 23rd day, in one patient with not so pronounced intestinal injuries, and for another with bone marrow deficiency, i.e., indicating the importance of considering the severity of the skin injuries.

UNSCEAR presents a complete schematic summary of the survival time and main causes of lethal outcomes for the 28 patients who died of ARD as the result of the Chernobyl accident (12, 15).

Furthermore, this material can be used to analyze the effectiveness of the therapy in relation to the pathomorphological transformations observed in cases of radiation disease, and the data can be compared to the previous international experience (15).

It is difficult to evaluate the effect of the separate treatment regimes. It is, however, possible to state, considering the clinical data retrospectively, that positive effects of prophylactic precautions and therapy were seen in cases of infection, especially in bacterial complications. As mentioned earlier, this was obtained by isolation of the patients at special aseptic conditions during the period of agranulocytosis, by prophylactic treatment, and, if needed, medical use of antibiotics, antimycotics, and in some cases medical prescription of antivirus drugs (acyclovir). The sepsis diagnosis was confirmed by only seven out of 27 patients with lethal outcome because of ARD degrees I-IV. This was confirmed by pathological inspection and postmortem microbiological surveys (in four cases there were mycotic and in 33 cases bacterial sepsis). The remaining cases were negative or the microorganisms in the tissues were not defined clearly. Only the presence of insignificant numbers of colonies on necrotic surfaces of skin and mucous membranes was noticed.

The substitution therapy with blood components was the other important part of the treatment regime. It is necessary to underline the direct and significant effectiveness of administration of allogenic and autologic, cryoconserved thrombocytes.

Diverse circulatory disorders in the capillaries, most often localized to the lungs, mucous membranes, and in the brain, were observed for many patients. Massive fatal hemorrhages, however, were exceptionally rare.

The efficiency of all the complex treatments, evaluated in relation to frequency and courses of the lethal outcomes, should be considered as rather satisfactory, if the severity and all the combinations of clinical syndromes are taken into consideration. The analysis of the influence of bone marrow transplantation for a selected group of 13 patients is given separately as a special report by one of the authors (11).

Patients with fatal outcomes had especially severe courses of their diseases. This was the case for practically all patients having combinations of 2-3 different radiation syndromes and complex spectra of toxic infections and complications of these as well as circulatory disorders.

The skin injuries, covering substantial areas of the body surface, were one of the main causes of death for more than 50% of all patients. In deaths before day 34, they were usually accompanied not only by severe impairment of the bone marrow function but also by early-identified intestinal syndromes.

The skin injuries, for the patients with a prolonged survival, were associated with one or two ARD syndromes (bone marrow or intestinal) or appeared independently.

The most diverse clinical appearance was seen in patients with combinations of syndromes in which the complications and direct courses of the lethal outcome came in the period from days 24 to 48 after the radiation exposure. In the cases of severe impairment of the bone marrow function, some individuals presented signs of a weak regeneration of the bone marrow, and the mucous membranes recovered partially.

From the end of the second month extremely heavy infectious complications (including viral) and morphological changes of the parenchymous organs were characteristic.

Observations during the two years following the accident indicated the effectiveness of the treatment for the acute radiation diseases. The process of restoring blood parameters to normal levels proceeded rather quickly. After 1-1.5 years restored hematological status was reached. A clear dependency of the completeness of recovery in relation to the severity of the disease (dose of general irradiation) was observed during the period of restoration.

A moderate nonstable leucopenia, and more seldom a moderate thrombocytopenia, was present at the end of the observation period with 9-15-30% of patients with ARD of degrees I, II, and III, respectively. Simultaneously, 50% of the patients without complete normalization already presented at the first day of investigation a decrease in leucocyte number (granulocytopenia and/or thrombocytopenia), i.e., initial impairment of hematological parameters.

Later the moderate, nonstable cytopenia was apparently aggravated by diseases in the gastrointestinal tract (hepatitis, gastritis, ulcers) which preceded ARD.

With ARD stage III all the patients presented local radiation injuries. Continued treatment was necessary, including plastic surgery which stabilized the moderate cytopenia.

An investigation of the physical capacity for work and energy consumption demonstrated a propitious progress with gradual increase during the course of recovery from ARD. The time and the completeness of the rehabilitation demonstrated a partial dependence on the severity of the disease (irradiation dose).

The investigation of the physical capacity in relation to energy consumption gave the following conclusions:

The group of persons without clinical signs of acute radiation disease retained at all observation periods (up to one year) the ability to perform with normal energy consumption-4.9 kcal/min; patients with ARD stage I in general have similar figures-4.3 kcal/min.

Patients with ARD stages II and III have lower indices of physical capacity in the early period of recovery in comparison to the normal level (3.5-3.8 kcal/min, respectively). Not even one year later had they reached normal values.

Comments on Uncertainty Analysis and Error Sources for Deterministic Effects

1. The given questionnaire corresponds to early radiation effects in humans only. We consider the usage of animal data to be one of the main sources of errors, if such data are applied to respond for the questions essentially for real radiation accident exposure circumstances (including exposure geometry, radiation types, dose rates, etc.). To eliminate this uncertainty we insist on the use of real data from human exposures in radiation accidents as much as possible. These data were accumulated from a wide range of different industries and stages in the nuclear energy production cycle. One has to be reminded that the Clinical Department of the Institute of Biophysics accumulated this specific information over more than 40 years. There are estimates that more than 1/3 of the information from all accidents that have happened worldwide is collected in the Clinical Department; these data are also supplemented by international experience. Moreover, it is necessary to mention that questions given in this project correspond to major radiation accidents in nuclear energy reactors, so the Chernobyl accident experience is essential to decrease uncertainty of project experts assessments. However, the other source of errors corresponded to statistics rises from approach mentioned above. We consider this statistical uncertainty to be of more acceptable than that occurring from animal data.

2. The diagnosis of severity of radiation injuries and selection of an adequate treatment scheme are extremely important. Some authors have assessed the treatment efficiency in Chernobyl in early-stage ARD patients from data provided by the Clinical Department. The treatment provided a 1.5-Gy increase of LD₅₀ in this group of patients, which frequently had aggravations of ARS from skin injuries. The accidental-exposure observed in our experience consisted of dose rates in the range of 10-100 Gy/h. Supportive treatment significantly modifies ARS outcomes. The lower dose rates correspond to the lower assurance of outcome, because the therapeutic irradiation dose rates used in our clinics (3-6 cGy/min) are not similar to those (1 Gy/h and 0.2 Gy/h) given in the questionnaire. The expressiveness of ARS gastrointestinal syndrome is more strict than that for hemopoietic syndrome versus dose rate.

3. The following clinical manifestations determine the severity and outcomes for local skin injuries:

- acute ulceration,
- acute necrosis,
- moist desquamation, and
- late radiation ulcers.

The outcome depends on exposure dose, area, depth of injury, the anatomical site of damage, and treatment used. The early outcomes of acute period are as follows:

- reepithelisation, and
- primary absence of healing.

The late period also includes late-radiation ulcers. The outcome for skin depends on anatomical localization of the damage and elaborated treatment.

4. The "standard dose curves" of lymphocyte counts and tables for initial reaction (12) are the basis for the assessment of Question 8. For homogeneous exposure and sufficient number of daily blood count analyses the confidence is equal to 95%. The 50% confidence level corresponds to lower number of blood counts and/or inhomogeneous exposure and/or for cases when the initial reaction severity does not relate to lymphopenia degree.

5. Fractionating and decrease of dose rate given in Question 9.2 will increase the threshold of the radiation injuries and indices of mortality, suggesting that the model does not correspond to real accidental experience. Therefore there is only 50% confidence in the estimate.

6. The models given in Question 9.3 are close to real accident conditions (at the Chernobyl power plant essentially). If skin exposure is present, then the skin damage determines the effects and outcomes.

References

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Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	2	2.3	3.5	5	5.7
LD10	2.5	3	3.5	7	8	9
LD50	3.0	4	4.5	7	10	11
LD90	5.0	6	6.5	9	11	13

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	2	2.3	3.5	5	5.7
LD10	2.5	3	3.5	7	8	9
LD50	3.0	4	4.5	7	10	11
LD90	5.0	6	6.5	9	11	13

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	2	2.3	3.5	5	5.7
LD10	2.5	3	3.5	7	8	9
LD50	3.0	4	4.5	7	10	11
LD90	5.0	6	6.5	9	11	13

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	2.3	3	4.3	4	6	7.5
LD10	3.5	4	5.5	6	9	10
LD50	4.0	6	7.5	8	10	11
LD90	6.0	8	9.5	10	12	14

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.05	0.1	0.2

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	<u>50</u>
10 Gy/hr	<u>60</u>
1 Gy/hr	<u>70</u>
0.2 Gy/hr	<u>70</u>

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	50	80
10 Gy/hr	1 Gy/hr	60	90
1 Gy/hr	0.2 Gy/hr	70	95

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	3.5	5	6.2	5	8	9.5
LD10 _{GI}	4.5	6	7.5	10	12	13
LD50 _{GI}	5.5	7	8.3	10	13	15
LD90 _{GI}	8	10	12	12	14	16

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	3.0	5	6.7	5	8	9.5
LD10 _{GI}	4.0	6	8.0	10	12	13
LD50 _{GI}	5.0	7	8.6	10	13	15
LD90 _{GI}	7.5	10	13	12	14	16

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5	7	9	9	12	14
LD10 _{GI}	6	8	10	10	13	15
LD50 _{GI}	8	10	12	11	14	16
LD90 _{GI}	10	12	14	12	15	17

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5.5	8	10	9	13	15
LD10 _{GI}	6	9	11	10.5	14	16
LD50 _{GI}	8	10	13	12	15	17
LD90 _{GI}	10	13	15	13	16	18

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.05	0.1	0.2

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	0
10 Gy/hr	0
1 Gy/hr	40
0.2 Gy/hr	50

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	0	60
10 Gy/hr	1 Gy/hr	0	70
1 Gy/hr	0.2 Gy/hr	50	75

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	30	40
10 Gy/hr	30	40
1 Gy/hr	40	50
0.2 Gy/hr	50	60

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration	17	19	20.5
Dose for effect in 10% of exposed skin area	19	21	22
Dose causing effect in 50% of exposed skin area	21.8	23	24.3
Dose causing effect in 90% of exposed skin area	22	25	27

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration	16	18	19
Dose for effect in 10% of exposed skin area	18	20	21
Dose causing effect in 50% of exposed skin area	19	21	22.5
Dose causing effect in 90% of exposed skin area	20	22	23.5

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration	15	17	18.5
Dose for effect in 10% of exposed skin area	16	18	19.5
Dose causing effect in 50% of exposed skin area	18	19	20
Dose causing effect in 90% of exposed skin area	18	20	21

5%, 50%, and 95% values for the fraction of the population

	Fraction that die*		
	5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin	0	5
	Acute Ulceration in 90% of Exposed Skin	0	10
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin	0	15
	Acute Ulceration in 90% of Exposed Skin	2	30
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin	25	28
	Acute Ulceration in 90% of Exposed Skin	35	50

* without supportive treatment

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis	23	25	26
Dose for effect in 10% of exposed skin area	23.5	26	27.5
Dose causing effect in 50% of exposed skin area	24	28	30
Dose causing effect in 90% of exposed skin area	25	≥30	32

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis	22	24	25
Dose for effect in 10% of exposed skin area	23	25	26
Dose causing effect in 50% of exposed skin area	24	26	27
Dose causing effect in 90% of exposed skin area	25	28	29

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis	21	23	24.5
Dose for effect in 10% of exposed skin area	21	24	25.5
Dose causing effect in 50% of exposed skin area	22	25	26
Dose causing effect in 90% of exposed skin area	24	27	28

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin	3	10	15
	Acute Epidermal Necrosis in 90% of Exposed Skin	18	25	29
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin	0	30	35
	Acute Epidermal Necrosis in 90% of Exposed Skin	50	70	80
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin	70	90	100
	Acute Epidermal Necrosis in 90% of Exposed Skin	93	97	100

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation	12	14	15
Dose for effect in 10% of exposed skin area	14	16	17
Dose causing effect in 50% of exposed skin area	16	18	19
Dose causing effect in 90% of exposed skin area	17	20	21

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation	11	13	14
Dose for effect in 10% of exposed skin area	13	15	16.5
Dose causing effect in 50% of exposed skin area	15	17	18
Dose causing effect in 90% of exposed skin area	17.5	19	20

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation	10	11	12
Dose for effect in 10% of exposed skin area	10.5	12	13
Dose causing effect in 50% of exposed skin area	11	13	14
Dose causing effect in 90% of exposed skin area	12	14	15.5

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0	2	4
	Moist Desquamation in 50% of Exposed Skin	0	3	5
	Moist Desquamation in 90% of Exposed Skin	70	85	95
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0	2	4
	Moist Desquamation in 50% of Exposed Skin	75	85	90
	Moist Desquamation in 90% of Exposed Skin	88	95	100
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin	0	2	4
	Moist Desquamation in 50% of Exposed Skin	88	95	100
	Moist Desquamation in 90% of Exposed Skin	94	98	100

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin	0	1.5	2.3
	Moist Desquamation in 90% of Exposed Skin	0	1	1.5
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin	3	5	7
	Moist Desquamation in 90% of Exposed Skin	25	35	40
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin	60	75	80
	Moist Desquamation in 90% of Exposed Skin	88	90	95

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.7	2.5	3.2	3.0	5.5	7.0
LD10	2.5	3.5	4.0	6.0	8.5	10.0
LD50	3.5	5.0	6.5	9.0	10.5	12.0
LD90	5.0	6.5	8.0	11.0	12.5	14.0

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

30

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	30	40
1 Gy/hr	40	50
0.2 Gy/hr	50	60

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.5	2.5	3.1	4.0	6.0	7.0
LD10	2.7	3.5	4.0	6.0	9.0	11.5
LD50	3.3	4.5	5.2	8.5	11.0	12.0
LD90	5.2	6.5	7.1	9.5	12.0	13.0

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

40

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Treatment Supportive Treatment

45

65

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	30	40	50	30	40	50
LD10	50	64	74	50	64	74
LD50	65	80	90	65	80	90
LD90	70	88	100	70	88	100

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

80

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr	50	40
1 Gy/hr	70	60
0.2 Gy/hr	80	70

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.4	1.5	1.6	1.5	3.0	4.5
LD10	2.2	2.3	2.4	3.0	4.5	6.0
LD50	2.4	3.1	3.8	5.2	6.0	7.7
LD90	4.2	4.7	5.0	9.0	10.0	11.5

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	0.7	0.8	0.6	1.0	1.2
LD10	0.6	0.8	0.9	0.7	1.1	1.3
LD50	0.8	1.0	1.2	0.8	1.4	1.8
LD90	1.1	1.5	1.7	0.9	1.5	1.9

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.45	0.55	0.6	0.65	0.80	0.9
LD10	0.5	0.60	0.65	0.75	0.90	1.0
LD50	0.55	0.65	0.7	0.85	1.0	1.1
LD90	0.6	0.70	0.75	0.88	1.05	1.2

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.40	0.50	0.55	0.45	0.56	0.66
LD10	0.45	0.55	0.60	0.50	0.60	0.67
LD50	0.50	0.60	0.65	0.55	0.65	0.70
LD90	0.55	0.70	0.75	0.60	0.73	0.80

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	<u>20</u>
20% skin exposed	<u>30</u>
40% skin exposed	<u>40</u>
60% skin exposed	<u>50</u>

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	1.5	1.6	2.0	3.0	3.6
LD10	1.8	2.3	2.4	3.5	4.5	5.0
LD50	2.4	3.1	3.2	4.2	6.0	7.2
LD90	4.0	4.7	4.8	7.8	10.0	11.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.62	0.7	0.75	0.85	1.0	1.1
LD10	0.7	0.8	0.87	0.9	1.1	1.25
LD50	0.91	1.0	1.6	1.2	1.4	1.5
LD90	1.0	1.5	1.8	1.3	1.5	1.6

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	0.55	0.57	0.72	0.8	0.86
LD10	0.55	0.6	0.62	0.75	0.9	1.0
LD50	0.6	0.65	0.67	0.85	1.0	1.1
LD90	0.65	0.7	0.73	0.9	1.05	1.2

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.4	0.5	0.55	0.45	0.56	0.6
LD10	0.45	0.55	0.6	0.5	0.60	0.7
LD50	0.5	0.60	0.65	0.55	0.65	0.7
LD90	0.55	0.70	0.75	0.6	0.73	0.82

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	<u>70</u>
20% skin exposed	<u>60</u>
40% skin exposed	<u>50</u>
60% skin exposed	<u>40</u>

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed	70	80
20% of Skin Exposed	60	70
40% of Skin Exposed	50	60
60% of Skin Exposed	40	50

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.46	0.5	0.54	0.48	0.55	0.62
LD10	0.56	0.6	0.64	0.58	0.65	0.72
LD50	0.61	0.65	0.69	0.62	0.7	0.78
LD90	0.66	0.7	0.74	0.71	0.8	0.90

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.06	0.08	0.14	0.10	0.14	0.16
LD10	0.07	0.11	0.15	0.11	0.15	0.18
LD50	0.10	0.14	0.17	0.15	0.19	0.23
LD90	0.13	0.21	0.25	0.16	0.21	0.25

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.05	0.07	0.08	0.085	0.11	0.13
LD10	0.06	0.08	0.09	0.095	0.12	0.14
LD50	0.07	0.09	0.10	0.11	0.14	0.16
LD90	0.085	0.095	0.105	0.12	0.145	0.165

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.06	0.07	0.075	0.056	0.07	0.077
LD10	0.065	0.075	0.08	0.066	0.08	0.088
LD50	0.07	0.08	0.085	0.07	0.09	0.10
LD90	0.08	0.09	0.095	0.075	0.10	0.12

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	<u>50</u>
20% skin exposed	<u>40</u>
40% skin exposed	<u>30</u>
60% skin exposed	<u>0</u>

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal 80 Supportive 90

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	3.3	3.8	4.3	5.6	6.2	6.6
LD10	3.8	4.3	4.8	6.2	6.7	7.2
LD50	4.3	4.8	5.3	6.3	7.1	7.9
LD90	4.6	6.2	6.8	7.0	7.6	8.2

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.05	0.08	0.09	0.09	0.14	0.16
LD10	0.07	0.11	0.13	0.1	0.15	0.18
LD50	0.1	0.14	0.16	0.14	0.19	0.21
LD90	0.17	0.21	0.23	0.16	0.21	0.24

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.04	0.07	0.08	0.08	0.11	0.12
LD10	0.05	0.08	0.09	0.09	0.12	0.14
LD50	0.06	0.09	0.11	0.1	0.14	0.16
LD90	0.065	0.095	0.12	0.11	0.145	0.17

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.04	0.07	0.09	0.09	0.11	0.12
LD10	0.05	0.08	0.1	0.10	0.12	0.13
LD50	0.055	0.09	0.12	0.11	0.14	0.15
LD90	0.07	0.095	0.13	0.115	0.145	0.17

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	50
20% skin exposed	40
40% skin exposed	30
60% skin exposed	0

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

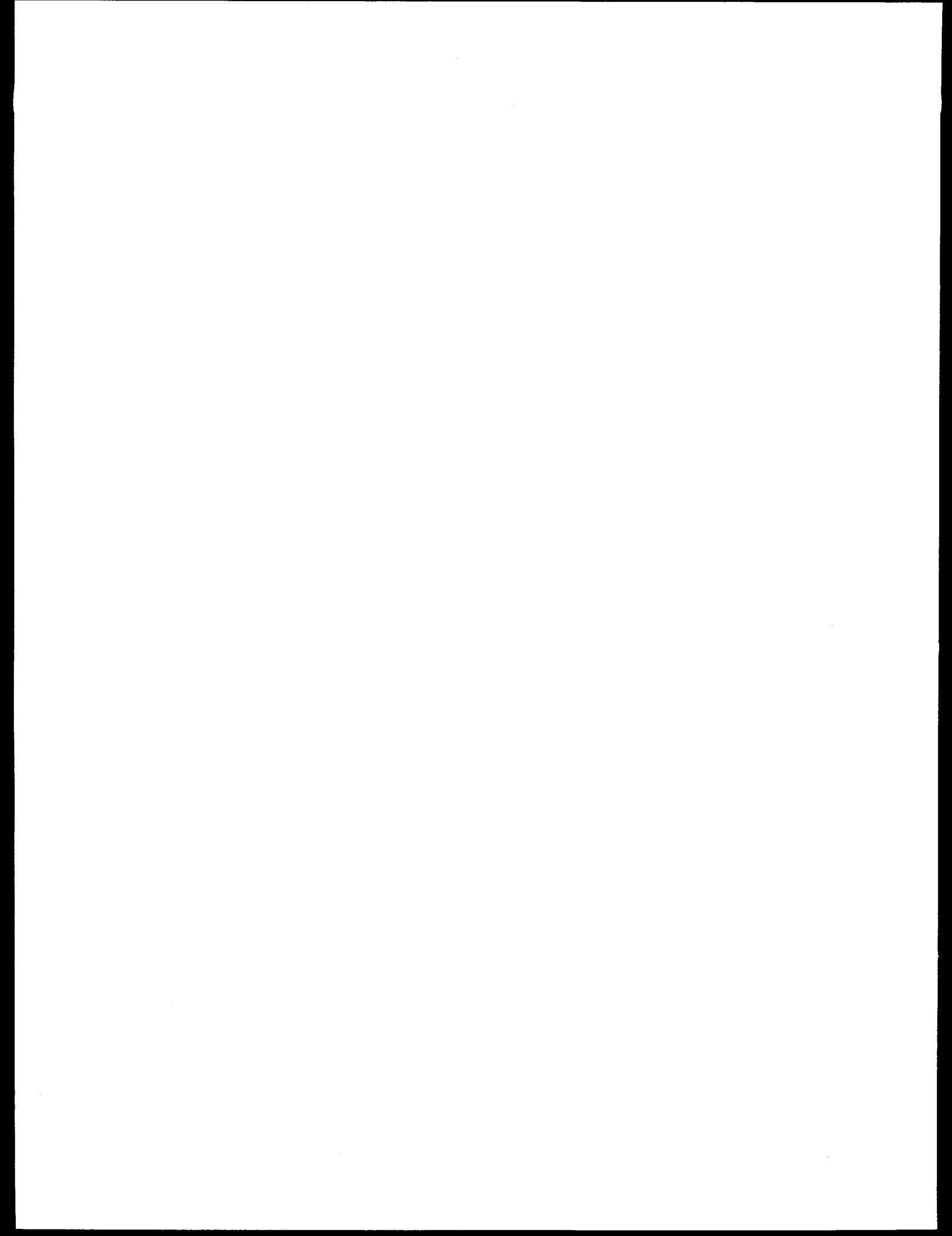
	Minimal Treatment	Supportive Treatment
No Skin Exposed	20	20
20% of Skin Exposed	80	90
40% of Skin Exposed	80	90
60% of Skin Exposed	70	75

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1	2.2	3.0	4.0
2	2.5	4.0	5.5
3	2.0	2.5	3.0
4	2.2	3.0	3.8
5	2.7	3.5	4.3
6	3.2	4.0	4.7
7	3.3	4.0	4.6
8	3.8	4.0	5.2
9	5.2	6.0	6.6
10	5.5	6.0	6.5



EXPERT G

Rationale

General Considerations

The goal of the joint study was to assess uncertainties associated with threshold effects and isoeffect doses at the 10%, 50%, and 90% incidence of deaths after total body irradiation at different dose rates and for different exposed organs. The data used to calculate the various isoeffect doses for hematopoietic syndrome, gastrointestinal syndrome and lung damage include published data from animal experimental systems which includes small rodents (i.e., mice and rats) canines, and primates. In addition, both published and unpublished data from my own laboratory was used since we have large amounts of data on the organs of interest allowing a good estimate of the uncertainty at the tails of the dose response curves. In addition, human data accrued from accidental overexposures, the atomic bomb incidents at Hiroshima and Nagasaki, the Chernobyl reactor accident in the Ukraine, and when appropriate, intentional exposure of humans to radiation in the treatment of cancer, were used. Because of the inherent uncertainties present in the data sets used, particularly regarding the data in humans, it was felt that rigorous mathematical modeling offered little benefit over my own approach (the "cold towel" method), in which I applied sound radiobiological principles to all available data to obtain estimates of the doses requested. In general, the estimates of doses on the steeply rising portions of dose response curves, i.e., the LD₅₀ with 5% and 95% confidence limits, can be accomplished with greater accuracy than those at the tails of the dose response curves, i.e., the LD₁₀s and LD₉₀s requested. In addition, the greatest uncertainty lies in these estimates. Since the goal of this report was to assess the degree of uncertainty in the estimates at the 3 isoeffects for the different endpoints, the greatest effort was put into the selection of the 5th and 95th percentiles for these estimates.

Range in Estimates of Uncertainties

Introduction

The uncertainties associated with estimates of LD's 10, 50 and 90 for humans are a result of: 1) the small number of individuals exposed; 2) errors in dosimetry and doses

received, 3) errors in extrapolating from the Japanese population to Western populations. For estimates of the 5th and 95th percentiles at the LD₁₀ and LD₉₀, I relied on the well-known steepness of dose response curves for the effects of interest as well as both published and unpublished data from my own laboratory. We have done a considerable amount of research on the tissues of interest. These data were compiled and, using both logit and Poisson fits to the data from individual experiments conducted over the past 20 years, estimates of the 5th and 95th percentiles at the three isoeffects were obtained. When extrapolating from animal data to man, the approach to estimate the LD₅₀ was to take the ratio of the doses from a large number of large animal experiments that produced measurable, very low or very high mortalities, e.g., LD₉₀/LD₁₀.

An important factor to consider when extrapolating from animals to man is that the coefficient of variation (CV) for the LD₅₀ among different species of large animals is similar. However, for irradiated cancer patients, the CV was shown to be much larger and was attributed to heterogeneity of responses among cancer patients. If the irradiated cancer population is assumed to be representative of the population at large, then the CV of a "normal" exposed population would be at least as great. However, the uncertainties in the dose estimates derived from experimental animals most often are obtained from inbred strains of animals, which are genetically identical and thus the estimates are smaller. In addition, the animals are housed and maintained under similar condition, further reducing the uncertainties in dose. Murine strain-dependent differences in LD₅₀/30 were reported as early as the 1950's. Most recently, strain dependent differences in lung damage have been reported by a number of laboratories, including ours. Thus, to account for heterogeneity in the human population, the dose response curves and the LD₅₀'s from different mouse models for the responses of interest were compared and the data compiled and an estimate of the LD₅₀, LD₁₀, and LD₉₀ with 5th and 95th percentiles obtained. A second important consideration was that mice that are sensitive to damage in one organ, as determined from dose response data, tend to exhibit a similar increased radiosensitivity in other organs, suggesting that radiosensitivity is genetically regulated, at least in part. It is now well-established that variations in radiosensitivity occur in the "normal" human population, which will account for at least some of the larger CV of variation observed in the radiotherapy patients.

Specific Elicitation Questions

Questions 9.1a and 9.1b. - Constant Dose Rates

Question 1a. Early fatalities due to a whole body dose delivered at 4 different dose rates.

The assumption was made that this question referred to deaths from hematopoietic syndrome. Based on animal experiments, little dose rate effect has been observed over the range of 100 Gy/h to 10 Gy/h. However, minimal treatment was assumed to be basic first aid only, while supportive treatment included standard measures, i.e., decontamination of skin and clothing, hospitalization, routine isolation, administration of blood products, etc., but did not include bone marrow transplantation or the administration of recombinant growth factors, such as GM-CSF, IL-6, etc. It has been suggested that bone marrow transplantation will be beneficial over a very small dose range, below 8 Gy. Conservative measures, i.e., supportive care only, will greatly increase the chance of survival, since it has been shown that these measures, i.e., antibiotic screen and careful nursing can increase the LD₅₀ by approximately two. Above 10 Gy death from the gastrointestinal syndrome is inevitable, and thus a bone marrow transplant would be of little value. Recombinant cytokines may be beneficial in the treatment of individuals exposed to high total body doses, although the data at this time are not clear. In animal experiments growth factors such as GM-CSF, IL-6 and IL-2 have been shown to protect hematopoietic progenitor cells in vitro, stimulate hematopoiesis in vivo, and in a few studies, increase the LD₅₀ from the hematopoietic syndrome. In humans however, the only growth factor that has been used is GM-CSF, which was administered to 8 patients exposed in the 1987 accident in Brazil who exhibited signs of acute radiation syndrome. In this small population, administration of GM-CSF did not improve the survival rate and thus the efficacy of this recombinant cytokine was not demonstrated. However, with improvements in recombinant technology and development of new cytokines, administration of recombinant cytokines to persons accidentally exposed to high total body doses of radiation will most likely become the standard of care for such individuals.

In terms of the dose rate question, bone marrow shows little dose rate effect. In the range of dose rates specified here (100 Gy/h to 0.2 Gy/h), however, dose rate effects have been demonstrated in animal systems. Most of these data derive from studies in murine models in the 1950's to 1970's but include more recent data from studies related to clinical protocols for bone marrow transplantation performed in

both murine and canine models. Little dose rate effect would be expected by a reduction in dose rate of one order of magnitude, from 100 Gy/h to 10 Gy/h. Based on the available data, reducing the dose rate from 10 Gy/h to 1 Gy/h would increase the dose for bone marrow syndrome by 20% to 40% by most reports, with only one reporting an increase of 70% in dose. Unfortunately, no studies used dose rates as low as the lowest specified in this report, 0.2 Gy/h, i.e., 0.003 Gy/min. Thus these estimates were derived from low dose rate studies in vitro.

Question 1b. Early fatalities due to gastrointestinal syndrome after a whole body dose delivered at 4 different dose rates.

Estimating the uncertainties in dose for deaths from the gastrointestinal syndrome at the three isoeffects specified is not clear since, in the dose range of the GI syndrome, death is inevitable. What differs is the time to death, occurring sooner, e.g., within 6 days, after the higher doses in the dose range and later, after 10 days but before 20 days, after doses in the low end of the dose range. Thus, each of the specified isoeffect doses will change with the time after irradiation. For the purposes of this report, the time of death from the GI syndrome will be considered to be 10 days. In addition, the gastrointestinal syndrome involves not only the GI tract, but the bone marrow as well. It has been shown in experimental animals that the LD₅₀ for the GI syndrome can be increased by either bone marrow transplantation or by shielding some portion of the active marrow. However, the data from Chernobyl indicate that bone marrow transplants had no effect on death from the GI syndrome although this was most likely due to the fact that the injuries in the GI tract were complicated by skin burns.

The assessment of dose uncertainties for the GI syndrome in man without other complicating factors, such as severe skin burns, is difficult because little data is available in man, including persons exposed at Chernobyl. Thus most of these estimates are derived from experimental models, specifically mice. Some of the same factors that apply to the hematopoietic syndrome apply here, e.g., genetic predisposition, but others are unique to this syndrome, e.g., it is well-established that the content of bacterial flora in the bowel significantly influences the LD₅₀ for GI death in mice. Thus, there is a large variation in the LD₅₀ for GI death even in experimental animals where standard conditions prevail between experiments in one lab but not for experiments between different labs. The influence of gut flora on the LD₅₀ for gut damage will have a significant impact on the LD₅₀ when conservative supportive care, i.e., antibiotic screen, is administered to over-exposed humans.

For the purposes of this report, such conservative care is assumed to increase the LD₅₀ for GI death by a factor ranging from 1.3 to 1.4.

Unlike the bone marrow, the gastrointestinal tract shows a large dose rate effect over the dose ranges specified. The estimates of the 3 isoeffects at dose rates specified were obtained using data from total body irradiation experiments in mice, since this experimental situation most closely approximates the conditions in question. The changes in dose values ranged from no change between 100 Gy/h and 10 Gy/h, to 1.5 to 1.6 between 10 Gy/h and 1 Gy/h, and 1.6 to 1.7 between 10 Gy/h and 1 Gy/h and, by extrapolation from in vivo data in mice and in vitro data for cells in culture, 1.8 to 2.0 for a decrease of dose rate from 10 Gy/h to 0.2 Gy/h.

Question 2a. Early fatalities due to Beta lung dose, same 4 dose rates, stratify by age <40 and >40.

The estimates for the lung were obtained from the only data available where doses and dosimetry are known, the data of van Dyk et al. The data regarding dose rate effects on lung deaths were obtained from murine experiments in which only the whole thorax was irradiated, consistent with the conditions in the elicitation question. The ages chosen for stratification of lung damage were puzzling. My assumption was that the underlying rationale is that older persons will have compromised lung and lung function due to a number of factors including environment, smoking habits, etc. However, there are no data in the literature, either in patients treated with radiation for malignant disease or animal experimentation, that allow an estimate in the change in LD₅₀ in an older age group. The obvious source of this information would be the radiotherapy literature, but the information sought cannot be obtained even from that literature. The other possibility is data on persons under the age of 18, particularly young children, under the age of three. The lungs of young children undergo rapid growth, particularly in terms of the numbers of alveoli. Unlike the airways, which are fully formed during gestation and increase only in size but not number during childhood, the number of alveoli increases rapidly during the first few years of life. Radiation would be expected to kill larger number of these dividing cells in a child than the non-dividing critical cells in an adult. However an analysis of the available data in the literature shows that, although progressive deterioration of lung function has been observed in children treated with curative doses of radiation for tumors such as Wilm's tumor, it was not due to changes in the lung but rather to skeletal

abnormalities resulting from irradiation of this rapidly proliferating system. Thus, the data are inconclusive regarding any increase in sensitivity of the lung in persons under the age of 18. However, because it is generally accepted that the lungs of this age group are more sensitive and because they are not treated to the same total doses as adults, I have assumed a 10% decrease in dose for the younger age group. My approach and rationale for the older age group was to assume that the various factors which might contribute to decreased lung function with age was not that the isoeffect value would change, but rather that such age-related changes would be manifested as an increase in the uncertainty for the dose estimate, i.e., the 95% confidence limits will be larger at all three isoeffects, but particularly at the high and low ends. The lung exhibits a substantial dose rate effect over the dose rates specified, and the estimates were derived from both animal experiments and clinical data after total body irradiation, although these data are more difficult to interpret because of immunosuppressive drugs such as cyclophosphamide are frequently given before TBI.

Question 2b. Morbidity Due to Beta Lung Dose

The same assumptions used in 2a were used here and similar bodies of data were used. However, it is well established in animal models and in humans that morbidity from pulmonary irradiation occurs at lower doses than does mortality. Thus all of the estimates of isoeffect doses are lower than for mortality in 2a. In addition, the issues of pre-existing lung disease or changes in lung function with age are more likely to have a larger impact on morbidity from radiation than mortality. However, little quantitative data are available to determine the influence of such factors on lung morbidity. Thus, these factors will be reflected in the uncertainty in the dose estimates.

Question 3. Not Done

Question 6.

The assumptions used to estimate these doses were: 1) the doses would be similar to those obtained in question 1a as questions 6a and 6b deal with a 10:1 and 100:1 reduction in dose rate. However, some consideration was given to the fact that the dose was given over a longer period of time and a time factor, 10% increase in dose, was used in the dose calculations. As in question 1, the increase in dose for supportive treatment was assumed to be 50%. The values for the doses in question 6 are similar to those for question 1 and assumed that death was due to hemopoietic syndrome.

Question 8. Seed Question

The data used to derive these values came from the 1988 UNSCEAR report. It was assumed that vomiting at 0:00 exposure time (case # 10) meant immediately after exposure or during exposure, rather than that the individual never vomited. The rationale use to estimate doses and rank these individuals from highest exposure to lowest was first that the earlier the onset of the symptoms of the prodromal phase, vomiting, the higher the dose. In addition however, the rate of decline and the shape of the curve for lymphocyte count as a function of time was also considered. Lastly, whether the dose to bone marrow was homogeneous or inhomogeneous was also considered since it is well established in animal models that the bone marrow can be repopulated by small numbers of sequestered cell. The lack of data on lymphocyte counts after 2 and 3 days for case numbers 2 and 8, respectively, was interpreted as indicating that these two individuals had died. However, I have also estimated doses in these two individuals assuming that the lack of data did not indicate that death had occurred. These numbers are given below the table. Using this scenario, both individuals would have received significantly lower doses, as indicated.

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Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.2	1.9	2.6	2	3	4.1
LD10	1.9	2.6	3.5	2.5	4	5.5
LD50	2.1	3.5	4.7	3.6	5	6.5
LD90	3.2	5	6.8	5.7	7	9

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.2	1.9	2.6	2	3	4.1
LD10	1.9	2.6	3.5	2.5	4	5.5
LD50	2.1	3.5	4.7	3.6	5	6.5
LD90	3.2	5	6.8	5.7	7	9

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.7	2.5	3.2	2.1	3.7	3.9
LD10	2.2	3.1	4.3	3.2	4.7	6
LD50	3.5	4.7	6.1	5.2	6.7	7.8
LD90	5	6.3	8	6.8	9	10.2

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.2	0.7	1

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	0.75
10 Gy/hr	0.75
1 Gy/hr	0.5
0.2 Gy/hr	_____

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr		
10 Gy/hr	1 Gy/hr	0.9	0.9
1 Gy/hr	0.2 Gy/hr	0.9	0.9

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	3.2	4.8	5.9	4.7	6.1	7.3
LD10 _{GI}	4.3	6	7.9	5.7	7.5	9.1
LD50 _{GI}	5.1	7.2	8.9	7.2	9.2	11
LD90 _{GI}	6.3	9.8	11.5	8.2	10.8	13

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	4.5	5.7	6.5	5.5	7	8.5
LD10 _{GI}	6.2	7.1	8.4	7	9.2	11.5
LD50 _{GI}	7	8.7	10.2	9.2	11.3	13.5
LD90 _{GI}	9	10.5	12.2	10.8	13.7	15.5

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	6	7.3	8.6	7.9	9.4	11
LD10 _{GI}	7.8	9.2	10.7	9.75	11.6	13.6
LD50 _{GI}	9.4	11.1	13	11.9	14.2	16.6
LD90 _{GI}	12.7	15.1	17.6	14	16.7	19.4

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	7.2	9	11	9.8	13	16.2
LD10 _{GI}	9	10.8	13.2	12	15.1	18.2
LD50 _{GI}	10	13.1	16.8	14	18.4	23.1
LD90 _{GI}	14.7	17.6	21.6	20.6	24.6	30.2

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.2	0.6	1

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	0.75
10 Gy/hr	0.75
1 Gy/hr	0.75
0.2 Gy/hr	0.75

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	0.75	0.9
10 Gy/hr	1 Gy/hr	0.75	0.9
1 Gy/hr	0.2 Gy/hr	0.9	0.9

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	0.5	0.5
10 Gy/hr	0.5	0.5
1 Gy/hr	0.5	0.5
0.2 Gy/hr	0.5	0.5

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				6	7	8
LD10				7.6	8.5	9.3
LD50				8.6	9.5	10.5
LD90				9.5	10.75	12

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				7.5	8.5	10.3
LD10				9.4	10.3	14.25
LD50				9.7	11.8	15.5
LD90				10.5	13.7	16

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				10	12	16.2
LD10				14.4	16.2	21
LD50				16.5	19.5	23.2
LD90				17.9	21.2	25.2

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				13.7	16.3	18.5
LD10				18.1	21.2	25
LD50				19.3	23.8	26.4
LD90				22	26.2	30

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	_____
10 Gy/hr	_____
1 Gy/hr	_____
0.2 Gy/hr	_____

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	0.9	0.9
10 Gy/hr	1 Gy/hr	0.9	0.9
1 Gy/hr	0.2 Gy/hr	0.9	0.9

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	0.5	0.5
10 Gy/hr	0.5	0.5
1 Gy/hr	0.5	0.5
0.2 Gy/hr	0.5	0.5

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				4.3	5.5	7.1
ED10				5.8	7.2	9
ED50				6.8	8.8	10.5
ED90				8.1	9.9	11.2

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				6.2	7	8.5
ED10				7.3	9.1	11.5
ED50				8.3	10.2	14
ED90				9.8	12	16.5

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				8.2	10.5	12.7
ED10				10.3	13.5	17.2
ED50				13.8	16.7	20
ED90				15.5	19.2	22

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				11.5	14.7	17.2
ED10				16	18.9	21
ED50				18	20	23.2
ED90				20.2	23.5	27

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				0.01	0.05	0.03
DR10				0.05	0.1	0.15
DR50				0.2	0.25	0.3
DR90				0.35	0.5	0.65

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr _____
10 Gy/hr _____
1 Gy/hr _____
0.2 Gy/hr _____

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	_____	0.5
10 Gy/hr	_____	0.5
1 Gy/hr	_____	0.5
0.2 Gy/hr	_____	0.5

Question 4a – DELETED**Question 4b – DELETED**

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

	Fraction that die		
	5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.3	2.3	3.3	2.2	3.4	4.6
LD10	2	3	4.7	3	5	6
LD50	3	4	5	5	6	7.8
LD90	4	5.5	6.5	5.8	7	8

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

0.9

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	0.9	0.9
1 Gy/hr	0.9	0.9
0.2 Gy/hr	0.9	0.9

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	2	2.9	3.8	2.8	4	5
LD10	2.5	3.4	5.9	3.6	5	6.5
LD50	4	5	6	5.8	7	8
LD90	5.8	6.7	7.9	7.5	9.5	10.8

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

0.9

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Treatment Supportive Treatment

0.5 0.5

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold				6	8.2	10.5
LD10				7.8	9.6	11
LD50				8.5	11.3	13.1
LD90				10.3	12.8	14.5

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		0.75
1 Gy/hr		0.9
0.2 Gy/hr		0.9

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

threshold	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____

20% skin exposed _____

40% skin exposed _____

60% skin exposed _____

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

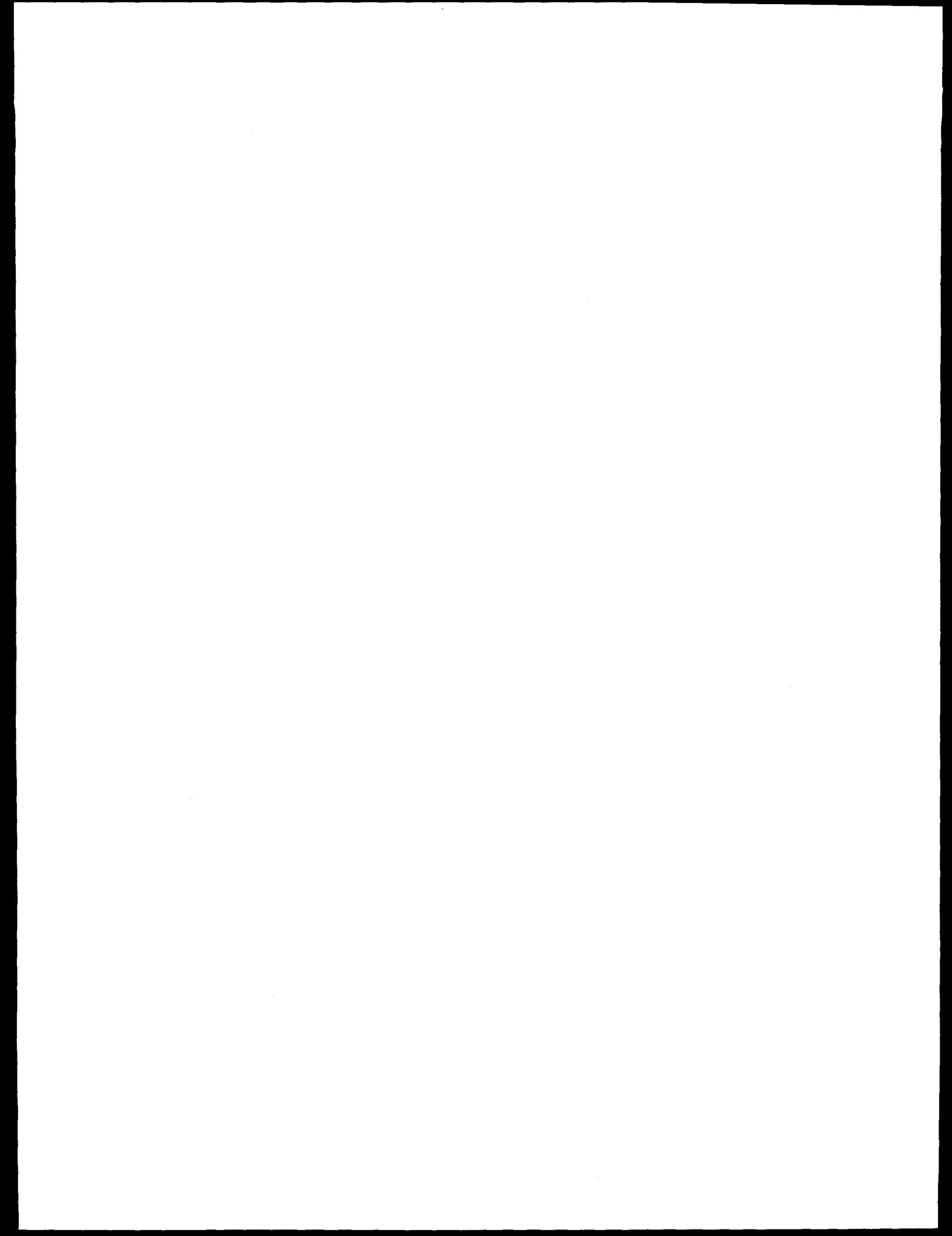
	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1	1.2	2.25	3.8
2	9.2	15	20
3	1.2	2	4
4	2	4	6
5	3.5	5.5	7
6	2	4	6.2
7	2.5	4.5	7
8	5	10	15
9	5.5	7.5	9.5
10	8	12	16



EXPERT H

Rationale

General Assumptions

It was considered that the population at risk is a general population including infants, aged, and ill (including genetically diseased and deleterious trait carriers, such as ataxia-telangiectasia families).

General Methods

My approach was to use dose-response data from my own clinical experience that has included patients with approximate whole body exposures of 100, 250, 300, 450, and 600 rads; and pertinent medical literature reports including those that I reviewed and used in WASH 1400 and NUREG 1446. I also used reports of IAEA, UNSCEAR and NCRP as well as current texts such as Mettler and Upton's *Medical Effects of Ionizing Radiation*. I did not perform mathematical analyses of the data although I may have been aware of the analytic results in those publications. Where clinical data were lacking, I considered relevant scientific literature reports on experimental animal radiation dose-response studies.

Uncertainties Considered

I considered the uncertainties listed on Page 6 of Revision 15 of the Early Health Effects Case Structure Document.

Rationale Specific to Individual Questions

Question 1a - Fatalities

Based on clinical experience and mainly on experimental animal data such as summarized by Scott et al., a decrease in effectiveness of about 10% could be expected at about 0.2 Gy/hr.

LD₅₀ doubling rate estimates are based on animal data.

The efficacy of supportive therapy may be greater than expected when the dose rate is lower, rather than an error in the LD₅₀ at the lower rate. On the other hand, data from the same exposed population could have a dose reconstruction error in common.

Question 1b - Gastrointestinal Fatalities

Although the GI tract is less radiosensitive than the hematopoietic system, when it is damaged, the efficacy of therapy is limited, well under a factor of two even under experimental conditions with animals. The Chernobyl data confirm this.

The benefit of protracted exposure in limiting GI morbidity is demonstrated in radiation therapy patients, but this is usually at dose rates below 1 Gy/day to the whole abdomen.

Supportive treatment may show differential efficacy at the lowest dose rate as noted in the "all causes" section above.

Regarding the GI LD₅₀ versus the "all causes" one, since the latter is dominated by the more radiosensitive hematopoietic system, it is hard to see how any error in the former determination could have any bearing on the latter one, other than a common mode failure in dosimetry. However, most of the human data are from different populations, e.g., the GI data are mainly from therapy patients, while the others are mainly from accidental exposures.

Question 2a - Early Fatalities due to Beta Lung Dose

The work of Scott et al. at ITRI has provided most of the available information in this specialized area. Others include WASH 1400 and NUREG 5198. The studies' LD₅₀ results range from 26 to 58 Gy in rats, to 45 to 110 Gy in dogs. Hobbs et al. found a threshold of 5.7 Gy in dogs. I used a judgmental number to resolve the differences.

I used a 10% reduction for the over-40 years group since an age effect has been seen, albeit not clearly.

Although dose rate decrease has been shown to decrease efficacy, I did not feel that I had enough data to fill in the over-40 category or the lower dose rate boxes. I reduced the probability of dose rate correlations because of the increased likelihood of there being different mechanisms at the lower rates.

While I felt that a correlation was possible at high dose rates, differences in mechanism and efficacy of supportive therapy at low dose rates decreased the possibility.

Question 2b – Pulmonary Mortality

I felt that I lacked enough expertise in this area to even guess at the answers to this set.

Question 3 – Deterministic Fatalities due to Alpha Lung Dose

The only human data are those of Okladnikova et al. presented at a Health Physics Society Plutonium Workshop in Washington, DC, 6–8 February 1996. She reported 6 deaths due to cardio-pulmonary insufficiency in a group of 11 young women with evidence of “Plutonium pneumosclerosis” who averaged 11.8 Gy absorbed lung dose from ^{239}Pu during an average 5.9 years of occupational exposure. I used 2.5 Gy assuming that there was wasted radiation near the end of the exposure period.

For the over-40 population, I assumed that the greatest consideration would be radiosensitivity of the lung, and therefore all responses would be altered in correlation.

Question 5 – Skin Effects

I did not feel competent to give probability estimates for skin effects.

Question 6a – Early Fatalities due to Whole Body Dose; 10:1 Decrease in Dose Rate

In the absence of any human data and of readily adaptable animal data, I used a judgmental 20% reduction in effectiveness of the irregularly reduced dose rate compared to the higher dose rates of Question 1. Estimated efficacy of supportive treatment, based on human and animal data is assumed to be about 1.5.

Question 6b – 100:1 Decrease in Dose Rate

Because 80% of the dose is absorbed in the first hour, I made a judgmental reduction of 10% from the higher dose effectiveness in Question 1.

Question 6c – Early Fatalities due to Lung Dose; 14:1 Decrease in Dose Rate

I lack the expertise and data with which to provide a response to this question.

Question 7 – Multiple Exposed Organs and Exposure Periods

The numbers generated in this response were based on the previous estimates for acute and protracted exposures to the bone marrow, etc., but the assumed interactions at various levels were essentially intuitive and not statistical because I felt that not enough has been done in human or even experimental animals (with additional extrapolation uncertainties) to calculate these estimates. When I tried to quantify the variables considered, I was unsuccessful in replicating the results or even producing consistent proportionate differences from the original. In other words, I really cannot provide a quantitative basis for the numbers or for the uncertainty range.

It has dawned on me that I really do not know enough to support my guesses of the doses, given the numbers of variables and the unknown and therefore unpredictable interactions that might result from the concurrent exposures. Setting aside pride of authorship and all the effort I expended in trying to encompass the considerations raised by this very difficult question, I would regretfully caution you about using my numerical responses to it.

References

No references provided.

Question 1a – Early Fatalities Due To Whole Body Dose

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	1.5	2.0
LD10	1.0	1.5	2.0	2.0	2.5	3.0
LD50	2.0	3.0	4.0	3.0	4.5	6.0
LD90	4.0	5.0	6.0	6.0	7.5	9.0

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	1.5	2.0
LD10	1.0	1.5	2.0	2.0	2.5	3.0
LD50	2.0	3.0	4.0	3.0	4.5	6.0
LD90	4.0	5.0	6.0	6.0	7.5	9.0

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.0	1.5	1.0	1.5	2.0
LD10	1.0	1.5	2.0	2.0	2.5	3.0
LD50	2.0	3.0	4.0	3.0	4.5	6.0
LD90	4.0	5.0	6.0	6.0	7.5	9.0

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.5	1.1	1.65	1.1	1.65	2.2
LD10	1.1	1.65	2.2	2.2	2.75	3.3
LD50	2.2	3.3	4.5	3.3	4.95	6.6
LD90	4.4	5.5	6.6	6.6	8.75	9.7

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.02	0.03	0.08

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	<u>0.9</u>
10 Gy/hr	<u>0.9</u>
1 Gy/hr	<u>0.9</u>
0.2 Gy/hr	<u>0.7</u>

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	0.9	0.9
10 Gy/hr	1 Gy/hr	0.9	0.9
1 Gy/hr	0.2 Gy/hr	0.9	0.7

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5.0	6.0	7.0	6.0	7.0	8.0
LD10 _{GI}	8.0	9.0	10.0	9.0	10.0	12.0
LD50 _{GI}	12.0	15.0	18.0	15.0	18.0	20.0
LD90 _{GI}	18.0	20.0	22.0	20.0	21.0	22.0

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5.0	6.0	7.0	6.0	7.0	8.0
LD10 _{GI}	8.0	9.0	10.0	9.0	10.0	12.0
LD50 _{GI}	12.0	15.0	18.0	15.0	18.0	20.0
LD90 _{GI}	18.0	20.0	22.0	20.0	21.0	22.0

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	5.0	6.0	7.0	6.0	7.0	8.0
LD10 _{GI}	8.0	9.0	10.0	9.0	10.0	12.0
LD50 _{GI}	12.0	15.0	18.0	15.0	18.0	20.0
LD90 _{GI}	18.0	20.0	22.0	20.0	21.0	22.0

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	6.0	7.0	8.0	7.0	8.0	9.0
LD10 _{GI}	9.0	10.0	11.0	10.0	11.0	12.0
LD50 _{GI}	13.0	16.0	19.0	14.0	17.0	20.0
LD90 _{GI}	20.0	22.0	24.0	21.0	23.0	25.0

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.08	0.1	0.15

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	<u>1.0</u>
10 Gy/hr	<u>1.0</u>
1 Gy/hr	<u>0.9</u>
0.2 Gy/hr	<u>.75</u>

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	0.9	0.9
10 Gy/hr	1 Gy/hr	0.9	0.9
1 Gy/hr	0.2 Gy/hr	0.7	0.7

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	0.5	0.5
10 Gy/hr	0.5	0.5
1 Gy/hr	0.5	0.5
0.2 Gy/hr	0.5	0.5

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	4	5	8	2	3	4
LD10	6	8	10	4	5	6
LD50	8	10	12	6	7.5	9
LD90	10	12	14	8	10	12

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	5	7	9	2.5	4	5.5
LD10	8	10	12	5.5	8	10
LD50	12	15	18	8	10	12
LD90	18	21	25	12	15	18

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	15	20	25	8	10	15
LD10	25	30	35	15	20	25
LD50	35	40	45	25	30	35
LD90	45	50	55	35	40	45

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	60	80	100	45	60	75
LD10	100	125	140	75	90	110
LD50	140	160	180	100	125	140
LD90	180	200	220	140	160	180

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	<u>0.9</u>
10 Gy/hr	<u>0.9</u>
1 Gy/hr	<u>0.9</u>
0.2 Gy/hr	<u>0.9</u>

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	<u>0.9</u>	<u>0.9</u>
10 Gy/hr	1 Gy/hr	<u>0.75</u>	<u>0.75</u>
1 Gy/hr	0.2 Gy/hr	<u>0.6</u>	<u>0.6</u>

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	<u>0.75</u>	<u>0.75</u>
10 Gy/hr	<u>0.75</u>	<u>0.75</u>
1 Gy/hr	<u>0.55</u>	<u>0.55</u>
0.2 Gy/hr	<u>0.55</u>	<u>0.55</u>

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	2	2.5	4	1	1.5	2
ED10	3	4	5	2	2.5	3
ED50	4	5	6	3	4	4.5
ED90	5	6	7	4	5	6

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	2.5	3.5	4.5	1.3	2	2.8
ED10	4	5	6	2.8	4	5
ED50	6	7.5	9	4	5	6
ED90	9	10.5	12.5	6	7.5	9

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	7.5	10	12.5	4	5	7.5
ED10	12.5	15	17.5	7.5	10	12.5
ED50	17.5	20	22.5	12.5	15	17.5
ED90	22.5	25	27.5	17.5	20	22.5

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	30	40	50	22.5	30	37.5
ED10	50	63	70	37.5	45	55
ED50	70	80	90	50	62.5	70
ED90	90	100	110	70	80	90

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	0.000034	0.000057	0.000068	0.000022	0.000035	0.000057
DR10	0.000091	0.000114	0.000171	0.000080	0.000103	0.000114
DR50	0.000228	0.000285	0.000342	0.000205	0.000251	0.000319
DR90	0.000342	0.000456	0.000571	0.000308	0.000411	0.000513

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	<u>0.9</u>
10 Gy/hr	<u>0.9</u>
1 Gy/hr	<u>0.8</u>
0.2 Gy/hr	<u>0.75</u>

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40
100 Gy/hr	<u>0.9</u>	<u>0.9</u>
10 Gy/hr	<u>0.9</u>	<u>0.9</u>
1 Gy/hr	<u>0.9</u>	<u>0.9</u>
0.2 Gy/hr	<u>0.9</u>	<u>0.9</u>

Question 4a – DELETED**Question 4b – DELETED**

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin			
	Acute Ulceration in 90% of Exposed Skin			

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin			
	Acute Epidermal Necrosis in 90% of Exposed Skin			

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	1.2	1.8	1.2	1.8	2.4
LD10	1.2	1.8	2.4	2.4	2.7	3.6
LD50	2.4	3.6	4.8	3.6	5.4	7.2
LD90	4.8	6.0	7.2	7.2	9.0	10.8

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

0.9

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr	0.9	0.9
1 Gy/hr	0.9	0.9
0.2 Gy/hr	0.75	0.75

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	1.1	1.7	1.1	1.7	2.2
LD10	1.1	1.7	2.2	2.2	2.75	3.3
LD50	2.2	3.3	4.4	3.3	5.0	6.6
LD90	4.4	5.5	6.6	6.6	8.3	9.9

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

0.9

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal Supportive
Treatment Treatment

0.9 0.9

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50						
LD90						

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	1.2	1.8	1.2	1.8	2.4
LD10	1.2	1.8	2.4	2.4	2.8	3.6
LD50	2.4	3.6	4.8	3.6	5.4	7.2
LD90	4.8	6.0	6.6	7.2	9.0	10.8

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.8	1.0	0.8	1.0	1.2
LD10	1.0	1.2	1.4	1.2	1.5	1.7
LD50	1.5	2.0	2.5	1.7	3.0	3.3
LD90	2.7	3.0	3.3	3.5	4.5	6.0

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.75	0.82	0.95	0.8	0.9	1.0
LD10	0.98	1.2	1.5	1.0	1.3	1.6
LD50	2.0	2.2	2.5	2.0	2.5	2.9
LD90	2.5	2.8	3.0	2.9	3.0	3.1

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.7	0.82	0.93	0.75	0.85	0.95
LD10	0.96	1.0	1.4	1.2	1.5	1.8
LD50	1.8	2.1	2.4	2.0	2.4	2.8
LD90	2.4	2.6	2.8	2.8	2.9	3.0

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	<u>0.9</u>
20% skin exposed	<u>0.7</u>
40% skin exposed	<u>0.6</u>
60% skin exposed	<u>0.5</u>

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.0*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	0.0*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.0*D	0
Total	2.1*D	3.1*D	2.1*D	0.0*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	1.2	1.8	1.2	1.8	2.4
LD10	1.2	1.8	2.4	2.4	2.6	2.8
LD50	2.4	2.5	3.0	2.8	3.0	3.5
LD90	3.0	3.5	4.0	3.5	4.0	4.5

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	0.8	1.0	0.8	1.0	1.2
LD10	1.0	1.2	1.4	1.4	1.6	1.8
LD50	1.6	2.2	2.6	2.0	2.8	3.0
LD90	2.7	3.2	3.4	3.2	3.7	4.0

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.75	0.82	0.95	0.8	0.9	1.0
LD10	0.98	1.2	1.5	1.0	1.3	1.6
LD50	2.0	2.2	2.5	2.0	2.5	2.9
LD90	2.5	2.8	3.0	2.9	3.0	3.1

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.7	0.82	0.93	0.75	0.85	0.95
LD10	0.96	1.0	1.4	1.2	1.5	1.8
LD50	1.8	2.1	2.4	2.0	2.4	2.8
LD90	2.4	2.6	2.8	2.8	2.9	3.0

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	<u>0.9</u>
20% skin exposed	<u>0.7</u>
40% skin exposed	<u>0.6</u>
60% skin exposed	<u>0.5</u>

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed	0.9	0.9
20% of Skin Exposed	0.9	0.7
40% of Skin Exposed	0.9	0.6
60% of Skin Exposed	0.9	0.5

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.7*D	6.3*D
balance of first day	0.7*D	1.2*D	0.7*D	9.3*D	144*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	3.6*D	0
Total	2.1*D	3.1*D	2.1*D	13.6*D	150.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.4	0.5	0.6	0.95	1.0	1.3
LD10	0.7	0.8	0.9	1.3	1.5	1.7
LD50	1.0	1.2	1.5	1.7	2.0	2.2
LD90	1.8	2.0	2.5	2.2	2.5	3.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.08	0.2	0.22	0.1	0.25	0.28
LD10	0.25	0.3	0.4	0.28	0.35	0.42
LD50	0.5	0.7	0.8	0.53	0.75	0.85
LD90	0.9	1.0	1.1	0.9	1.2	1.5

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.1	0.15	0.18	0.25	0.3	0.35
LD10	0.2	0.25	0.35	0.4	0.45	0.6
LD50	0.45	0.6	0.7	0.7	0.8	0.9
LD90	0.7	0.8	0.9	0.95	1.0	1.2

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.05	0.1	0.15	0.15	0.2	0.25
LD10	0.15	0.2	0.25	0.28	0.3	0.4
LD50	0.3	0.4	0.5	0.55	0.6	0.7
LD90	0.6	0.7	0.8	0.75	0.8	1.0

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed 0.9
20% skin exposed 0.7
40% skin exposed 0.6
60% skin exposed 0.5

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.0*D	6.3*D
balance of first day	0.7*D	1.2*D	0.7*D	0.0*D	144*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.0*D	0
Total	2.1*D	3.1*D	2.1*D	0.0*D	150.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.6	1.2	1.8	1.2	1.8	2.4
LD10	1.2	1.8	2.4	2.4	2.6	2.8
LD50	2.4	2.5	3.0	2.8	3.0	3.5
LD90	3.0	3.5	4.0	3.5	4.0	4.5

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.09	0.1	0.3	0.4	0.5	0.7
LD10	0.4	0.5	0.6	0.8	1.0	1.2
LD50	0.8	1.0	1.2	1.3	1.5	1.7
LD90	1.3	1.5	1.7	1.8	2.0	2.2

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.2	0.3	0.4	0.4	0.5	0.6
LD10	0.5	0.7	0.8	0.7	0.8	1.0
LD50	0.9	1.1	1.2	1.0	1.2	1.3
LD90	1.3	1.4	1.5	1.3	1.5	1.7

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	0.08	0.09	0.1	0.35	0.4	0.45
LD10	0.2	0.3	0.4	0.45	0.5	0.6
LD50	0.5	0.6	0.7	0.7	0.8	0.9
LD90	0.8	0.9	1.0	0.9	1.0	1.2

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	<u>0.9</u>
20% skin exposed	<u>0.7</u>
40% skin exposed	<u>0.6</u>
60% skin exposed	<u>0.5</u>

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed	0.9	0.9
20% of Skin Exposed	0.9	0.8
40% of Skin Exposed	0.9	0.7
60% of Skin Exposed	0.9	0.6

Question 8 – Seed

Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1	2	3	4
2	5.5	6.5	7.5
3	4	5	6
4	5	6	7
5	5	6	7
6	5.5	6.5	7.5
7	6	7	8
8	9	10	11
9	9	10	11
10	1.5	2.5	3.5

EXPERT I

My rationale for quantification of deterministic radiation effects comes from both an academic and experimental perspective. Since I am not a physician-clinician, much of my perspective is from my four decades of animal experimentation, especially with long-lived radionuclides and with basic hematopoietic research.

In addition, my experience with the Russian data from Chernobyl and Chelyabinsk, on deterministic effects will alter some of my perceptions. I have been there some 25 times over the last decade, and their database is much more impressive than anything I am familiar with in the West. Their dosimetry in some cases leaves much to be desired and thus may temper some of the evaluations.

While I have a fairly firm feeling about the median values for certain effects, I am less confident of my quantification of the variance and bounds surrounding these values. I believe them to be sincere but soft. My rationale will not cover skin or GI effects, but will cover lung and bone marrow-hematopoietic effects.

I believe that there is a significant dose rate effectiveness factor for deterministic consequences in lung. Because of the repair potential for lung injury, chronic exposures may accumulate a considerable total dose if administered at modest rates. For low LET radiations such as in long-lived mixed fission products, large doses can be absorbed before functional impairment occurs. How to define a threshold for functional impairment is difficult, but I do not mean the minimal detectable decrease in vital capacity or tidal volume. For practical purposes I have chosen a 10% decrease in vital capacity as a threshold for the effect; call it minimal morbidity. Maximal lung morbidity is at 50% decrease.

For actinides, there is little difference in response as a function of particle size, i.e., for deterministic decrement to have taken place, the respirable sizes will provide a rather uniform lung exposure. There is a threshold for alpha morbidity which is about 0.7 that of low LET exposure. There is no dose rate effect since the exposures are continuous. The range of exposures between the morbidity threshold and lethality is about 3x for alpha emitters and about 2x for low LET radionuclides.

The response curve is quite steep, the 10 and 90% morbidity points are about $\pm 30\%$ around the median for the actinides and a bit broader for low LET, i.e., about $\pm 40\%$ of the median. My reading of the limited data from Chelyabinsk suggests that except for the different time constants, the mortality and morbidity values derived from dogs are quite close to human values.

The ratio of $LD_{90/10}$ for both actinides and low LET radiations is about 2:3; the response is quite steep. I make no distinction between the $LD_{0.10}$ or the $LD_{0.01}$; it's a real "hockey stick." I don't think we should put much emphasis on the extremes of the distributions. The dog curves show this steepness for most radiations. I think the perceived shallower slope for humans is an anomaly related to lack of tight dosimetry, since most human dose estimates are derived retrospectively.

For marrow responses there is an age sensitivity for both morbidity and mortality. Much has been derived from basic radiobiology experiments on injury and repair rates and patterns. In my experience, I have found the data on dose response best fits a logistic curve rather than a Wiebel. As with lung my low level indicator does not distinguish an ED 0.01 from 0.10. By the way, I found that the initial leukopenia could be fitted to a logistic, and so could the subsequent cancer incidence. In the lifetime dog studies, where groups were all given the same dose, this leukopenia factor was an excellent predictor of all incidence of tumors some 10 years later in the dog's life.

In March 1996, I was at a European conference on growth factors, and I am impressed at their potential for treating maximally dosed cases. When there are only a few stem cells left in the marrow, the growth factors can have a significant impact on survival probabilities. Where the dose is so high as to have destroyed much tissue, an apparent threshold for effectiveness seems to be operative.

References

No references provided.

Question 1a – Early Fatalities Due To Whole Body Dose

(Note: Data are with growth factors; data without growth factors are shown in parentheses.)

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.5	2.0	3.0	3.0	4.0	5.0
LD10	2.5	3.0	3.5	4.0 (6.0)	5.0 (7.0)	6.0 (8.0)
LD50	4.0	5.0	6.0	5.0 (7.0)	6.0 (8.0)	7.0 (9.0)
LD90	7.0	8.0	9.0	8.5	9.0	9.5

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.5	2.0	3.0	3.0	4.0	5.0
LD10	2.5	3.0	3.5	4.0 (6.0)	5.0 (7.0)	6.0 (8.0)
LD50	4.0	5.0	6.0	5.0 (7.0)	6.0 (8.0)	7.0 (9.0)
LD90	7.0	8.0	9.0	8.5	9.0	9.5

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.5	2.0	3.0	3.0	4.0	5.0
LD10	2.5	3.0	3.5	4.0 (6.0)	5.0 (7.0)	6.0 (8.0)
LD50	4.0	5.0	6.0	5.0 (7.0)	6.0 (8.0)	7.0 (9.0)
LD90	7.0	8.0	9.0	8.5	9.0	9.5

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	2.5	3.0	4.0	3.0	4.0	5.0
LD10	3.0	3.5	4.5	4.0	5.0	5.5
LD50	5.0	5.5	6.5	6.0	6.5	7.5
LD90	7.5	8.0	9.0	8.5	9.0	9.5

Dose Rate at Which LD50 Doubles

5%, 50%, and 95% estimates of the dose rate at which LD50 would be twice its value at 100 Gy/hr.

5%	50%	95%
0.01	0.02	0.03

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

100 Gy/hr	0.9
10 Gy/hr	0.9
1 Gy/hr	0.9
0.2 Gy/hr	0.75

Dose Rate Effects: Probability that the true LD50 is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	1.0	1.0
10 Gy/hr	1 Gy/hr	1.0	1.0
1 Gy/hr	0.2 Gy/hr	0.75	0.6

Question 1b – Early Fatalities Due to Gastrointestinal Syndrome

Whole body dose rate of 100 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	4.0	6+	8.0	4.4	6.6	8.8
LD10 _{GI}	6.0	7.0	8.5	6.6	7.7	9.3
LD50 _{GI}	7.0	8.5	10.0	7.7	9.3	11.0
LD90 _{GI}	9.0	10.0	11.0	9.9	11.0	12.1

Whole body dose rate of 10 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	4.0	6+	8.0	4.4	6.6	8.8
LD10 _{GI}	6.0	7.0	8.5	6.6	7.7	9.3
LD50 _{GI}	7.0	8.5	10.0	7.7	9.35	11.0
LD90 _{GI}	9.0	10.0	11.0	9.9	11.0	12.1

Whole body dose rate of 1 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}	4.0	6+	8.0	4.4	6.6	8.8
LD10 _{GI}	6.0	7.0	8.5	6.6	7.7	9.3
LD50 _{GI}	7.0	8.5	10.0	7.7	9.3	11.0
LD90 _{GI}	9.0	10.0	11.0	9.9	11.0	12.1

Whole body dose rate of 0.2 Gy/hr

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold _{GI}						
LD10 _{GI}						
LD50 _{GI}						
LD90 _{GI}						

Dose Rate Where LD50_{GI} Doubles

5%, 50%, and 95% estimates of the whole body dose rate at which LD50_{GI} would be twice its value at 100 Gy/hr.

5%	50%	95%
0.03	0.05	0.1

Dependencies

Minimal and Supportive Treatment: Probability that the true LD50_{GI} with minimal treatment is above the 50% value.

100 Gy/hr	High
10 Gy/hr	High
1 Gy/hr	High
0.2 Gy/hr	Med.

Dose Rate Effects: Probability that the true LD50_{GI} is above the 50% value for the lower dose rate.

Higher Dose Rate	Lower Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr	10 Gy/hr	1.0	1.0
10 Gy/hr	1 Gy/hr	1.0	1.0
1 Gy/hr	0.2 Gy/hr	0.75	0.6

LD50_{GI} Versus LD50: Probability that the true LD50 for Question 1a (all causes of death) is above the 50% value.

Whole Body Dose Rate	Minimal Treatment	Supportive Treatment
100 Gy/hr		
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Question 2a – Early Fatalities Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	100	150	175	100	150	175
LD10	100	200	300	100	200	300
LD50	200	300	400	200	300	400
LD90	400	450	500	400	450	500

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	100	150	175	100	150	175
LD10	100	200	300	100	200	300
LD50	200	300	400	200	300	400
LD90	400	450	500	400	450	500

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	100	150	175	100	150	175
LD10	100	200	300	100	200	300
LD50	200	300	400	200	300	400
LD90	400	450	500	400	450	500

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	100	150	175	100	150	175
LD10	100	200	300	100	200	300
LD50	200	300	400	200	300	400
LD90	400	450	500	400	450	500

Dependencies

Age Groups: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	High
10 Gy/hr	High
1 Gy/hr	High
0.2 Gy/hr	High

Dose Rate: Probability that the true LD50 is above the 50% value for the lower dose rate.

		Under 40	Over 40
100 Gy/hr	10 Gy/hr	1	1
10 Gy/hr	1 Gy/hr	1	1
1 Gy/hr	0.2 Gy/hr	0.75	0.75

Beta Lung Dose Versus Whole Body Dose: Probability that the true LD50 for this question is above the 50% value.

	Under 40	Over 40	
100 Gy/hr	_____	_____	Medium
10 Gy/hr	_____	_____	Medium
1 Gy/hr	_____	_____	Medium
0.2 Gy/hr	_____	_____	Medium

Question 2b – Morbidity Due to Beta Lung Dose

Lung dose rate of 100 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	25	50	75	25	50	75
ED10	30	55	65	30	55	65
ED50	60	70	80	60	70	80
ED90	90	100	150	90	100	150

Lung dose rate of 10 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	25	50	75	25	50	75
ED10	30	55	65	30	55	65
ED50	60	70	80	60	70	80
ED90	90	100	150	90	100	150

Lung dose rate of 1 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	25	50	75	25	50	75
ED10	30	55	65	30	55	65
ED50	60	70	80	60	70	80
ED90	90	100	150	90	100	150

Lung dose rate of 0.2 Gy/hr

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	25	50	75	25	50	75
ED10	30	55	65	30	55	65
ED50	60	70	80	60	70	80
ED90	90	100	150	90	100	150

Question 3 – Deterministic Fatalities Due to Alpha Lung Dose

	Persons Under 40 Years Old			Individuals Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	0.0002	0.00027	0.00038	0.0002	0.00027	0.00038
DR10	0.00038	0.00057	0.00076	0.00038	0.00057	0.00076
DR50	0.00095	0.00114	0.00133	0.00095	0.00114	0.00133
DR90	0.00133	0.00152	0.00171	0.00133	0.00152	0.00171

Under-40 Versus Over-40: Probability that the true LD50 for individuals under 40 years old is above the 50% value.

100 Gy/hr	High
10 Gy/hr	High
1 Gy/hr	High
0.2 Gy/hr	_____

Alpha Versus Beta Lung Dose: Probability that the true LD50 for alphas in this question is above the 50% value.

	Under 40	Over 40	
100 Gy/hr	_____	_____	High to Medium
10 Gy/hr	_____	_____	High to Medium
1 Gy/hr	_____	_____	High to Medium
0.2 Gy/hr	_____	_____	High to Medium

Question 4a – DELETED

Question 4b – DELETED

Question 5a – Early Fatalities by Acute Ulceration from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute ulceration			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

	Fraction that die		
	5%	50%	95%
20% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		
40% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		
60% of Skin Exposed	Acute Ulceration in 50% of Exposed Skin		
	Acute Ulceration in 90% of Exposed Skin		

Question 5b – Early Fatalities by Acute Epidermal Necrosis from Beta Skin Dose

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for acute epidermal necrosis			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population

	Fraction that die		
	5%	50%	95%
20% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin		
	Acute Epidermal Necrosis in 90% of Exposed Skin		
40% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin		
	Acute Epidermal Necrosis in 90% of Exposed Skin		
60% of Skin Exposed	Acute Epidermal Necrosis in 50% of Exposed Skin		
	Acute Epidermal Necrosis in 90% of Exposed Skin		

Question 5c – Early Fatalities by Lesion of Moist Desquamation and Secondary Ulceration

20% Skin Exposed (6% hands, 14% face and neck)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

40% Skin Exposed (6% hands, 20% face and neck, 14% arms)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

60% Skin Exposed (6% hands, 20% face and neck, 14% arms, 20% lower legs)

	5%	50%	95%
Threshold for moist desquamation			
Dose for effect in 10% of exposed skin area			
Dose causing effect in 50% of exposed skin area			
Dose causing effect in 90% of exposed skin area			

5%, 50%, and 95% values for the fraction of the population that would develop secondary ulceration.

		Fraction developing secondary ulceration		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 10% of Exposed Skin			
	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

5%, 50%, and 95% values for the fraction of the population that would die.

		Fraction that die		
		5%	50%	95%
20% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
40% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			
60% of Skin Exposed	Moist Desquamation in 50% of Exposed Skin			
	Moist Desquamation in 90% of Exposed Skin			

Two Distinct Exposure Periods, Decreasing Dose Rates

Question 6a – Early Fatalities Due to Whole Body Dose; 10:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.65	2.2	3.3	3.3	4.4	5.5
LD10	2.75	3.3	3.85	4.4	5.5	6.6
LD50	4.4	5.5	6.6	5.5	6.6	7.7
LD90	7.7	8.8	9.9	9.35	9.9	10.45

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is above the 50% value.

Question 2a Dose Rate	Minimal Treatment	Supportive Treatment
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Question 6b – Early Fatalities Due to Whole Body Dose; 100:1 Decrease in Dose Rate.

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	1.65	2.2	3.3	3.3	4.4	5.5
LD10	2.75	3.3	3.85	4.4	5.5	6.6
LD50	4.4	5.5	6.6	5.5	6.6	7.7
LD90	7.7	8.8	9.9	9.35	9.9	10.45

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

High

10:1 Versus 100:1 Dose Rate Decrease: Probability that the corresponding LD50 for this question is above the 50% value.

Minimal
Treatment

Supportive
Treatment

Question 6c – Early Fatalities Due to Lung Dose; 14:1 Decrease in Dose Rate.

	Persons Under 40 Years Old			Persons Over 40 Years Old		
	5%	50%	95%	5%	50%	95%
threshold	13.0	19.5	22.75	13.0	19.5	22.75
LD10	13.0	26.0	39.0	13.0	26.0	39.0
LD50	26.0	39.0	52.0	26.0	39.0	52.0
LD90	52.0	58.5	65.0	52.0	58.5	65.0

Under-40 Versus Over-40: Probability that the true LD50 is above the 50% value for the over-40 age group.

Constant Versus Decreasing Dose Rate: Probability that the true LD50 for this question is also above your 50% value.

Question 2a Dose Rate	Under 40	Over 40
10 Gy/hr		
1 Gy/hr		
0.2 Gy/hr		

Multiple Exposed Organs and Exposure Periods

Question 7a1 – Lung Dose Two Times Larger Than Bone Marrow Dose.

	Red Bone Marrow	Lower Intestine	Small Intestine	Lungs	Exposed Skin
cloud passage (1 hour)	0.3*D	0.3*D	0.3*D	0.4*D	1.2*D
balance of first day	0.7*D	1.2*D	0.7*D	1.6*D	20.1*D
1 day to 7 days	1.1*D	1.6*D	1.1*D	0.6*D	0
Total	2.1*D	3.1*D	2.1*D	2.6*D	21.3*D

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	2.5	3.0	4.0	2.5	3.5	4.0
LD10	2.8	3.5	4.0	2.5	4.0	4.5
LD50	3.0	4.0	4.5	3.0	4.5	5.2
LD90	5.0	5.5	6.0	5.5	5.8	6.0

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	2.5	3.0	3.5	2.5	3.0	3.5
LD10	2.5	3.5	4.0	3.0	3.5	4.0
LD50	3.0	4.0	4.5	3.5	4.0	4.5
LD90	4.5	5.0	6.0	4.0	4.5	5.0

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold	2.0	2.5	3.0	2.0	3.0	3.5
LD10	2.5	2.8	3.3	2.5	3.0	4.0
LD50	2.8	3.2	3.5	3.0	3.8	4.2
LD90	3.8	4.0	4.2	3.5	4.0	4.5

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold		2.0			2.0	
LD10		2.5			2.5	
LD50		3.0			3.0	
LD90		3.5			3.5	

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	High
20% skin exposed	High
40% skin exposed	High
60% skin exposed	High

Question 7a2 – Zero Lung Dose, Otherwise Same as Question 7a1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		2.5			3.0	
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		2.5			3.0	
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		2.2			2.5	
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10		2.0			2.0	
LD50						
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7a1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed	0.5	
20% of Skin Exposed	0.5	
40% of Skin Exposed	0.5	
60% of Skin Exposed	0.5	

Question 7b1 – Lung Dose Ten Times Larger Than Bone Marrow Dose.

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		1.0			1.5	
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		1.0			1.5	
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		1.0			1.5	
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		0.5			1	
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed	0.6
20% skin exposed	0.6
40% skin exposed	0.7
60% skin exposed	0.8

Smaller Versus Larger Lung Dose: Probability that the true LD50 for this question is above the 50% value.

Minimal _____ Supportive _____

Question 7b2 – Zero Lung Dose, Otherwise Same as Question 7b1

No Skin Exposed

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		3.0			4.0	
LD90						

20% of Skin Exposed - Assume only 20% of skin is exposed (face, neck, and hands).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		3.0			4.0	
LD90						

40% of Skin Exposed (face, neck, hands, and arms).

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		2.8			3.0	
LD90						

60% of Skin Exposed (face, neck, hands, arms, and lower legs)

	Minimal Treatment			Supportive Treatment		
	5%	50%	95%	5%	50%	95%
threshold						
LD10						
LD50		2.5			2.8	
LD90						

Minimal Versus Supportive Treatment: Probability that the true LD50 with minimal treatment is above the 50% value.

No skin exposed _____
20% skin exposed _____
40% skin exposed _____
60% skin exposed _____

With Versus Without Lung Dose: Probability that the true LD50 with the lung dose specified in Question 7b1 is above the 50% value.

	Minimal Treatment	Supportive Treatment
No Skin Exposed		
20% of Skin Exposed		
40% of Skin Exposed		
60% of Skin Exposed		

Question 8 – Seed

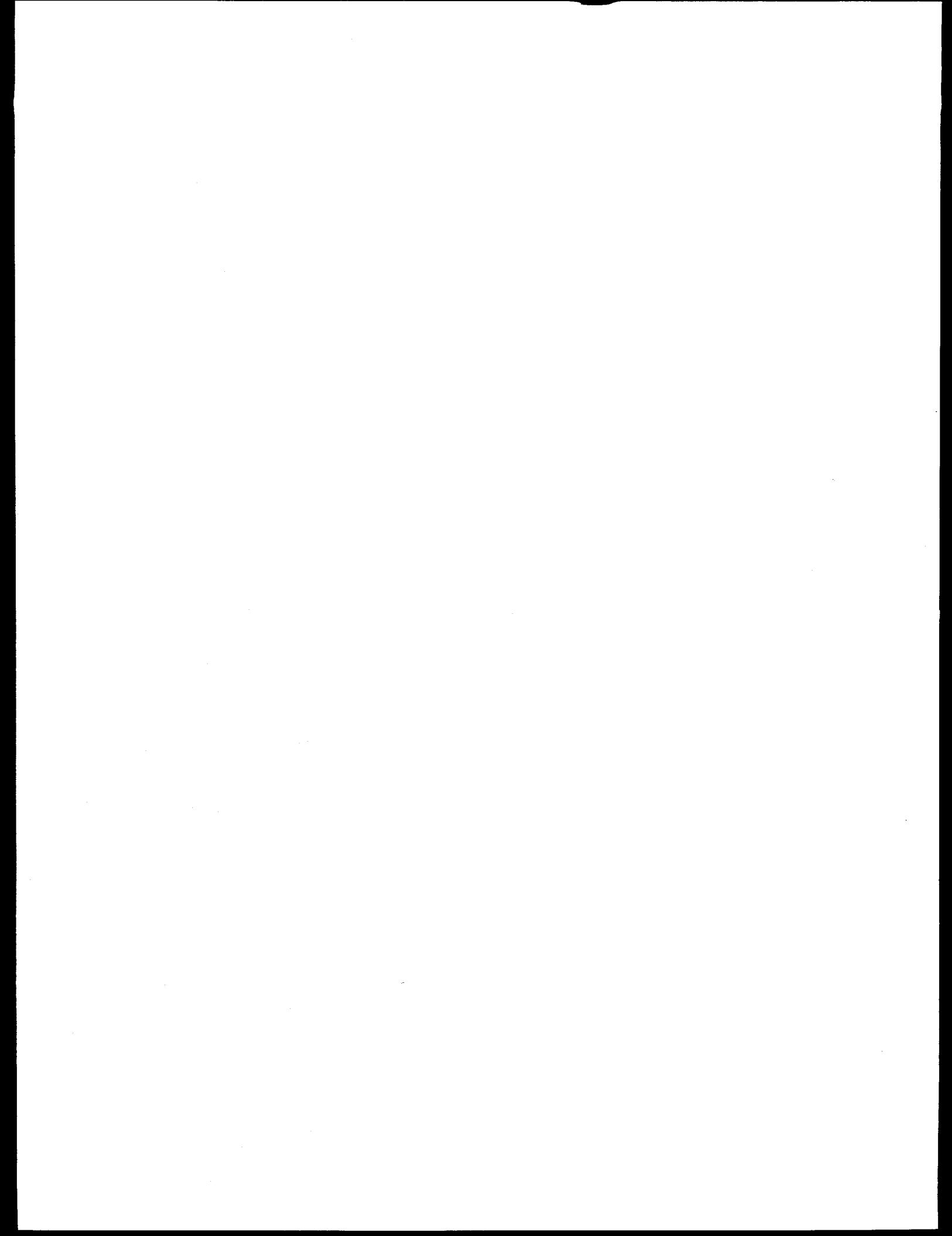
Dose estimates of the average dose to the red bone marrow (100 Gy/hour).

Doses (Gy) to red bone marrow and gastrointestinal system

case number	average dose to RBM (Gy)		
	5%	50%	95%
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

APPENDIX D

Short Biographies of the Early Health Effects Experts



Short Biographies of the Early Health Effects Experts

Johannes J. Broerse, The Netherlands

Prof. Broerse is a graduate in Nuclear and Molecular Physics at the University of Amsterdam, where he earned his Ph.D. in 1966. Until 1991 he was doing research on neutron dosimetry, neutron radiobiology, biophysics, tumor radiobiology and experimental radiotherapy at the Radiobiological Institute TNO. Since 1986 he is a part-time professor of Medical Radiation Physics at the Department of Clinical Oncology of the Academic Hospital in Leiden. He was a member of many committees in the field of Nuclear Physics, of which he chaired a considerable number. He is an Honorary member of the Swedish Radiobiological Society as well as of the British Association for Radiation Research. In 1994 Prof. Broerse received a Knighthood in the Order of Orange Nassau for his outstanding service to the state and society. Prof. Broerse enlisted the input of two colleagues, Anthony Hermens and Henk Kal. Their biographies are given at the end of Appendix D.

Marvin Goldman, USA

Marvin Goldman is Emeritus Professor of Radiological Sciences in the Department of Surgical and Radiological Sciences of the University of California-Davis. He has an AB from Adelphi University (NY, '49), an MS [physiology] from University of Maryland ('51) and his Ph.D. in Radiation Biology and Biophysics from the School of Medicine at the University of Rochester (NY, '57).

He has been at UC-Davis since 1958 and has published over 150 scientific papers, patents and reports on radiation dosimetry and effects of exposure to radioactive materials, including the first global summary (1957 DOE report) of the environmental and medical impact of the Chernobyl accident. He has been to the former Soviet Union 23 times in the last decade and helped develop the scientific cooperative research program between US and CIS.

In 1972 he received the EO Lawrence Award of the Atomic Energy Commission for work on the dosimetry and medical effects of radioactivity, and in 1988 he received the Distinguished Scientific Achievement Award of the Health Physics Society. He has received a NASA citation for his work on space nuclear (Pu) safety. Dr. Goldman is immediate past president of the Health Physics Society and

is now Secretary of the Council of Scientific Society Presidents.

Jolyon H. Hendry, UK

Prof. Hendry received his BSc in Physics at St. Andrews University in 1966 and in 1968 received his MSc in Radiation Biology at London University, where he was awarded his Ph.D. in 1971 and his DSc in 1991. Since 1976 he has been head of the Cancer Research Campaign in the Department of Experimental Radiation Oncology of the Paterson Institute for Cancer Research in Manchester. He has received numerous awards and honorary positions, including Honorary Professor of the Chinese Academy of Medical Science at the Institute of Radiation Medicine in Tianjin and Honorary Professor in the Faculty of Medicine of the University of Manchester. Prof. Hendry is a member of many scientific societies and committees. He is also involved in editorial activities, including being past chief editor of the *International Journal of Radiation Biology*, a member of the editorial boards of *Radiotherapy and Oncology*, and *Clinical Oncology* and joint editor of several books including most recently *Radiation and Gut*, and *Radiation Toxicology: Bone marrow and Leukemia*.

John W. Hopewell, UK

Professor Hopewell has a joint BSc in Botany and Zoology and obtained his Ph.D. in Radiation Biology at the University of London in 1968. He was awarded an MRCR (Hon) by the Royal College of Radiologists in 1994. Currently Professor Hopewell is Director of Radiobiological Research at the University of Oxford and Chairman of the Management Committee of the Churchill Hospital Research Institute, Oxford. He is a member of various scientific societies and has published a considerable number of papers in peer-reviewed journals.

Natalja M. Nadejina, Russia

Dr. Nadejina earned her Ph.D. in Medicine in 1982 at the Institute of Biophysics of the Ministry of Health where she completed her education for Senior Researcher in 1983. Since 1989 she has been head of the Division of Acute Radiation Injuries and Consequences of Accident Radiation exposures of the Radiation Medicine Department of the

Scientific Research Centre of the Institute of Biophysics. Her area of specialization is the diagnosis and treatment of radiation injuries, assessment of health status in victims of different range of radiation accidents at early or late period of acute radiation syndrome and local radiation injuries at early and late consequences period. She is a certified expert of the international project "Radiological Consequences of the Chernobyl Accident in the USSR - Assessment of Health and Environmental Effects and Evaluation of Protective Measures."

Bobby R. Scott, USA

Dr. Scott received his Ph.D. in Biophysics in 1974 from the University of Illinois. After conducting post-doctoral research, at the Argonne National Laboratory, related to modeling neutron and gamma ray toxicity in animals, he joined in 1977 and has remained at the Inhalation Toxicology Research Institute (ITRI). While at the ITRI, Dr. Scott has conducted both theoretical and experimental research related to stochastic and deterministic effects of exposure of biological systems (cells, tissue, organs, organisms) to ionizing radiation. Models he developed for early occurring and continuing radiological health effects in humans are used in MACCS and COSYMA computer codes and are also used by the National Radiological Protection Board in the UK for assessing possible health effects of nuclear accidents. His current research includes using data for nuclear workers in Russia chronically exposed to large radiation doses to validate models used in MACCS and COSYMA codes for specific deterministic effects or irradiation.

Elizabeth L. Travis, USA

Dr. Travis received her Ph.D. in Experimental Pathology and Radiation Biology from the Medical University of South Carolina. Following three years as Research Scientist and Lecturer in England and another three as a Cancer Expert with the National Institutes of Health, National Cancer Institute, she joined the University of Texas MD Anderson Cancer Center, where she is currently a Radiobiologist and Professor of Experimental Radiation Oncology. Dr. Travis's research focuses on understanding the mechanisms and pathogenesis of radiation and drug-induced damage in normal tissues. The majority of her research has centered on late responding tissues, specifically the lung, as well as acutely responding tissues such as the GI tract, skin, and bone marrow. Her current research involves investigating the genetic basis of radiation- or

drug-induced fibrosis in a number of normal tissues, including the lung, colon, and kidney, using murine models with varying susceptibilities to these agents. In addition, other studies are focused on the role of cytokines and growth factors in the process of tissue repair and remodeling in the lung and in two types of late effects: fibrosis and in the colon.

Niel Wald, USA

Dr. Wald received an AB from Columbia College, an M.D. from New York University, and post-graduate hospital training in internal medicine and hematology. He served with the US Air Force in the Department of Radiobiology at its School of Aviation Medicine, with the National Academy of Science's Atomic Bomb Casualty Commission as Senior Hematologist in Hiroshima, and with the Health Physics Division of Oak Ridge National Laboratory. He then joined the University of Pittsburgh's faculty in 1958 and is Professor of Environmental and Occupational Health at the University of Pittsburgh, with joint appointments as Professor of Human Genetics and of Radiology. He was the first Chairman of the Department of Radiation Health from 1969 until 1989, and is Director of the Radiation Medicine Department of Presbyterian-University Hospital. His research interests have included early diagnostic tests and clinical treatment of acute radiation injury and internal radionuclide contamination, radiation-induced mouse leukemia, clinical and radiation cytogenetics including the automation of radiation-induced aberration scoring, and irradiated population studies. His research has been funded by the National Aeronautics and Space Agency, the US Public Health Services, the National Institutes of Health and the Department of Energy. He has contributed over 160 articles and chapters to the scientific literature on hematology, cytogenetics, radiation medicine and radiation health. His professional activities have included service as President of the Health Physics Society, and Associate Editor of *Radiation Research* and the *Journal of Nuclear Medicine*, a consociate member of the National Council of Radiation Protection and Measurement and a consultant to the US Nuclear Regulatory Commission, the US Navy, and various nuclear industries and utilities.

Dr. Robert W. Young, USA

Dr. Young graduated from the Catholic University of America where he earned his Ph.D. in Neurobehavioral Toxicology, Radiation Biology, and Statistical Analysis. His thirty-year research career has focused on the early

effects of radiation on human health, the nervous system, and behavior. During his sixteen years at the Armed Forces Radiobiology Institute, he was the head of the division that conducted research into the effects of mixed-spectrum ionizing radiation on the nervous system and behavior. Dr. Young has chaired the NATO Project Group on Radiation studying anti-emetic drugs and served as a member of the President's Committee on the Chernobyl nuclear accident.

He has published numerous papers and three book chapters on the early effects of radiation. For the last fifteen years, his work has focused on defining and modeling the early effects of ionizing radiation on humans, first as the director of the biomedical research program for the Defense Nuclear Agency, and currently as a consultant on human health effects.

* * * * *

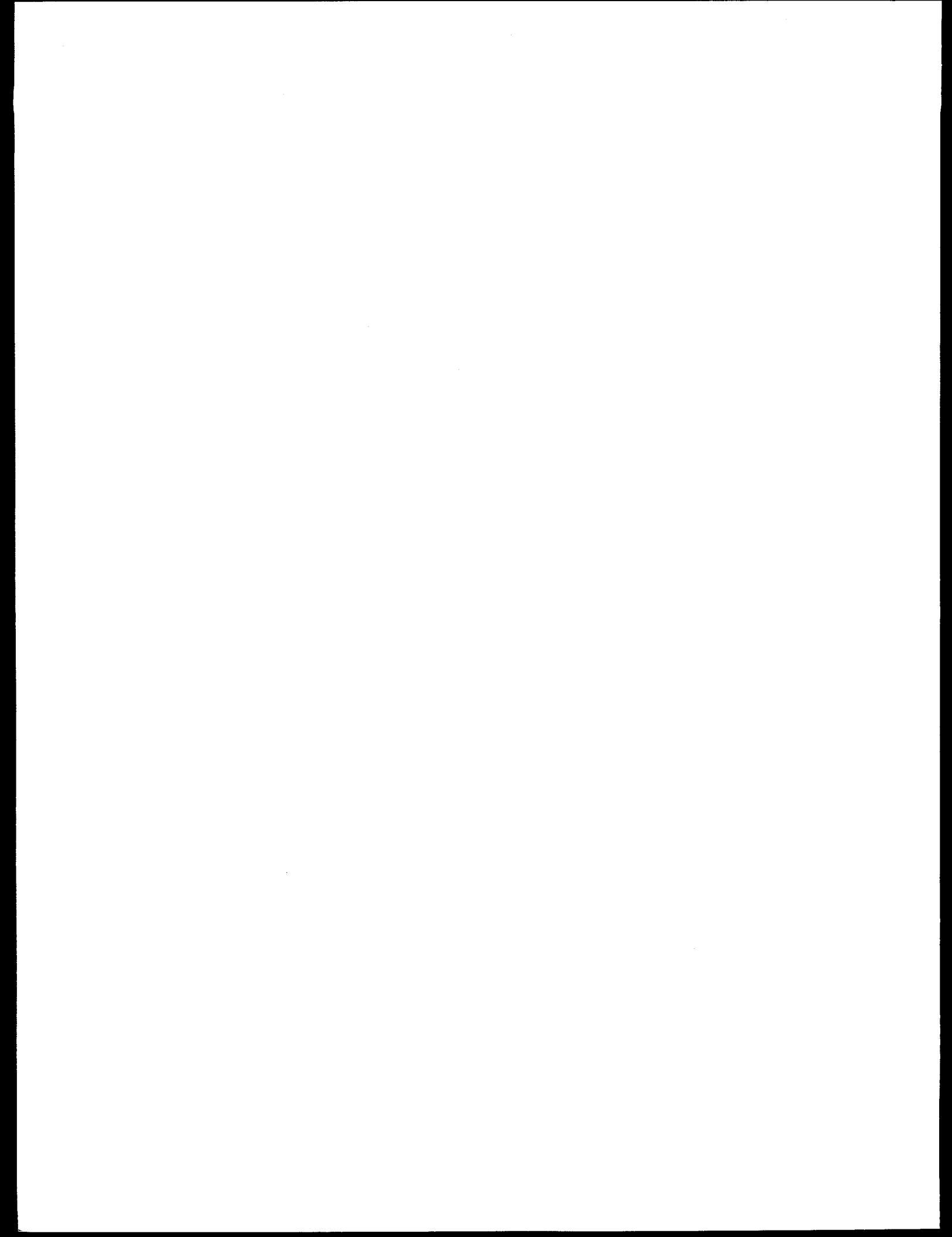
Anthony F. Hermens, The Netherlands

Dr. Hermens graduated from the Municipal University of Amsterdam and its medical school in 1961. After fulfilling his military service, he was trained in radiotherapy (1963–1965) at the Rotterdam Radio-Therapeutic Institute. This training was prelude to a research position at the Radiobiological Institute of the Health Organisation, TNO, at Rijswijk, which he held from 1965 through 1993. The main field of his research encompassed tumour cell kinetics and radiation effects of tumours and normal tissues. He received his Ph.D. in 1973 from the Medical Faculty of the Municipal University of Amsterdam. Since 1980 Dr. Hermens has contributed to medical post graduate teaching courses in Radiation Protection, organized by the J.A. Cohen Institute, Inter-University Research Institute for Radiopathology and Radioprotection, at Leiden. In 1985 he was appointed a member of the board of programme advisors to these courses. He has been an associate research member of the Experimental Radiotherapy Research Group of the Department of Clinical Oncology, University of Leiden since 1993.

Henk B. Kal, The Netherlands

Dr. Kal is a graduate in Nuclear Physics of Delft University of Technology, The Netherlands. He earned his Ph.D. in 1974 at the University of Amsterdam on the subject "Responses of a rat tumour and skin irradiation with low dose rate gamma rays and fast neutrons." In 1974–1975, he was Fellow of the American Cancer Society, Eleanor Roosevelt, at Stanford University, USA. He has been doing research on effects of different types of ionizing radiation on biological systems, tumour radiobiology, hyperthermia, experimental radiotherapy and risk assessments at the Radiobiological Institute TNO (until 1991) and at the TNO Centre for Radiological Protection and Dosimetry (from 1991 to present), both at Rijswijk, The Netherlands. Dr. Kal was a member of many committees of the Dutch Health Organization and is council member of committees in the field of radiobiology.

APPENDIX E
Aggregated Results of Expert Responses



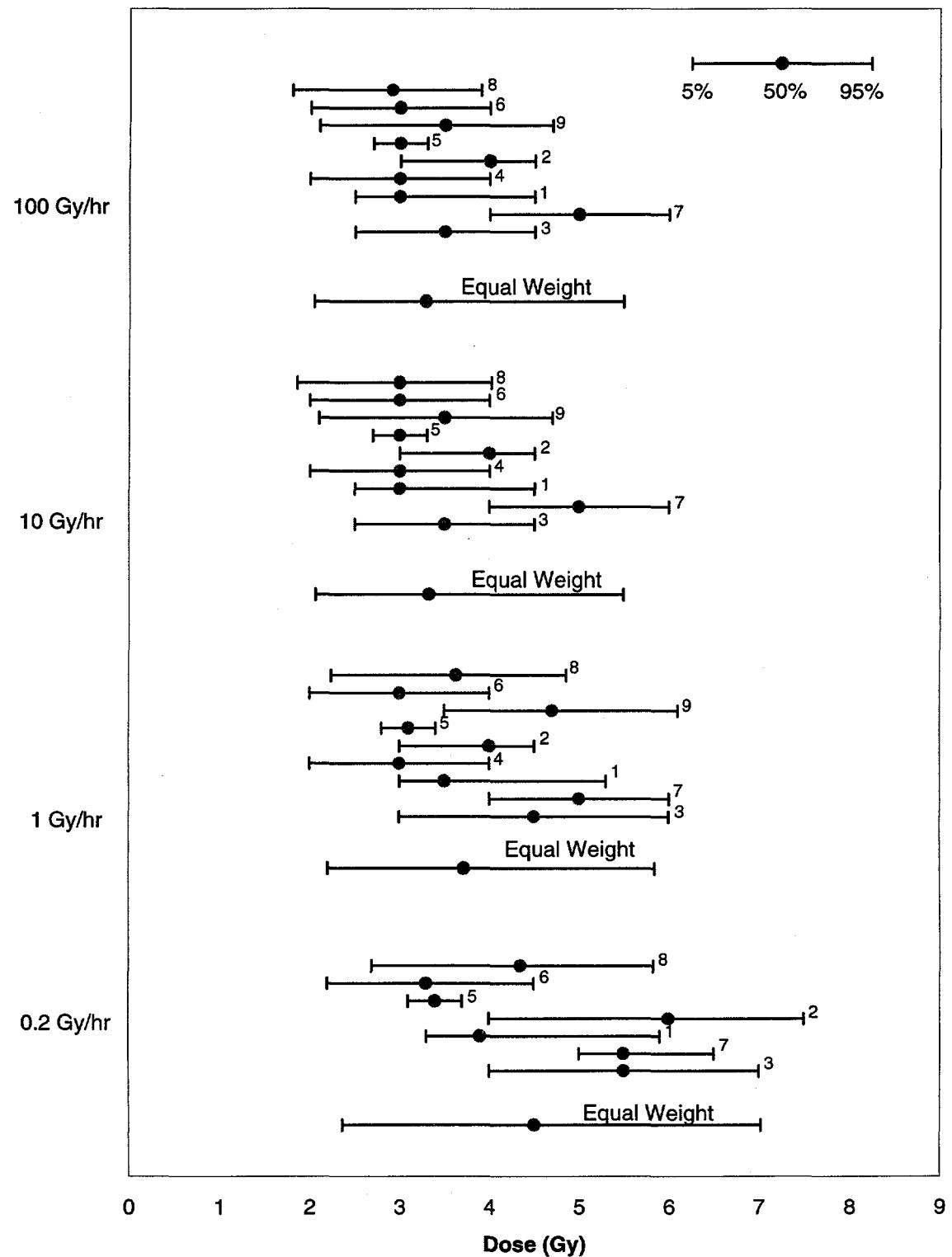


Figure E.1. LD₅₀ for whole-body gamma exposure, minimal medical treatment.

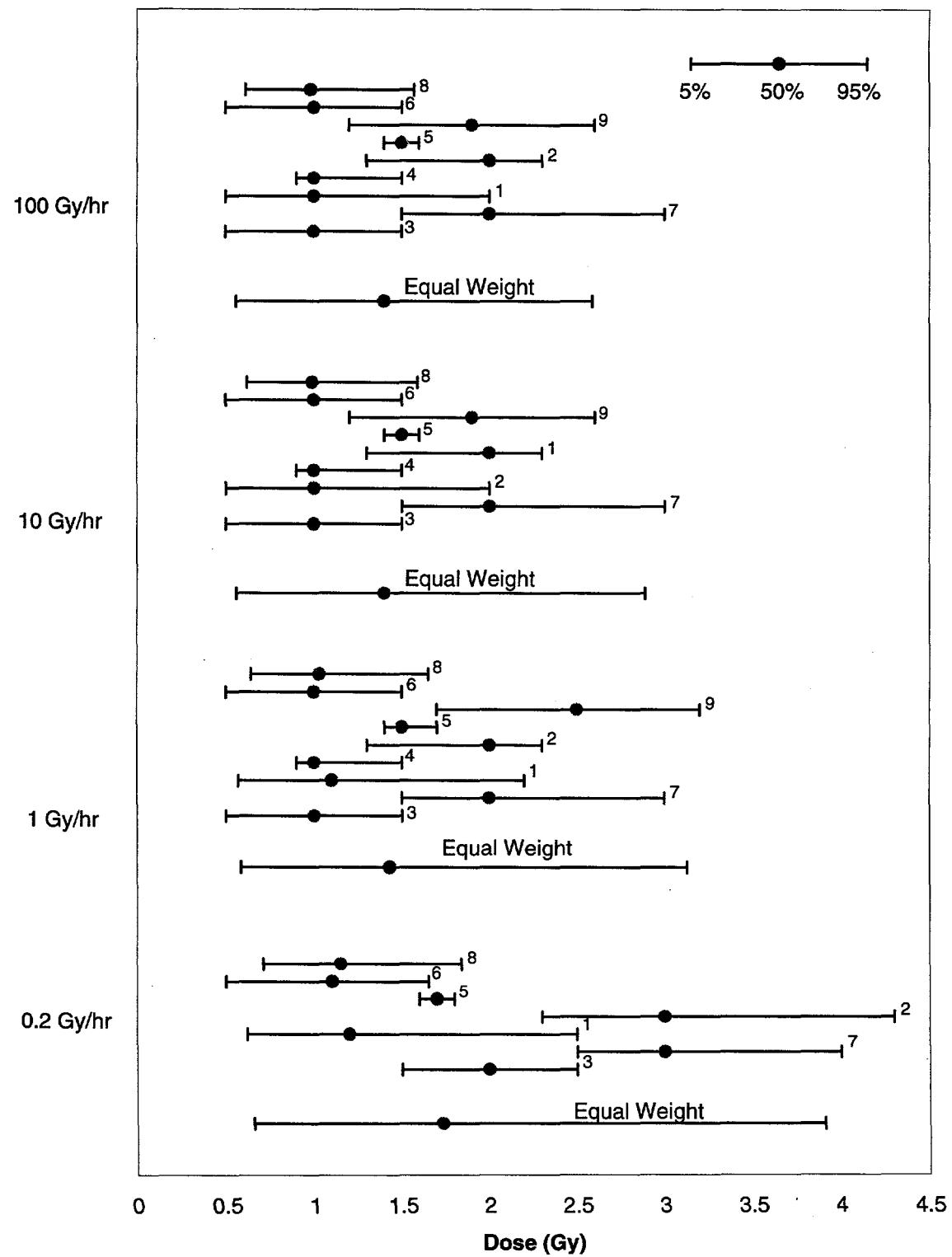


Figure E.2. Threshold for fatalities from whole-body gamma exposure, minimal medical treatment.

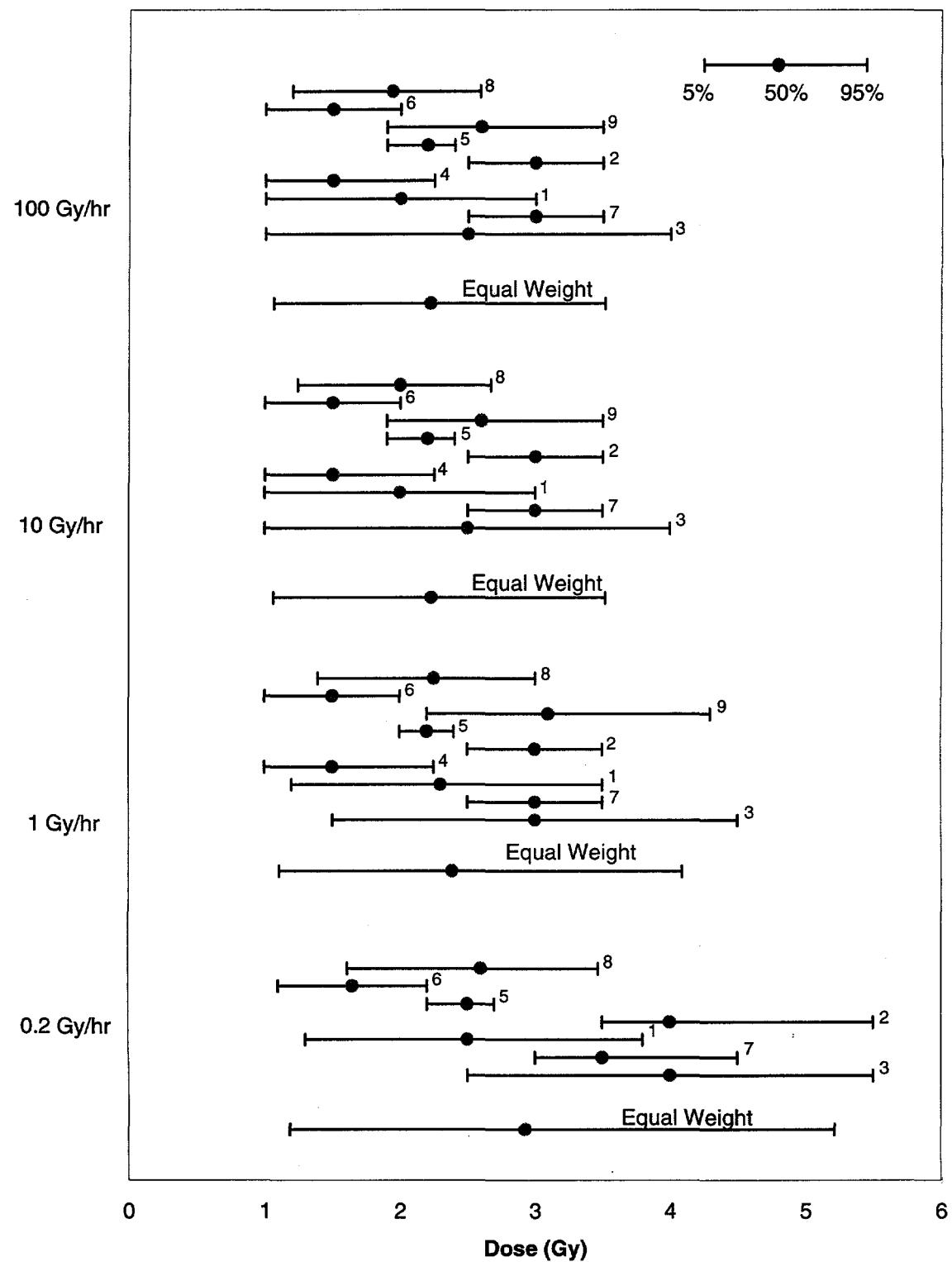


Figure E.3. LD₁₀ for whole-body gamma exposure, minimal medical treatment.

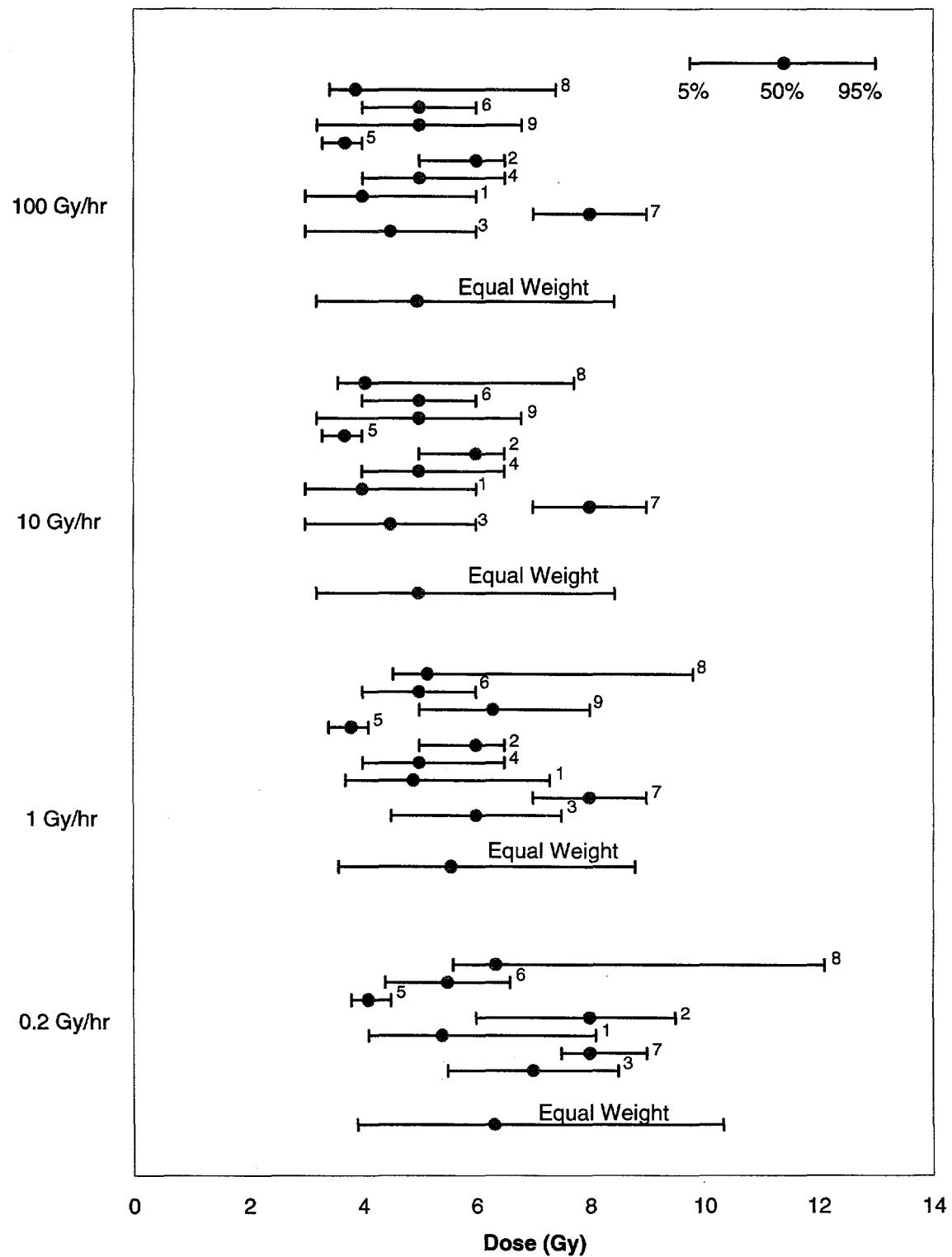


Figure E.4. LD₉₀ for whole-body gamma exposure, minimal medical treatment.

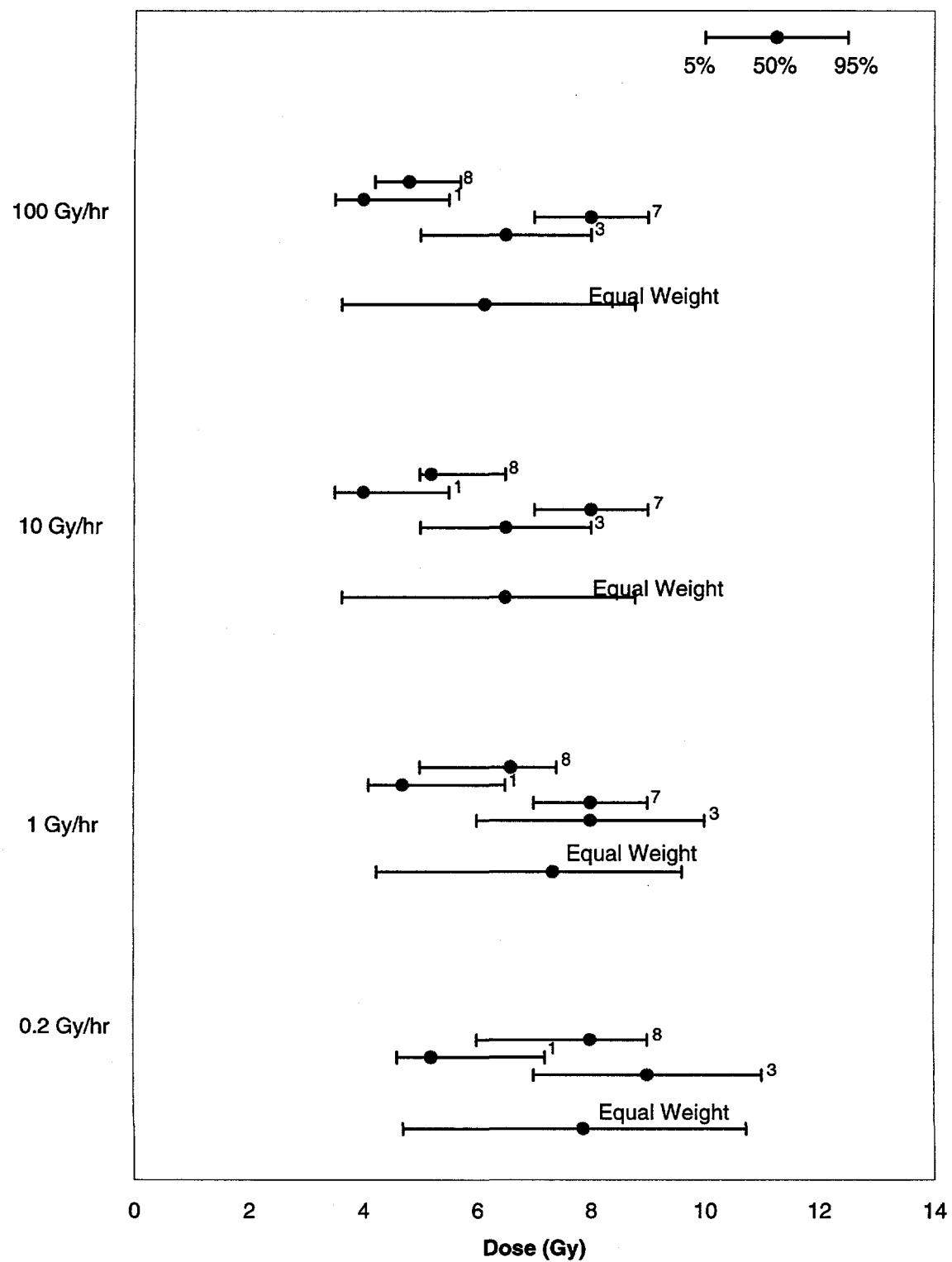


Figure E.5a. LD₅₀ for whole-body gamma exposure, supportive medical treatment, with growth factors.

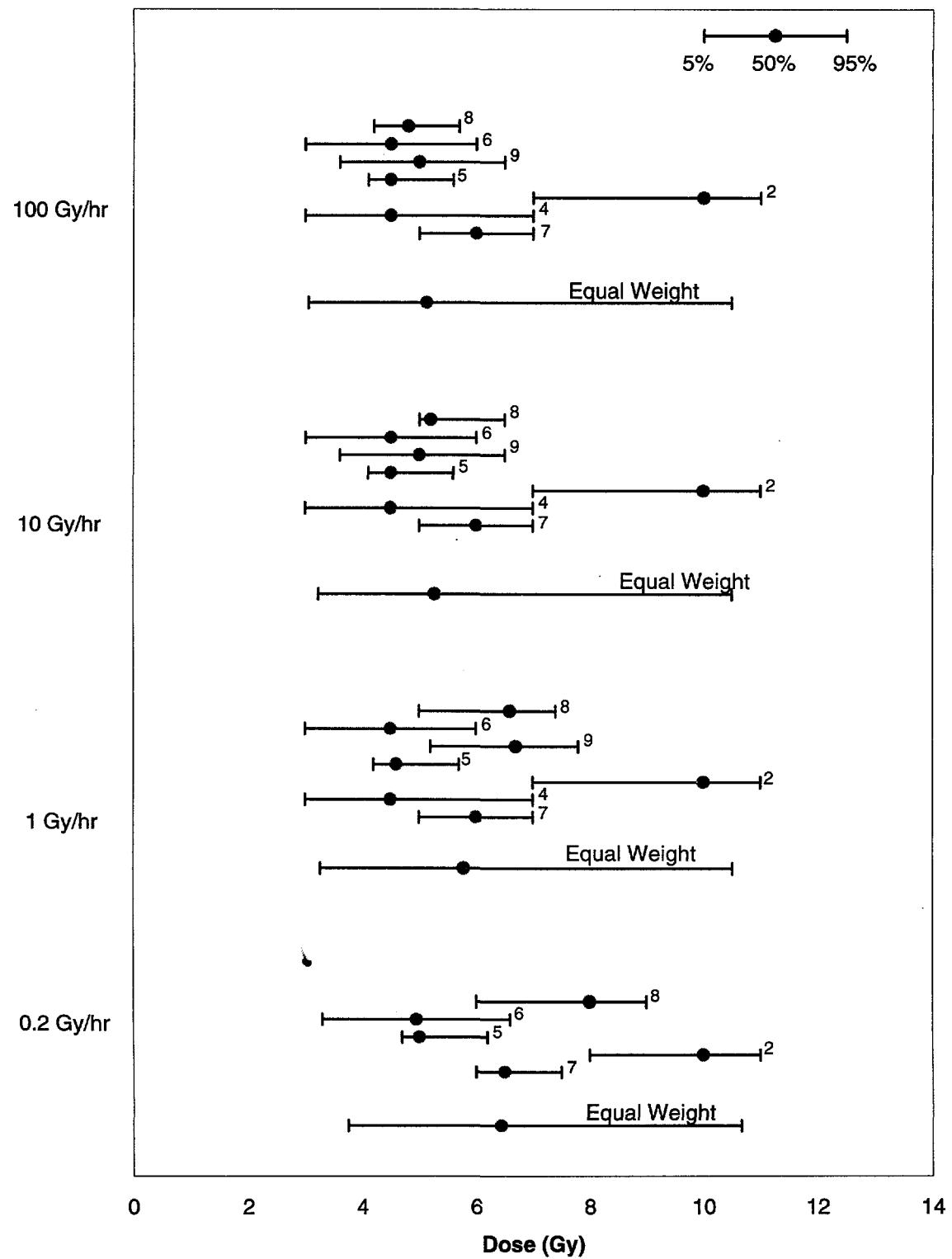


Figure E.5b. LD₅₀ for whole-body gamma exposure, supportive minimal medical treatment, without growth factors.

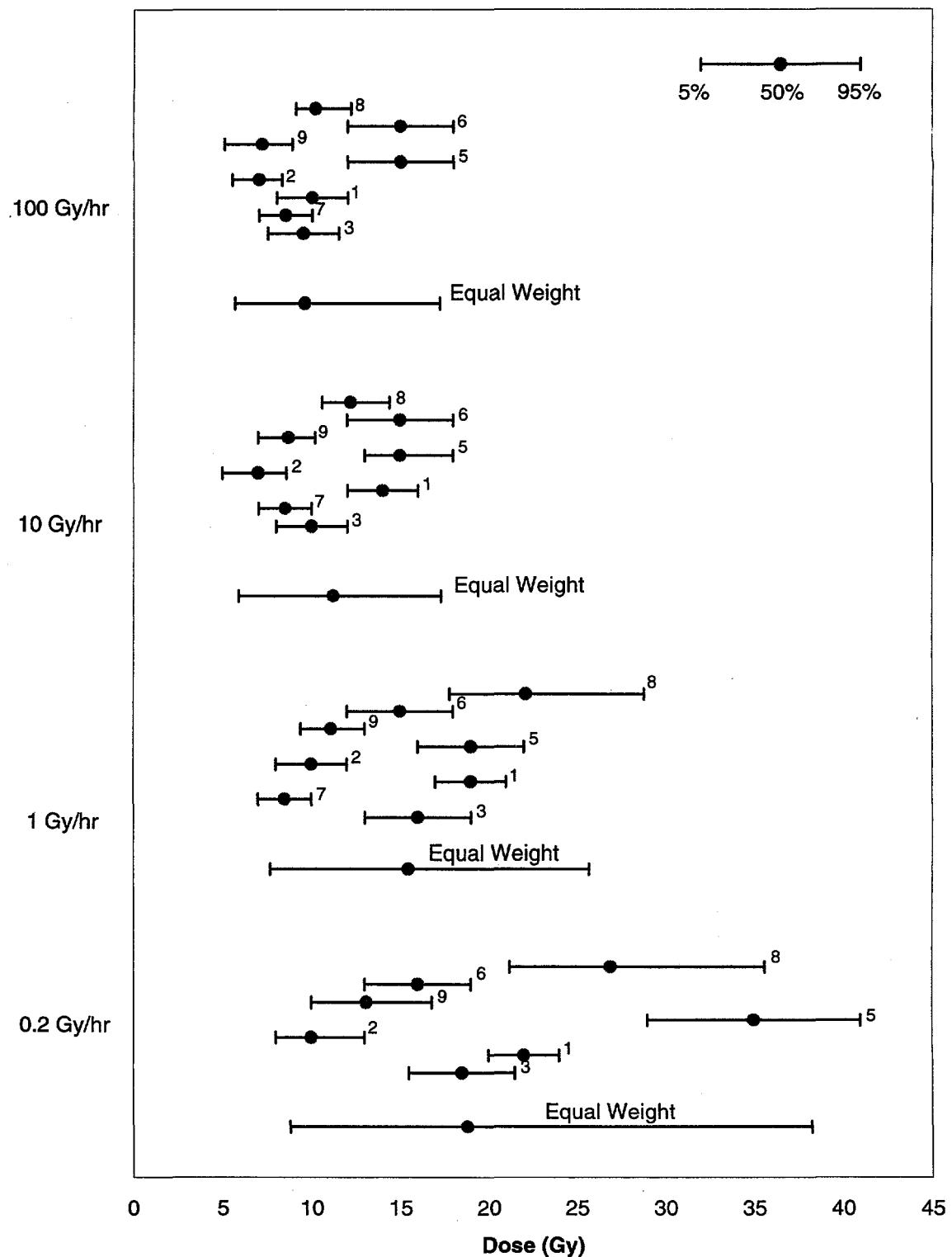


Figure E.6. LD_{50} for gastrointestinal syndrome, minimal medical treatment.

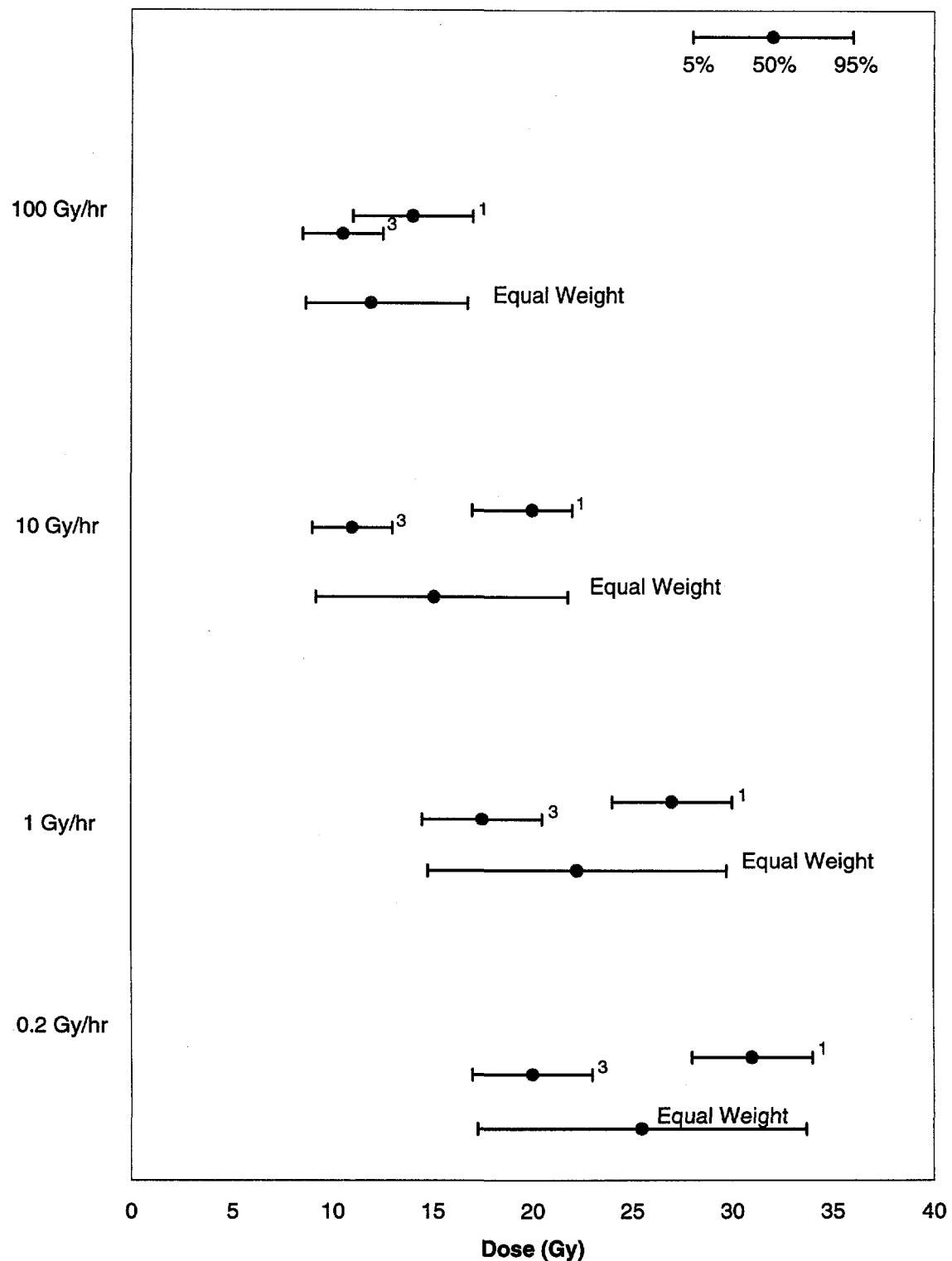


Figure E.7a. LD_{50} for gastrointestinal syndrome, supportive medical treatment, with growth factors.

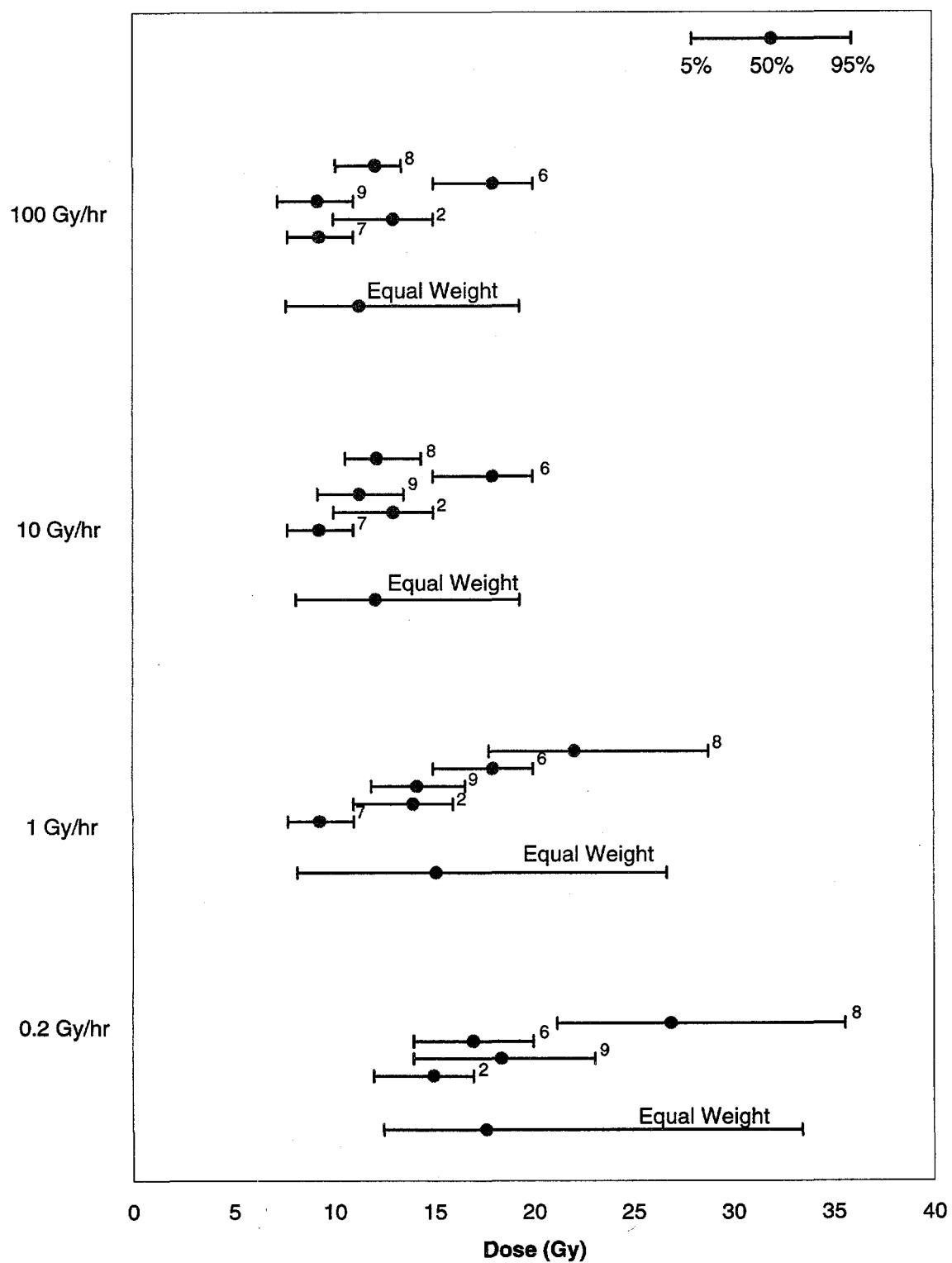


Figure E.7b. LD₅₀ for gastrointestinal syndrome, supportive medical treatment, without growth factors.

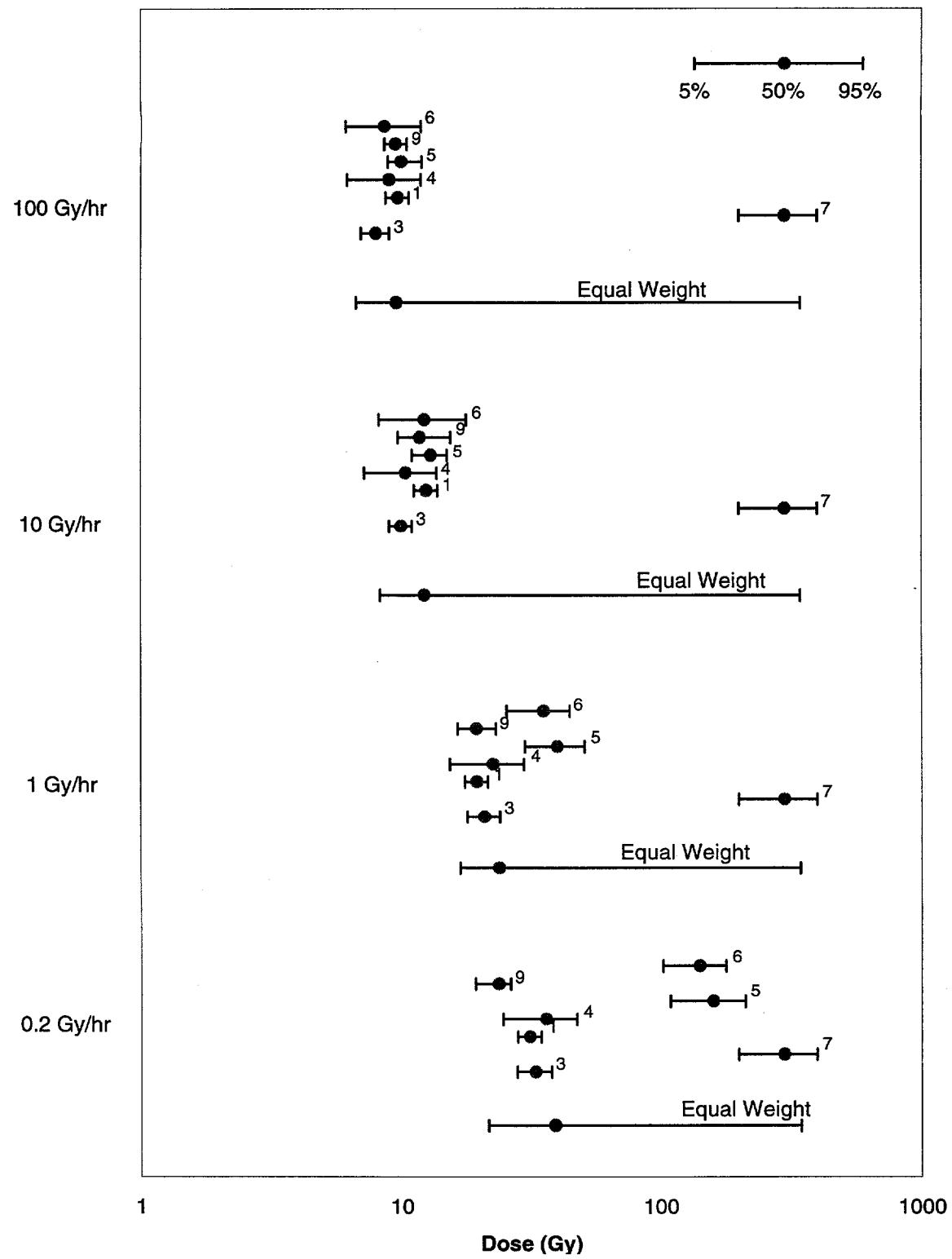


Figure E.8. LD₅₀ for beta lung exposure.

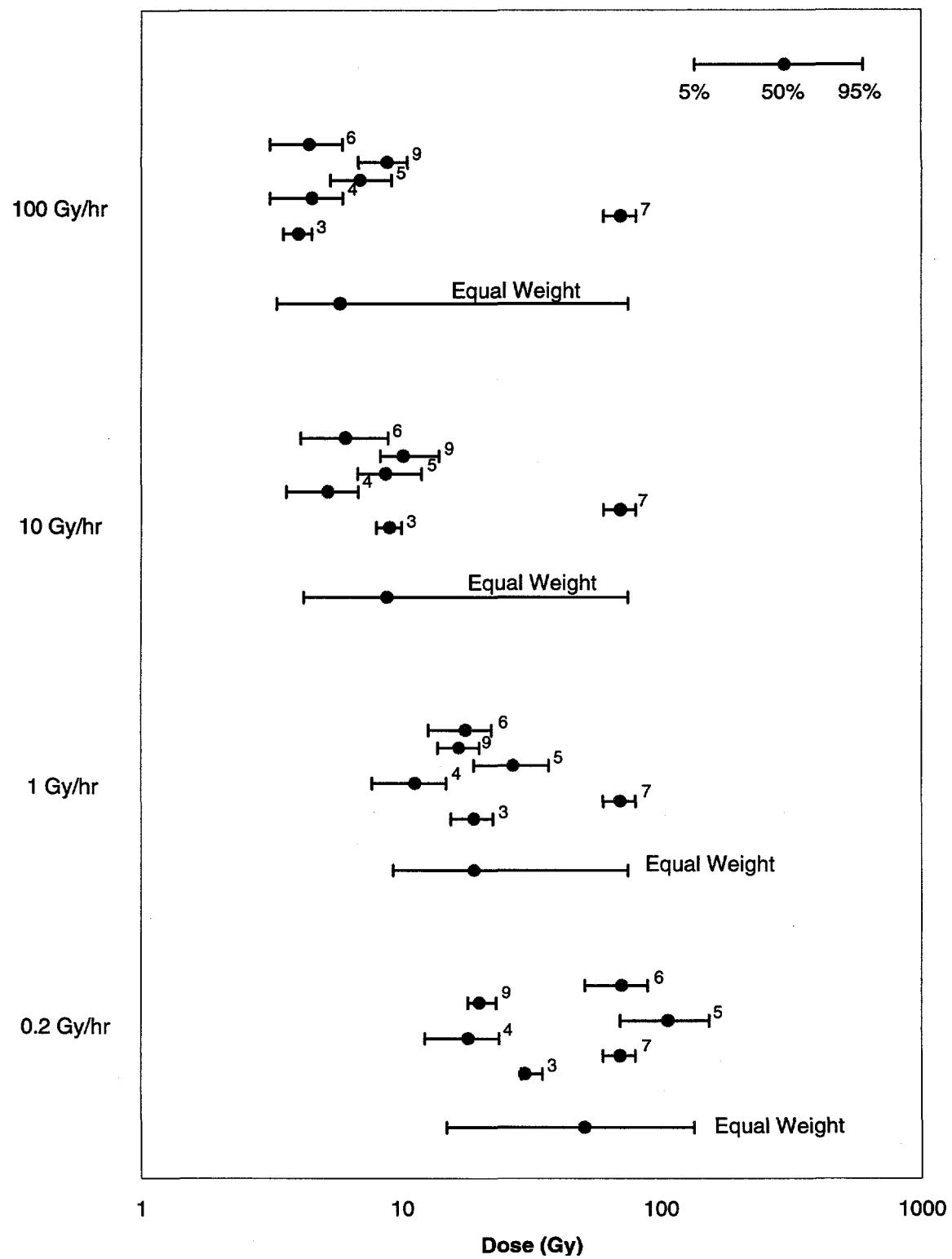


Figure E.9. LD_{50} for morbidity due to beta lung exposure.

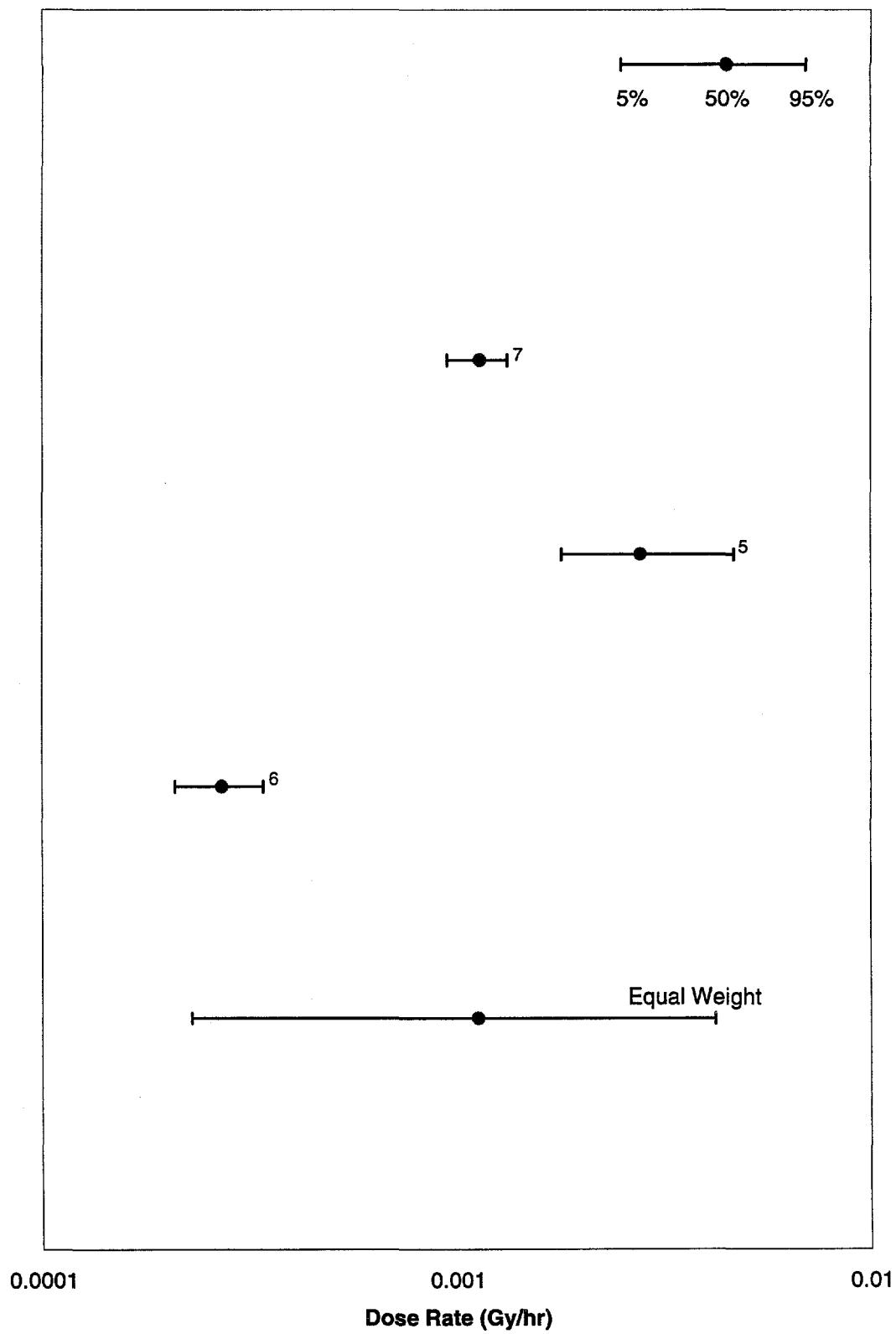


Figure E.10. LD₅₀ for alpha lung exposure.

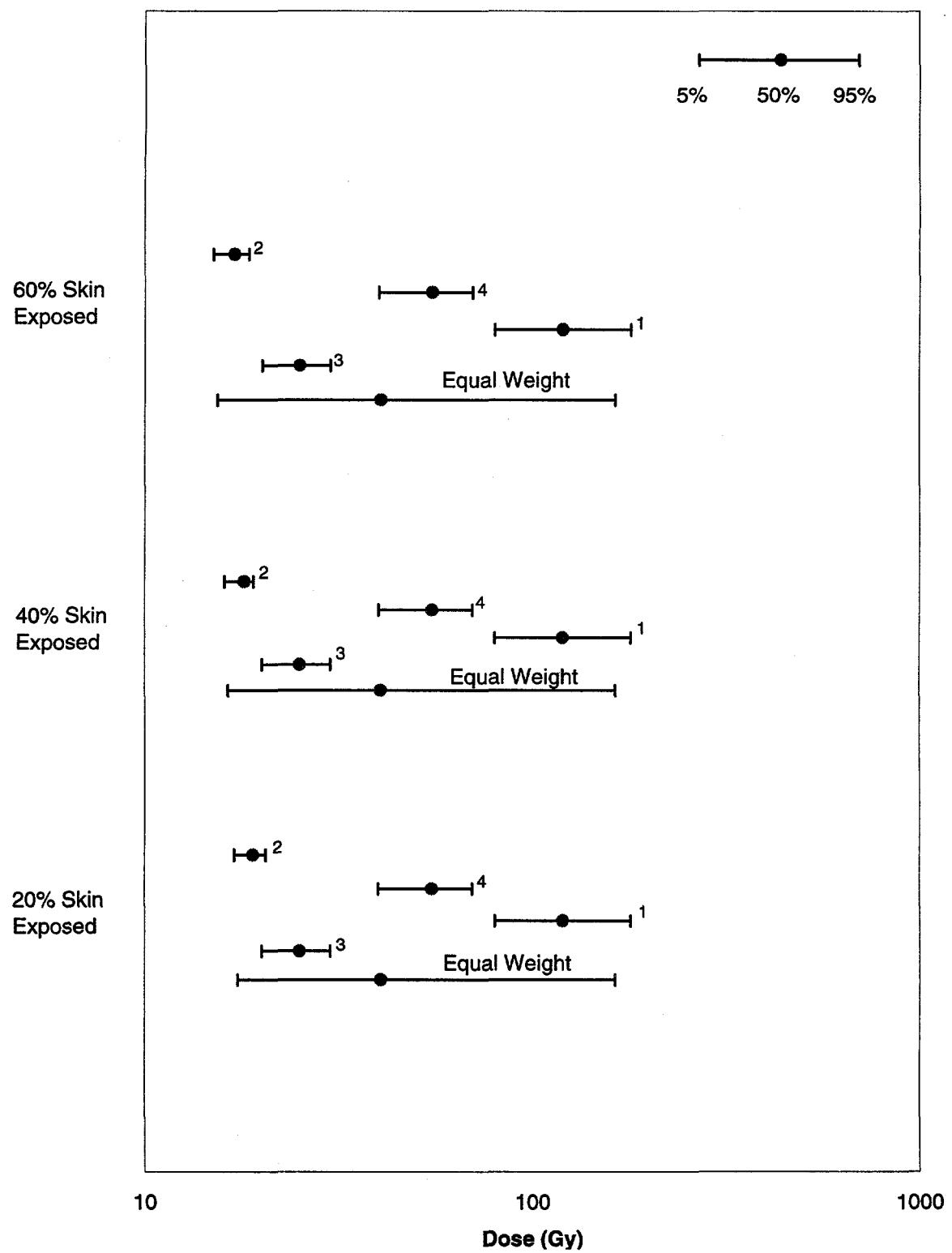


Figure E.11. Threshold for acute ulceration from 24-hour beta skin dose.

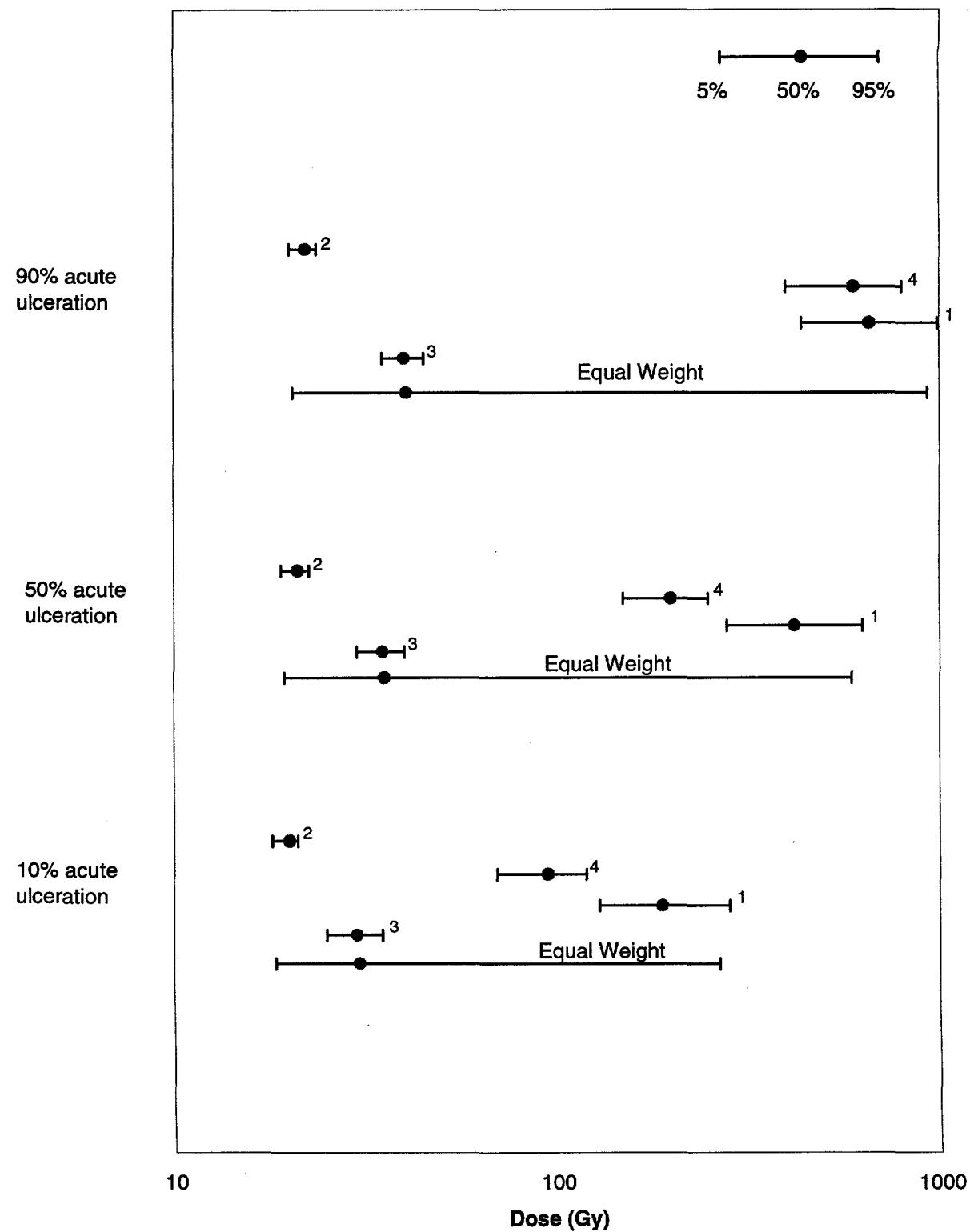


Figure E.12. 24-hour beta skin dose for acute ulceration in specified fraction of exposed skin (40% of total skin exposed), supportive medical treatment.

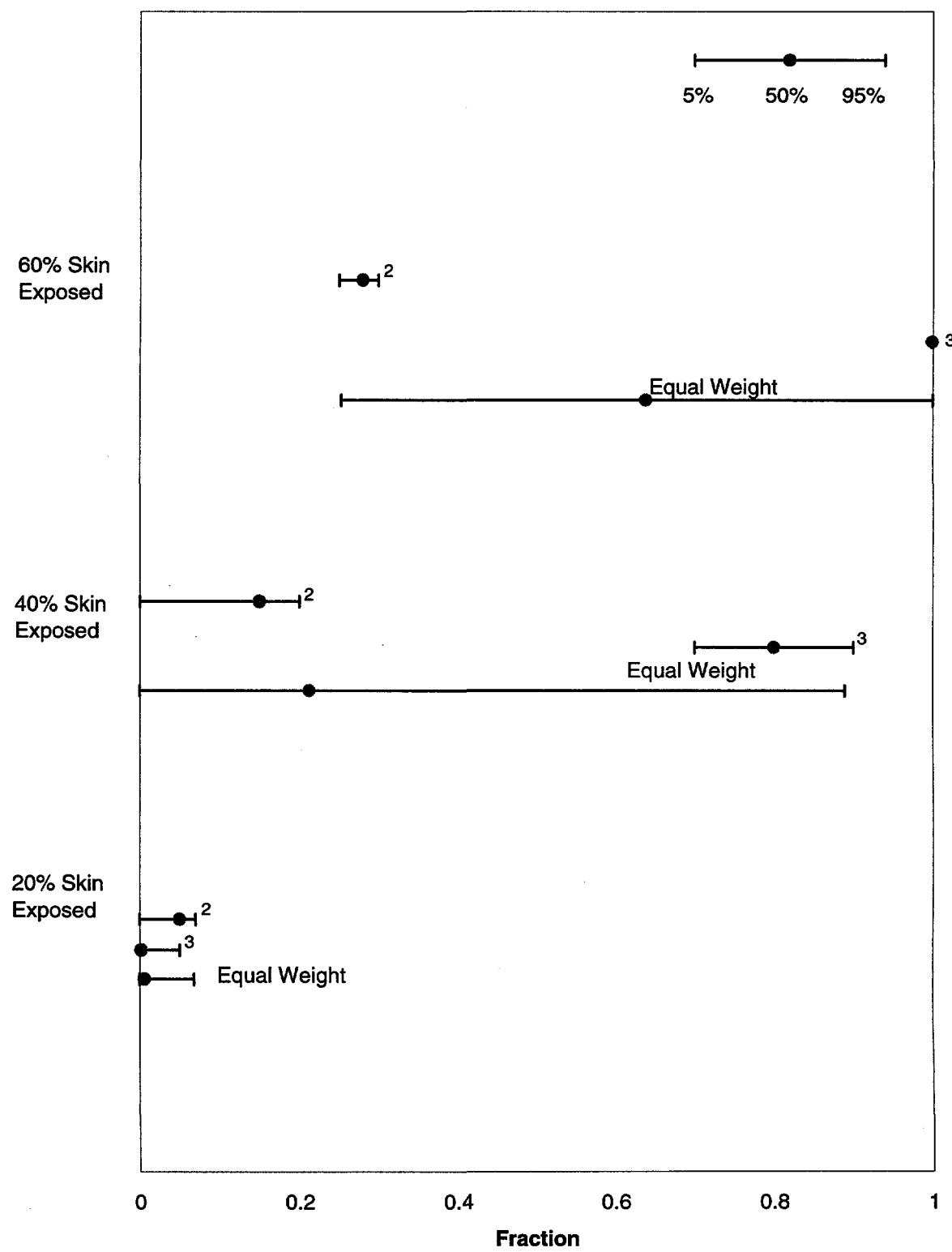


Figure E.13. Fraction that die from 50% acute ulceration of exposed skin following 24-hr beta skin dose.

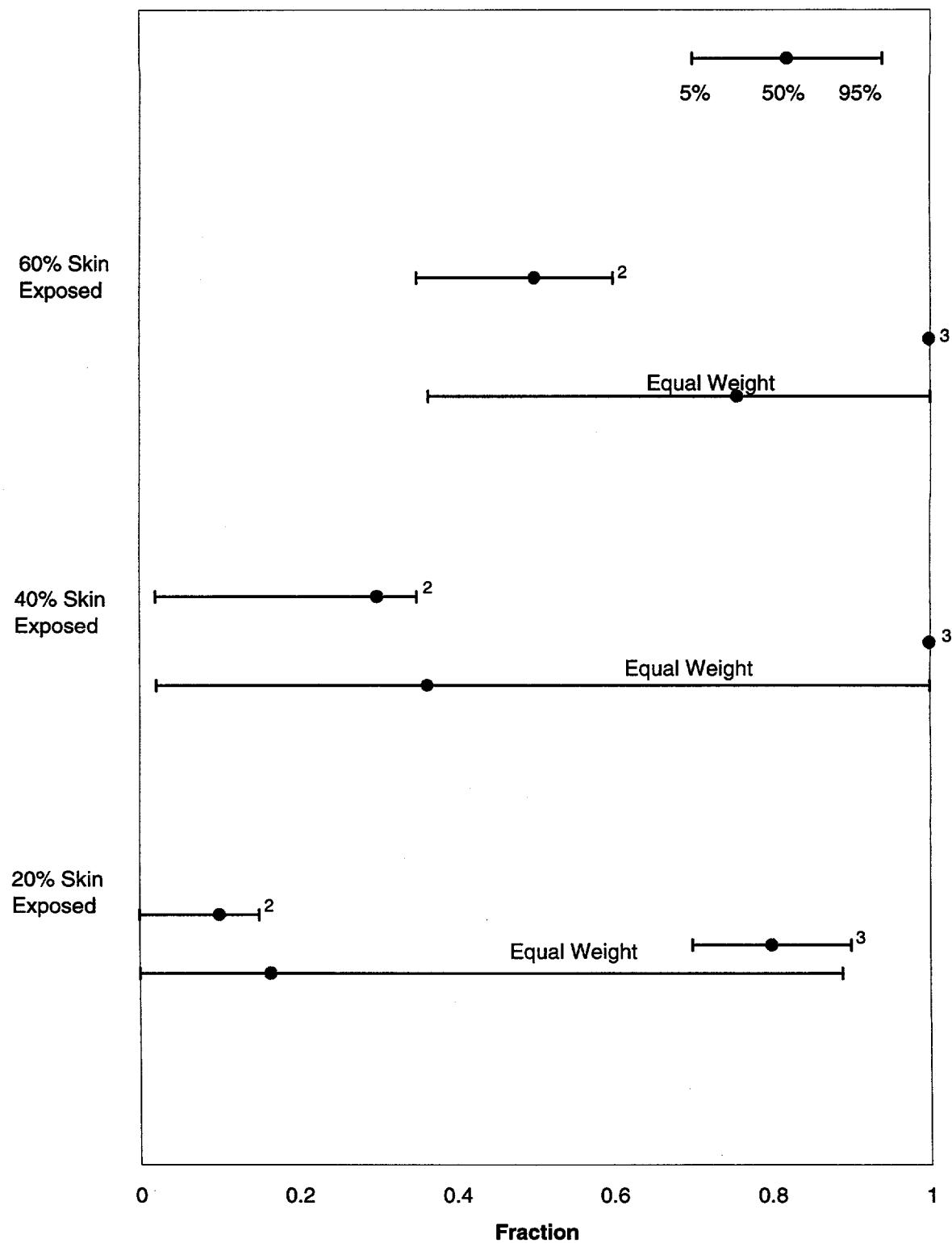


Figure E.14. Fraction that die from 90% acute ulceration of exposed skin following 24-hr beta skin dose.

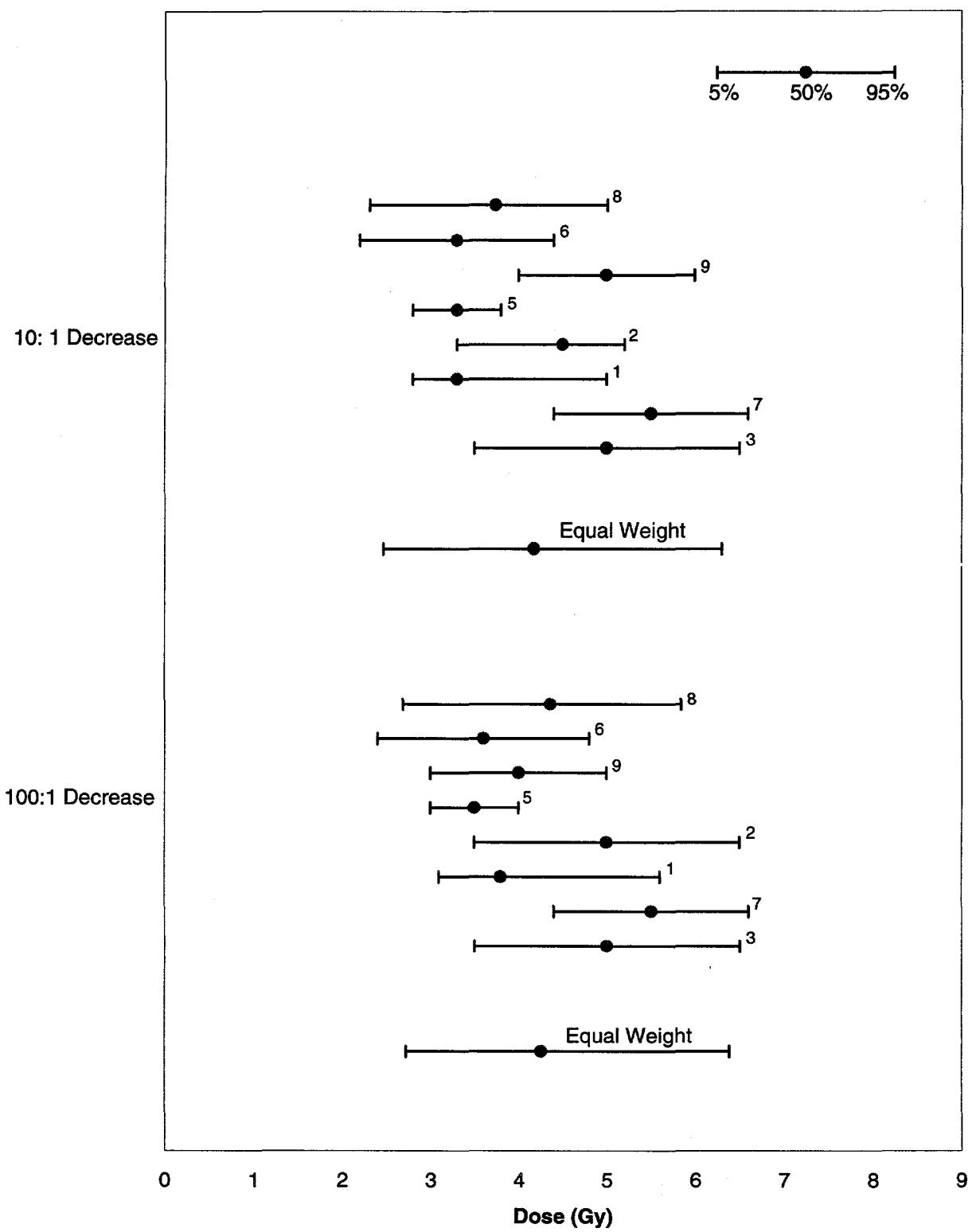


Figure E.15a. LD₅₀ for two-step 24-hour whole-body gamma dose, 10:1 and 100:1 relative dose rates, minimal medical treatment.

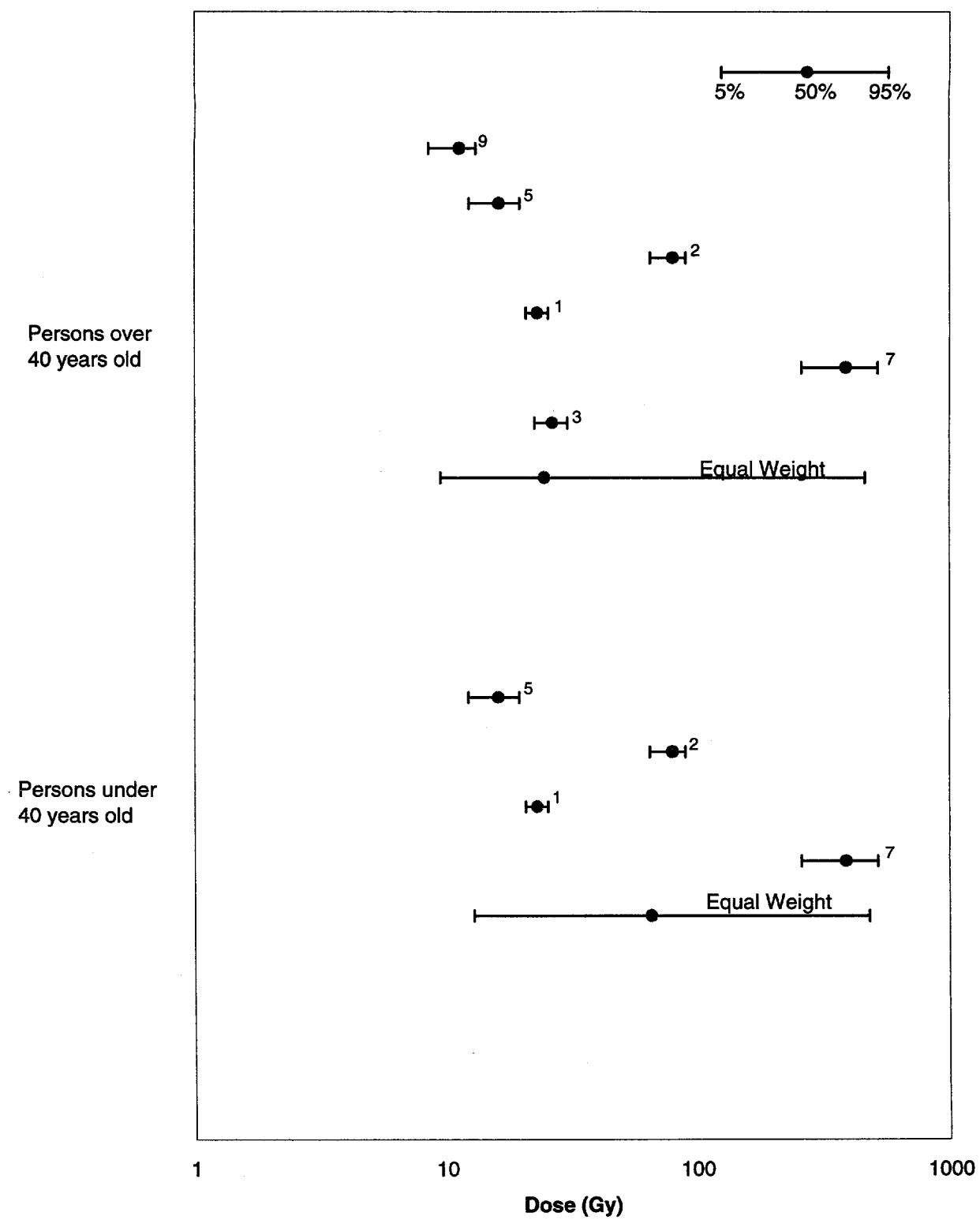


Figure E.15b. LD₅₀ for two-step 7-day beta lung dose 14:1 relative dose rates by age groups supportive medical treatment.

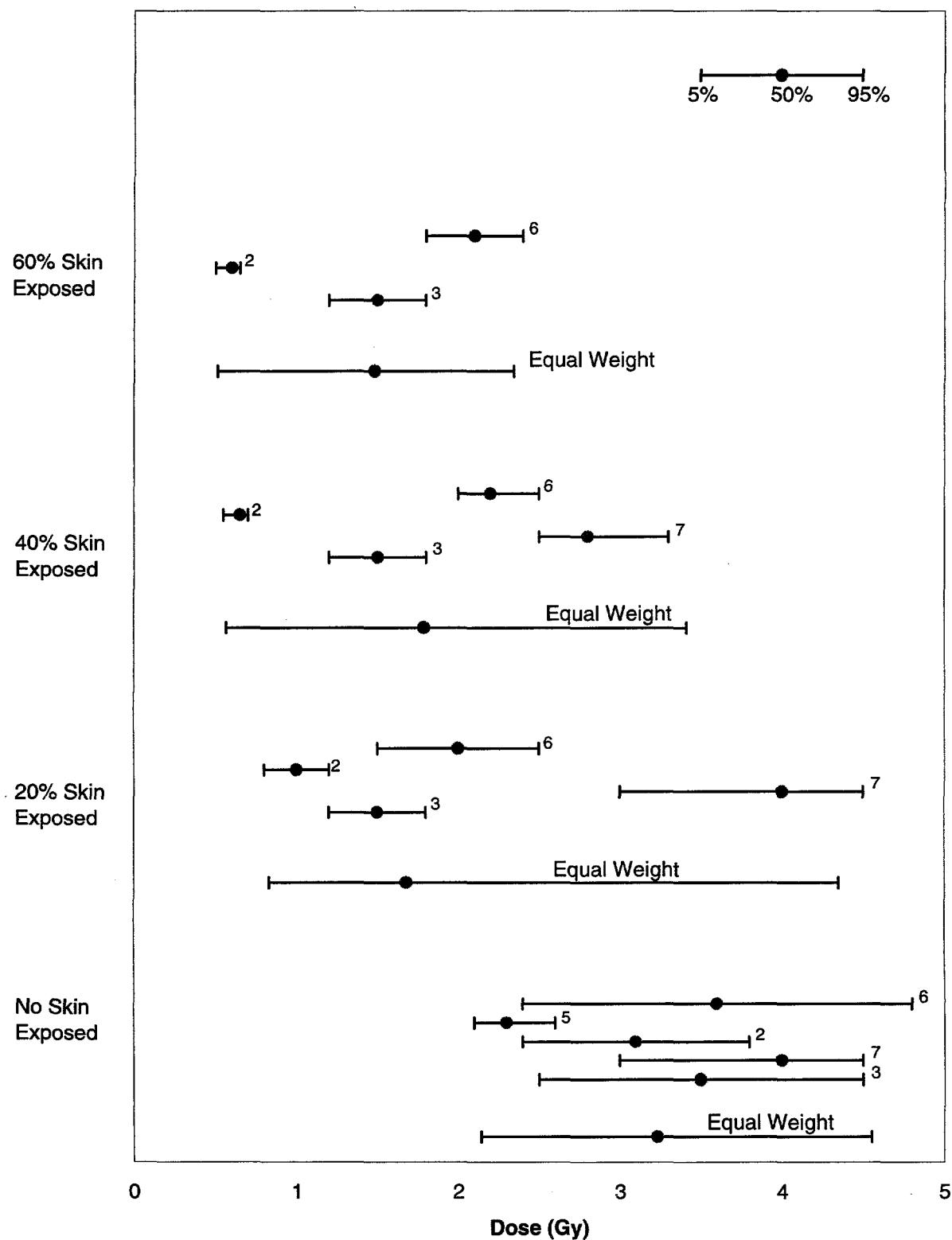


Figure E.16. LD₅₀ red marrow dose for composite exposure: D_{LU} = 2D_{RM}, D_{SK} = 21D_{RM}, minimal medical treatment.

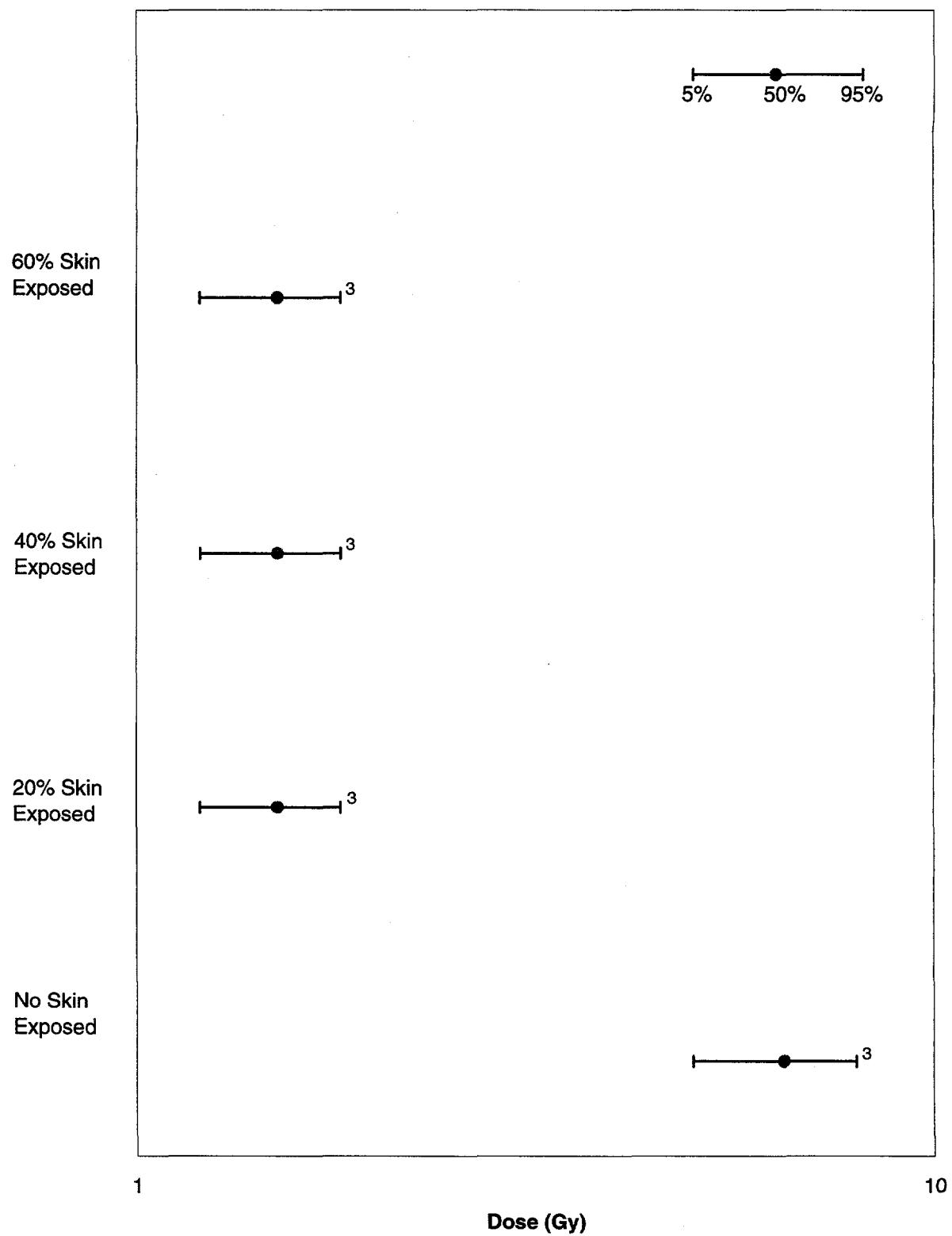


Figure E.17a. LD₅₀ red marrow dose for composite exposure: D_{LU} = 2D_{RM}, D_{SK} = 21D_{RM}, supportive medical treatment, with growth factors.

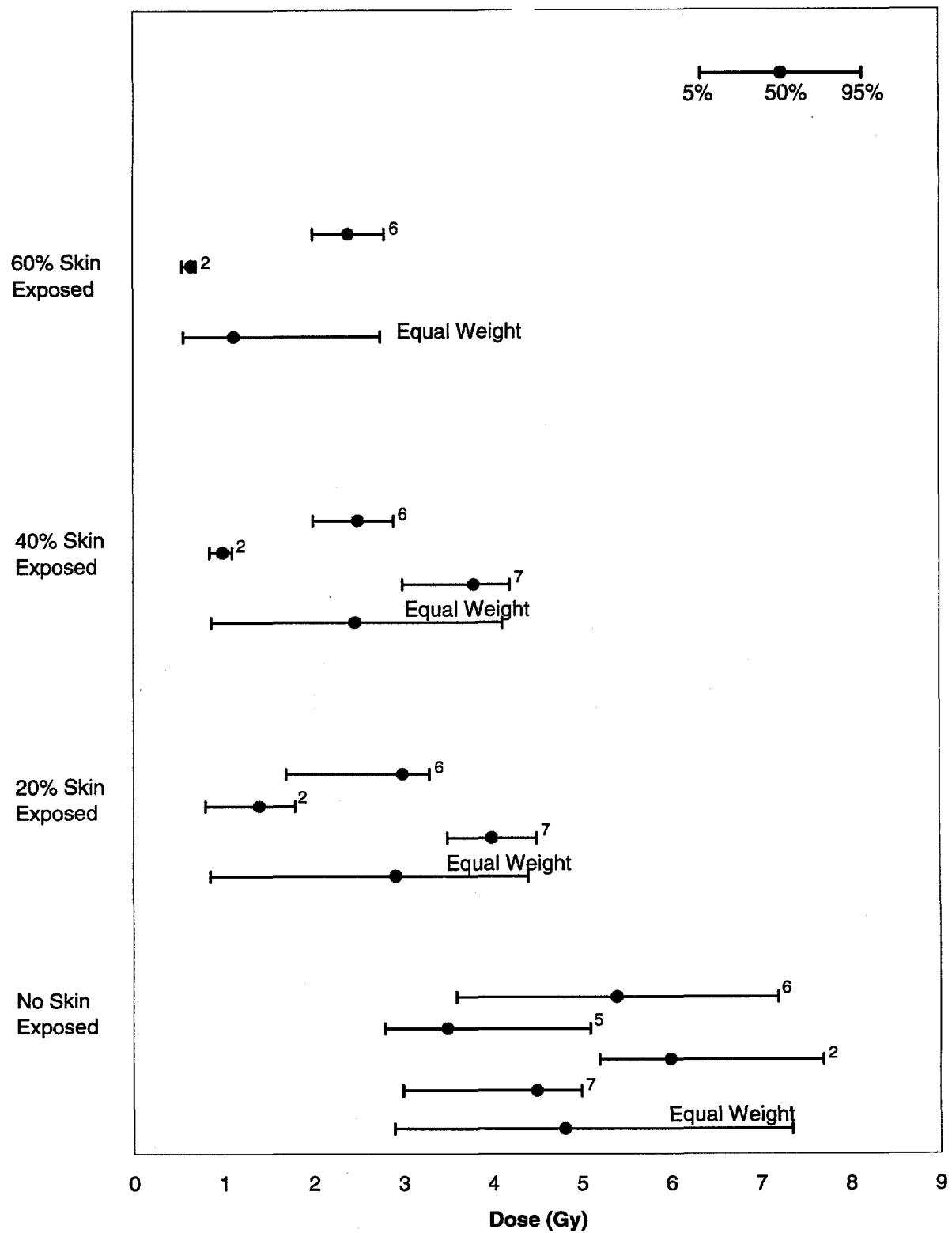


Figure E.17b. LD_{50} red marrow dose for composite exposure: $D_{LU} = 2D_{RM}$, $D_{SK} = 21D_{RM}$, supportive medical treatment, without growth factors.

BIBLIOGRAPHIC DATA SHEET

(See instructions on the reverse)

2. TITLE AND SUBTITLE

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Early Health Effects Uncertainty Assessment
Appendices

5. AUTHOR(S)

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B.C.P. Kraan (TUD)

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B-1049 Brussels, Belgium

10. SUPPLEMENTARY NOTES

J. Randall, NRC Project Manager

11. ABSTRACT (200 words or less)

The development of two new probabilistic accident consequence codes, MACCS and COSYMA, was completed in 1990. These codes estimate the consequences from the accidental releases of radiological material from hypothesized accidents at nuclear installations. In 1991, the U.S. Nuclear Regulatory Commission and the Commission of the European Communities began cosponsoring a joint uncertainty analysis of the two codes. The ultimate objective of this joint effort was to systematically develop credible and traceable uncertainty distributions for the respective code input variables. A formal expert judgment elicitation and evaluation process was identified as the best technology available for developing a library of uncertainty distributions for these consequence parameters. This report focuses on the results of the study to develop distribution for variables related to the MACCS and COSYMA early health effects models.

12. KEY WORDS/DESCRIPTIONS (List words or phrases that will assist researchers in locating the report.)

uncertainty analysis, early health effects, radiological health effects, deterministic health effects, accident consequence analysis, nuclear accident analysis, probabilistic analysis, expert elicitation, MACCS, COSYMA, consequence uncertainty analysis

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