kers have risks that are about 10 times those for non-smokers, while according to the NIH Report a dose of 10 rad would not increase the risk of lung cancer by more than a factor of 1.3. The exact manner in which radiation affects risks in smokers and non-smokers is difficult to determine from available epidemiological data. For low-LET radiation (i.e., gamma ray) exposure, PCs given in the NIH Report are based on data which support the assumption that risks due to smoking and risks due to radiation are independent or "additive." This means that the risk of lung cancer due to a given radiation exposure for a smoker will be a much smaller proportion of his total risk than will the risk due to that same exposure for a nonsmoker.

All of these sources of uncertainty are recognized in the NIH Report and have been considered in developing the PC methodology and determining the estimates of PC for the various types of cancers. While the methodology is general, estimates of the NIH Working Group are for the "average individual" having the characteristics of a group that can be defined by condition of sex, age at exposure, etc. and the uncertainties described in the NIH Report. For the claimant, however, individual characteristics and other relevant factors may increase or decrease not only the estimated PC value but also the uncertainties surrounding the PC value.

V. A PROPOSED SCREENING PROCEDURE FOR CLAIMS

Introduction

In this section, a procedure is described for screening claims of radiation-induced cancer. This procedure is designed to insure that cases which have even a small chance of a true PC, that is 0.5 (50 percent) or greater (i.e., that meet the "at least as likely as not" criterion), are developed for assessment of causality, yet will avoid detailed development of those cases for which there is virtually no chance that the true PC would be as large as 50 percent. The screening process is not a decision-making process that should result in automatic compensation.

The screening procedure both favors the claimant and allows for consideration of uncertainties. It intends to separate virtually certain, non-meritorious claims for causality (i.e., "those of pure speculation or remote possibility") from those that have some chance of being adjudicated as meritorious (i.e., are "within the range of possibility"). In the latter cases, additional scientific and medical evidence which is specific for the individual cases will need to be analyzed, and at that time reasonable doubt is taken into account for those claims in which it is approximately "as likely as not" that the cancer was caused by radiation exposure received during the time of the claimant's service.

It was noted in section IV that the estimated PCs provided in the NIH Report are subject to several sources of uncertainty. This means that for an individual case, the true PC will lie within a range of PCs that is reasonably consistent with the available evidence in the case. Therefore, although the PC given in the NIH Report may be less than 50 percent, the possibility that the true PC exceeds this percentage cannot be ruled out with certainty, as the upper end of the associated range of uncertainty may exceed 50 percent. However, if the PC calculated from the NIH Report is close to zero, then, even with a large degree of uncertainty, one can be reasonably certain that the true PC does not exceed 50 percent, i.e., that it does not satisfy the "at least as likely as not" criterion.

It is expected that the vast majority of potential claimants for Veterans Administration benefits will have received doses of less than 5 rad (0.05 Gy), and that most claimants will have received doses of less than 1 rad (0.01 Gy). In most cases, the PCs given by the NIH Report for doses of 1 rad (0.01 Gy) or less are less than one percent, while the PCs for doses of 5 rad (0.05 Gy) or less are usually less than five percent. Because the PCs for these exposures are so small, the derived screening procedure could help to limit greatly the number of cases needing detailed development for causality without jeopardizing claims with medical and radiation exposure records that merit evaluation.

In order to accomplish this objective, it is necessary to quantify the various uncertainties discussed in Chapter VII of the NIH Report. Some of these uncertainties can be quantified objectively from the available data, while others require a more

subjective evaluation. It is possible also to estimate the effect of these several uncertainties acting jointly on the calculated PC. With this approach, an upper limit can be derived for any given PC. The level of credibility in this upper limit can be specified with 90, 95, and 99 percent being common levels.

If all sources of uncertainty could be quantified in a rigorous statistical manner from available data, the interpretation of an upper limit of (for example) 95 percent would be that there is only a five percent chance that the observed data could have resulted if the PC were as large or larger than the stated upper limit. This is the usual interpretation associated with "confidence" limits. However, because some sources of uncertainty must be evaluated subjectively, the term "credibility" limit, a term which reflects a more subjective concept of probability, is used instead. For practical purposes, a 95-percent upper limit can be interpreted as meaning that there is only a five percent chance that the true PC exceeds this value.

For screening purposes, it is then possible to determine the dose (specific to the cancer type, age at exposure, etc.) such that the upper 95-percent (or other specified level) credibility limit for the PC associated with that dose will be no greater than 50 percent. These doses will be referred to as screening doses. For any dose less than the appropriate screening dose, it follows that there is less than a 5 percent chance that the true PC exceeds fifty percent. The determination of such screening doses forms the basis of this screening procedure.

Determination of Screening Doses

The determination of screening doses requires the following three steps:

1. Quantifying uncertainties;
2. Combining these uncertainties to determine upper credibility limits for PCs; and
3. Determining the doses corresponding to a PC upper limit of 50 percent.

The methodology for determining these screening doses is described in Appendix B, which includes the derivation of a screening dose model to accomplish steps 2 and 3 above and an explanation of the mathematical treatment of uncertainties in the model. Also, an example is provided, showing the determination of the screening dose for stomach cancer given certain conditions.

In Tables 1-3, screening doses for the radiogenic cancers listed in Section III are given for three credibility levels, 90, 95, and 99 percent. Entries are shown for ages at exposure of 20, 30, and 40 years. Kidney and urinary bladder cancers are treated as urinary tract cancer. Radiation dose is expressed in rad and is the average absorbed dose received by the target organ or tissue.

Application of the Screening Procedure

A claimant's dose is compared with the screening dose indicated in Tables 1-3 for the appropriate type of cancer and age at exposure. If the claimant's dose exceeds the screening dose the claim should receive further development of causality.

Linear interpolation can be used for ages at exposure intermediate to those given in the NIH Report. The screening doses given for exposure at age 20 can be used for those younger than age 20 at exposure. Likewise, the screening doses given for exposure at age 40 can be used for those over age 40 at exposure. Two sets of screening values are given for each type of leukemia shown, one to be used if the case occurred within 20 years of exposure and the other for 20 or more years. For other types of cancer, the screening doses apply to all cases occurring five or more years after exposure. For lung cancer, there are also two sets of values in order to account for differences in smoking histories. The first set of values should be used if the potential claimant is known to be a smoker, while the second set of values should be used if the claimant's smoking habits are unknown at the time of screening, or claimant is known to have stopped smoking 5 years or more prior to diagnosis, or claimant is known to be a nonsmoker.

The choice of credibility level is an administrative decision which resides within the responsibility of the VA. The VA could also select higher, lower or in-between credibility levels, but such a selection would require additional calculations. In practice, it seems very unlikely that claims excluded from consideration of causality based on the "90-percent screening doses," but allowed consideration based on the "99-percent screening doses," would be found meritorious after the individualized claims are fully evaluated.

Table 4 lists the doses required to yield a PC of 50 percent if the NIH Report is applied directly. The fact that these doses are much larger than the screening doses developed by the Science Panel reflects the conservative assumptions that have been made in developing the screening procedure to meet the intent of the VA's "reasonable doubt" policy.

The screening dose methodology has the following characteristics:

* It allows for the possibility that the claimant has a lower baseline rate than average, corresponding to the 10th percentile of male rates (except for female breast cancer) for all counties in the United States. That is, consideration of individual characteristics of the claimant is very unlikely to raise the PC for doses at screening levels to 50 percent or more.

* It allows for the possibility of future adjustments of PCs as a result of new dose estimates for the Japanese atomic bomb survivors. This source of uncertainty is treated in the same manner as in Chapter VII, Section O of the NIH Report.

* It allows for additional uncertainty from a variety of sources, including all sources considered in Section O of the NIH Report and discussed in Appendix B of this report. Given these allowances and an allowance for a lower baseline rate than average, even a claimant with a low baseline rate who fails to pass the screening criteria would have a less than 1 in 100 chance (if 99-percent credibility limits are used) that his true PC exceeds 50 percent. With 95-percent credibility limits the chance would be 1 in 20, while with 90-percent credibility limits the chance would be 1 in 10. For a claimant with the average baseline rate, the chance of the true PC exceeding 50 percent will be much less than these values.

The following examples, based on the 95-percent screening doses in Table 2, illustrate the application of the screening procedure.

Example 1: A male claimant alleges that he received a dose of 12 rad at age 20 and developed acute leukemia at age 30. The screening dose in this case is 1.8 rad. Since the claimant's dose exceeds 1.8 rad, his case would be further developed for causality. The calculated PC for this case is 34 percent. Thus, based on the NIH Report alone, his PC is not as large as 50 percent, and causality would not be established if the decisional criterion "as least as likely as not" is applied at this 50 percent level. It is possible, however, that evaluation of the details of this claim could provide reason to adjust the PC upward.

Example 2: A male claims he received a dose of 1.2 rad at age 25 and developed cancer of the stomach at age 50. The screening dose for stomach cancer is 10.8 rad for exposure at age 20 and 21.2 rad for exposure at age 30. Thus, the screening dose is 16.0 rad for age 25 based on linear interpolation. Therefore, using the screening conditions described, his claim would not be further developed for causality because his dose did not exceed the 16.0 rad. In this case the calculated PC from the NIH Report is 0.46 percent. From the NIH Radioepidemiological Tables a dose of 126.3 rad is required to yield a PC of 50 percent for 25 years of age at exposure. This dose of 126.3 rad can be derived by interpolation between ages 20 and 30 for doses shown in Table 4.

Example 3: Claimant alleges that he received a dose of 17 rad at age 25 and developed cancer of the stomach at age 50. Since this dose exceeds the screening dose of 16.0 rad, the claim, in this case, just passes the screening criteria for further development of the causality issue. Using the NIH Report, the calculated PC is 6.9 percent. A claim based on a 15 rad dose would not have passed the screening criteria for further development of causality.

Passing the screening criteria should not be equated with having established significant causality. A claim based on an exposure to radiation that just passes the screening criteria has only a very remote chance of resulting in a meritorious finding after further development of causality.

Suppose the claimant in Example 3 were able to demonstrate that he lived in a section of the country that had especially low stomach cancer rates. For stomach cancer, the 10th percentile of all U.S. counties is a factor of 1.9 lower than the average rate. As discussed in the NIH Report (pp. 51-52), it is not clear whether or not adjustment should be made for this reason. However, if it were, the new PC would be raised from 6.9 to 12 percent, still well below a PC of 50 percent. If an additional adjustment is made for revised dosimetry in Japan by the factor of 1.62 (suggested in the NIH Report) the claimant's PC would increase from 12 to 19 percent.

Thus, even if this claimant's PC were adjusted for a low baseline and for revised Japanese dosimetry, the PC is still well below 50 percent. This would be expected since the screening dose of 16.0 is far below the dose of 126 rad (interpolated for age 25, Table 4) needed to obtain a PC of 50 percent if the NIH Report is used directly.

VI. ROLE OF THE PC TABLES IN ADJUDICATING INDIVIDUAL CASES

The NIH Report represents an extensive effort to utilize relevant scientific knowledge and data for the purpose of estimating risks due to radiation, and, in turn, estimating probabilities of causation for certain types of cancer. Since the report reflects a consensus of scientists with expertise in several relevant scientific fields, it is not unreasonable to view it as an opinion deserving greater weight than that of individual experts. In those cases warranting further development of causality, the NIH Report provides a reasonable basis for assessing the significance of the risk associated with a given radiation exposure to an individual with a specific cancer of the type treated in the Report. However, the scientists responsible for developing the NIH Report could not give detailed consideration to every possible individual situation that might arise. Thus, it is possible that in individual cases some modifications of the PCs provided by the NIH Report might be warranted. It is also important that use of the NIH Report does not exclude consideration of the specifics of each claimant's case, including the type of radiation involved.

Most of the uncertainties reflect limitations in available data for developing scientific understanding and, thus, cannot be overcome by some other system of assessing risks due to radiation. It is important to understand that most uncertainties are bidirectional, so that the PC can be overestimated as well as underestimated.

The NIH Report should be considered an important piece of evidence that can contribute to the VA's requirement to take into account "sound scientific and medical evidence" in the adjudication of those veterans' claims for compensation for diseases allegedly resulting from radiation exposure. Further use of the NIH Report in developing causality for those cases that exceed the appropriate screening doses would be harmonious with and supportive of the rules of the Veterans Administration in adjudicating claims of service connected radiogenic cancer.

VII. RECOMMENDATIONS

In response to the request of the Veterans Administration (VA) to the Committee on Interagency Radiation Research and Policy Coordination (CIRRPC) for guidelines on using the National Institutes of Health's (NIH) report on radioepidemiological tables in the adjudication of veterans' claims of radiation injury, the Science Panel of CIRRPC proffers the following recommendations:

1. The NIH Report is directly applicable only to the following cancers listed as "radiogenic" diseases in the VA's final rules for adjudicating veterans' claims:

All forms of leukemia, except chronic lymphatic leukemia;
Colon cancer;
Esophageal cancer;
Female breast cancer;
Kidney cancer;
Liver cancer;
Lung cancer;
Pancreatic cancer;
Stomach cancer;
Thyroid cancer; and
Urinary bladder cancer.

2. For purposes of screening claims, Tables 1-3 in this Science Panel report may be used to deny causality for those claims which have "no reasonable possibility" of meeting the decisional criterion of "at least as likely as not." The selection of an appropriate credibility level (90%, 95%, or 99%) to be used for applying this criterion is a choice left to the Veterans Administration.

3. The NIH Report should be considered a scholarly and scientifically responsible document and accepted as a valid basis not only for the screening procedure developed, but also as a learned opinion of medical scientists in evaluating, along with other evidence, cases not eliminated by the screening procedure.

Table 1. Screening Doses (in rad) to the Affected Organ/Tissue Based on Upper 90-Percent Credibility Limit [1/]

Type of Cancer	Age at Exposure		
	<20	30	>40
Chronic granulocytic leukemia [2/]			
within 20 years of exposure	1.8	2.6	2.8
20 or more years post-exposure	5.3	6.3	11.7
Acute leukemia [2/]			
within 20 years of exposure	2.3	3.7	8.2
20 or more years post-exposure	7.0	8.2	10.8
Leukemia (excl. chronic lymphatic)			
within 20 years of exposure	2.3	3.5	6.6
20 or more years post-exposure	6.6	7.7	10.8
Colon cancer	32.0	59.1	98.9
Esophageal cancer	14.1	33.2	52.2
Female breast cancer	32.0	60.0	120.6
Kidney and bladder cancer	26.5	43.7	63.3
Liver cancer	2.1	6.9	16.5
Lung cancer			
known smokers [3/]	46.1	83.4	119.3
others [4/]	8.6	18.0	28.2
Pancreatic cancer	13.8	30.7	51.5
Stomach cancer	13.7	26.5	42.8
Thyroid cancer	6.0	13.0	15.4

1/ A claim should be further developed for causality if the claimant's organ/tissue dose exceeds the values given in the table. Screening doses between age 20 and 30 or between 30 and 40 should be obtained by linear interpolation. A claimant with a dose less than the screening dose would have less than a 10 percent chance of having a true PC exceeding 0.5 (50%).

2/ Dose to active bone marrow.

3/ Known to have been a regular smoker (10 or more cigarettes per day) within 5 years of diagnosis. Screening doses are calculated based on the assumption that the claimant is a member of the average U.S. population that includes smokers and nonsmokers.

4/ Claimant's smoking habits are unknown, or claimant is known to have stopped smoking 5 years or more prior to diagnosis, or claimant is known to be a nonsmoker. Screening doses are calculated based on the assumption that the claimant is a nonsmoker.

Table 2. Screening Doses (in rad) to the Affected Organ/Tissue Based On Upper 95-Percent Credibility Limit [1/]

Type of Cancer	Age at Exposure		
	<20	30	>40
Chronic granulocytic leukemia [2/]			
within 20 years of exposure	1.4	2.0	2.2
20 or more years post-exposure	4.2	5.0	9.3
Acute leukemia [2/]			
within 20 years of exposure	1.8	2.9	6.5
20 or more years post-exposure	5.5	6.5	8.5
Leukemia (excl. chronic lymphatic)			
within 20 years of exposure	1.8	2.8	5.2
20 or more years post-exposure	5.2	6.1	8.5
Colon cancer	25.9	48.6	82.7
Esophageal cancer	9.1	22.2	35.8
Female breast cancer	26.7	50.9	104.3
Kidney and bladder cancer	21.1	35.2	51.7
Liver cancer	1.6	5.4	12.9
Lung cancer			
known smokers [3/]	37.8	69.6	100.6
others [4/]	6.8	14.4	22.8
Pancreatic cancer	10.3	23.4	40.0
Stomach cancer	10.8	21.2	34.8
Thyroid cancer	4.9	10.7	12.7

1/ A claim should be further developed for causality if the claimant's organ/tissue dose exceeds the values given in the table. Screening doses between age 20 and 30 or between 30 and 40 should be obtained by linear interpolation. A claimant with a dose less than the screening dose would have less than a five percent chance of having a true PC exceeding 0.5 (50%).

2/ Dose to active bone marrow.

3/ Known to have been a regular smoker (10 or more cigarettes per day) within 5 years of diagnosis. Screening doses are calculated based on the assumption that the claimant is a member of the average U.S. population that includes smokers and nonsmokers.

4/ Claimant's smoking habits are unknown, or claimant is known to have stopped smoking 5 years or more prior to diagnosis, or claimant is known to be a nonsmoker. Screening doses are calculated based on the assumption that the claimant is a nonsmoker.

Table 3. Screening Doses (in rad) to the Affected Organ/Tissue Based on Upper 99-Percent Credibility Limit [1/]

Type of Cancer	Age at Exposure		
	<20	30	>40
Chronic granulocytic leukemia [2/]			
within 20 years of exposure	0.9	1.3	1.4
20 or more years post-exposure	2.7	3.2	5.9
Acute leukemia [2/]			
within 20 years of exposure	1.1	1.8	4.1
20 or more years post-exposure	3.5	4.1	5.5
Leukemia (excl. chronic lymphatic)			
within 20 years of exposure	1.1	1.7	3.3
20 or more years post-exposure	3.3	3.9	5.5
Colon cancer	17.0	33.1	58.1
Esophageal cancer	3.9	9.9	16.7
Female breast cancer	18.8	37.0	78.6
Kidney and bladder cancer	13.4	23.1	34.7
Liver cancer	1.0	3.3	8.2
Lung cancer			
known smokers [3/]	25.5	48.8	72.1
others [4/]	4.3	9.3	15.0
Pancreatic cancer	5.8	13.7	24.3
Stomach cancer	6.9	13.8	23.2
Thyroid cancer	3.3	7.4	8.8

1/ A claim should be further developed for causality if the claimant's organ/tissue dose exceeds the values given in the table. Screening doses between age 20 and 30 or between 30 and 40 should be obtained by linear interpolation. A claimant with a dose less than the screening dose would have less than a one percent chance of having a true PC exceeding 0.5 (50%).

2/ Dose to active bone marrow.

3/ Known to have been a regular smoker (10 or more cigarettes per day) within 5 years of diagnosis. Screening doses are calculated based on the assumption that the claimant is a member of the average U.S. population that includes smokers and nonsmokers.

4/ Claimant's smoking habits are unknown, or claimant is known to have stopped smoking 5 years or more prior to diagnosis, or claimant is known to be a nonsmoker. Screening doses are calculated based on the assumption that the claimant is a nonsmoker.

Table 4. Organ/Tissue Doses (in rad) Corresponding to a PC of 50 Percent Based on the NIH Radioepidemiological Tables

Type of Cancer	Age at Exposure		
	<20	30	>40
Chronic granulocytic leukemia			
peak time of risk	11.5	16.0	17.6
15 years post-exposure	30.8	35.7	59.4
Acute leukemia			
peak time of risk	14.7	22.4	44.5
15 years post-exposure	38.7	44.5	55.6
Leukemia (excl. chronic lymphatic)			
peak time of risk	14.4	21.4	37.1
15 years post-exposure	37.1	42.4	56.6
Colon cancer	209.4	331.8	497.4
Esophageal cancer	183.8	331.8	458.6
Female breast cancer	92.3	157.0	287.3
Kidney and bladder cancer	258.1	368.3	483.5
Liver cancer	28.0	72.6	138.0
Lung cancer			
smokers	258.1	409.0	546.8
nonsmokers	73.2	128.0	178.6
Pancreatic cancer	112.4	202.2	297.9
Stomach cancer	95.6	157.0	225.9
Thyroid cancer	28.9	56.6	63.9

APPENDIX A

SCIENCE SUBPANEL ON RADIOEPIDEMIOLOGICAL TABLES

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APPENDIX B[1]

DETERMINATION OF SCREENING DOSES

Derivation of Screening Dose Model

The PC is calculated as $R/(1+R)$ where R is the relative excess risk and is defined as the ratio of the risk due to radiation and the baseline risk. R can be written as the product of two factors, F(D) and G. F(D) is a function of dose (D) in rad and is taken to be $D+D^2/116$ in the NIH Report, except for breast and thyroid cancer following low LET radiation. Note that F(1) is approximately equal to one, so that G can be regarded as the relative excess risk for a one rad exposure and will sometimes be referred to in this manner.

For the purpose of evaluating uncertainties, G can be assumed to be the product of several factors G(i). G(1) is taken to be the overall risk coefficient (for a particular type of cancer), and the remaining G(i) indicate possible modifying effects of various factors as follows: G(2), baseline values; G(3), age at exposure; G(4), time response; G(5), dose-response relationship; and G(6), Japanese dosimetry.

$\hat{G}(i)$ denotes the estimate of G(i) that is used in the NIH report, and it is assumed (as in section O of Chapter VII of the NIH Report) that the $\hat{G}(i)$ follow independent lognormal distributions, with geometric means given by G(i)/B(i) and geometric standard deviations S(i), where B(i) denotes bias. Note that if $B(i)=1$, the uncertainty is unbiased, and that if B(i) is greater than one, then B(i) is the factor by which G(i) is underestimated. Specifically, the above model is based on the assumption that $\log \hat{G}(i)$ is normally distributed with mean ($\log G(i) - \log B(i)$) and standard deviation $\log S(i)$. [Note: log means the natural logarithm, i.e. $\log_e$.]

Since $\hat{G}(i)$ are assumed independent, an upper 95 percent credibility limit for $\log \hat{G}$ is given by

$$\sum_i [\log \hat{G}(i) + \log B(i)] + 1.645 * [\sum_i \log^2 S(i)]^{1/2}$$

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[1] This Appendix was prepared by Dr. Ethel S. Gilbert, Battelle, Pacific Northwest Laboratories, at the request of the Subpanel on Radioepidemiological Tables, in order to provide the scientific basis and mathematical methodology for the determination of screening doses. Minor editorial changes were made by the Subpanel which, however, did not affect the scientific content of the Appendix. It assumes familiarity with the NIH Report, particularly Chapter VII, Section O. The Appendix is intended for the reader who is interested in the technical details of the procedure used to determine screening doses.

and the upper 95-percent credibility limit, which will be denoted by R95, for $\hat{G}$ is given by

$$\{\prod_i B(i)*\hat{G}(i)\}*\exp\{1.645*[\sum_i \log^2 S(i)]^{1/2}\}$$

$$= \hat{G} * X95, \text{ where } X95 = \{\prod_i B(i)\}*\exp\{1.645*[\sum_i \log^2 S(i)]^{1/2}\} \quad (1).$$

More generally, to obtain a Z percent upper credibility limit, the upper Z percentile of a standard normal distribution would be substituted for 1.645.

Once the B(i) and S(i) are specified, the factor X95 can be calculated. $\hat{G}$ may be calculated as $PC_1/(1-PC_1)$ where PC_1 is the probability of causation given in the NIH Report for a one rad exposure.

The upper limit for G, the relative excess risk for a one rad (0.01 Sv) exposure, is given by $R95=\hat{G}*X95$ where R95 is the relative excess risk at the upper 95 percent credibility level. The upper limit for the relative excess risk for a dose D is given by R95 * F(D), and the corresponding upper limit for the PC for dose D is given by

$$R95 * F(D)/[1 + R95 * F(D)] \quad (2)$$

To calculate the dose corresponding to an upper credibility limit on the PC of 50 percent, the expression in (2) is set equal to 0.50, and solved for D. This leads to the following quadratic equation:

$$R95 * D^2/116 + R95 * D - 1 = 0$$

It remains to determine the specific B(i) and S(i) needed to evaluate the factor X95. This is done in the discussion that follows on evaluating sources of uncertainty with S(i) referred to as the GSD (geometric standard deviation), and B(i) as bias. The values of B(i) and S(i) used to determine the screening doses are presented in Table A.

Treatment of Uncertainties

a. Baseline Values

When the individual characteristics of a claimant are examined, it is possible that in some cases it will be determined that the person's baseline risk is different from the average, leading to possible adjustment of the PC. It is important that a screening procedure allow for this possibility.

If it is determined that an individual has been exposed to other substances associated with the type of cancer at issue, or if it is determined that the individual has a

family history of the cancer, the direction of the adjustment (if any) would be to raise the baseline risk and thus lower the PC from those given in the NIH Report. Potential adjustment in this direction is not of concern for screening purposes.

Consideration of the individual characteristics of a person could result in increasing the PCs given in the NIH Report only if the person could demonstrate that he or she were unusually free of exposures associated with the disease, or if the person demonstrated that rates from the area in which he or she had resided were substantially lower than the national average. (It was noted in the NIH Report that if the factors contributing to these differences act multiplicatively with radiation, the PCs as given in the NIH Tables are in fact appropriate, but in the interest of allowing the benefit of a doubt, it is possible one would want to adjust PCs based on such considerations.) To allow for this possibility, the proposed screening procedure is based on the assumption that the claimant has a baseline rate that is equal to the 10th percentile of male rates (except for female breast cancer) for all U.S. counties for the cancer type involved (Atlas 1975). That is, the screening PC is set sufficiently low that adjustment for a baseline risk that was at the 10th percentile of all counties would not yield a PC as great as 50 percent. It is unlikely that a person could make a solid case that his baseline was lower than this. The ratios of the average U.S. rate to the 10th percentile for several cancer types are given in Table A in the column headed B(2).

b. Age at Exposure

In the NIH Report, a geometric standard deviation (GSD) of 1.23 is used to reflect uncertainty resulting from age at exposure. This may not be adequate to reflect uncertainty in estimates of risk for those who are young at exposure. Much of the exposure of potential Veterans Administration claimants would have been received in their early 20's. For example, the overall GSD for all digestive cancer calculated from results presented by Land is 1.28 (Land 1986). By contrast, the GSD's for estimated age-specific coefficients are in the order of 2 or more. In order to increase the GSD of 1.28 to the level of 2, a GSD for age at exposure of about 1.9 is required. However, similar calculations based on breast cancer estimates presented in BEIR III suggest a GSD for age at exposure of 1.3.

As another means of assessing uncertainty, the ratios of the relative excess risks (from the NIH Report) for those exposed at age 20 and age 10 have been examined. This ratio is about 3 for lung and stomach cancer, but is somewhat smaller for acute leukemia, breast cancer, and thyroid cancer. Results for age 10 at exposure are not given for most cancer types.

In short, the uncertainty from this source is difficult to assess, and probably is not the same for all cancer sites. A GSD of 1.75 has been used allowing for a factor of 3 in the 95 percent two-sided credibility interval.

c. Time Response

For cancers other than leukemia, this uncertainty has been handled in the same manner as in the NIH Report (Chapter VII, Section O) with a GSD of 1.15. For leukemia, risk shows a wave-like response with a peak time at risk that depends on the type of leukemia and age at exposure. For the purposes of screening only, all cases occurring within 20 years of exposure are assumed to have the PC associated with this peak or maximum time of risk. For cases occurring more than 20 years after exposure, the PC associated with 15 years post-exposure is used. This approach may be unduly conservative, but leukemia is a sufficiently uncommon disease that it is unlikely to lead to large numbers of cases needing detailed consideration.

d. Dose Response Relationship

In the NIH Report, except for breast and thyroid cancer, linear risk coefficients derived mainly from BEIR III are multiplied by 0.4 to allow for reduced effectiveness of exposure when received at low doses and dose rates. There is uncertainty concerning whether there should be any reduction at all since a pure linear response cannot be ruled out based on epidemiological data. In preparing the tables of screening doses for various cancers (Tables 1-3, pp. 27-29), it has been assumed that the probability of linearity is 0.33 while the probability for the need for reduction is 0.67. A GSD of 1.43 is used for the uncertainty regarding the degree of reduction as in the NIH Report.

To apply these assumptions, two factors X95 are calculated as indicated in (1). For the first factor, X95A, B(5) is taken to be 2.5 and S(5) taken to be 1.0. For the second factor, X95B, B(5) is taken to be 1.0 and S(5) taken to be 1.43. X95 is then calculated as 0.33 * X95A + 0.67 * X95B.

e. Latent Period

For leukemia, this source of uncertainty is included by using the peak PC (as described above) for all leukemia cases occurring within 20 years of exposure. For cancers other than leukemia, the PCs associated with 10 or more years post-exposure are used for all cases occurring 5 or more years post-exposure. Thus, there is no need for including uncertainty from this source in calculating the overall GSD.

f. Japanese Dosimetry

Uncertainty resulting from the revision in the Japanese dosimetry is treated in the same manner as in Section O of the NIH Report where it is listed under "Risk Coefficient." However, unlike Section O, the correction has not been applied to breast cancer; in this case estimates have been verified in Caucasian populations. The treatment also differs from Section O in that the correction has been applied to liver

cancer. Even though data from thorotrast patients were considered in deriving PCs for liver cancer, with this data there is the additional uncertainty in extrapolating from high to low-LET radiation. Thus, the estimate for liver cancer is dependent on the Japanese data.

g. Risk Coefficients

Statistical uncertainty in the estimated coefficients was not included in the evaluation given in Chapter VII, Section O of the NIH Report. Since estimates for specific cancer types may involve considerable uncertainty, it is important to include this source of uncertainty in this Science Panel assessment. The estimate of the GSD requires the standard error of the logarithm of the estimate, which can be approximated by the standard error of the estimate divided by the estimate. The estimated GSD is then the exponential of this ratio.

As a rule, standard errors are not presented in the NIH Report, and it is difficult to trace the exact source of each estimate used and to determine its standard error. The sources indicated in Table B should provide a reasonably valid assessment of this source of error. With the exception of leukemia, uncertainty in the estimated relative biological effectiveness (RBE) of neutrons for estimates based on Japanese data was not included. To some extent, this source of uncertainty may be included in the uncertainty resulting from Japanese dosimetry, noted above; without consideration of RBE uncertainty, the GSD for leukemia would have been 1.05 (Kato and Schull 1982). Uncertainty in the separate estimates for different types of leukemia has not been considered.

Screening Dose Example

CONDITIONS: 95-percent screening dose for stomach cancer, male, age at exposure is 20 years, time from exposure is 5 or more years.

The PC given in the NIH Report for a one rad (0.01 Sv) exposure for the situation in the example is 0.0057. Thus G, the estimated relative excess risk for a one rad exposure, is $0.0057/(1- 0.0057) \approx 0.0057$. The factors X95A and X95B (see above subsection d on dose response relationship) are calculated as follows:

$$X95A = 1.9*2.5*1.62*\exp\{1.645\ (\log^2 1.33+\log^2 1.75+\log^2 1.15+\log^2 1.17)^{1/2}\}$$
$$= 7.70 *\exp(1.645*0.6623) = 22.89$$

$$X95B = 1.9*1.62*\exp\{1.645(\log^2 1.33+\log^2 1.75+\log^2 1.15+\log^2 1.43+\log^2 1.17)^{1/2}\}$$
$$= 10.63$$

X95 is then given by $\{22.89 + 2(10.63)\}/ 3 = 14.72$

The upper limit for the relative excess risk G of a one rad (0.01 Sv) exposure is then given by 0.0057*14.72 = 0.084. The screening dose is determined by solving

$$\frac{0.084(D+D^2/116)}{1+0.084(D+D^2/116)} = 0.50.$$

The dose 10.8 rad (0.108 Sv) is found to satisfy this equation, and is the screening dose given in Table 2 for stomach cancer for exposure at age 20.

Table A. Bias, B(i), and Geometric Standard Deviations, S(i), used in Determining Screening Doses.

Cancer Type	S(1)	B(2)	S(3)	S(4)	S(5)	B(5)	S(6)	B(6)
Female Breast	1.15	1.9	1.75	1.15	1.00	1.0	1.00	1.00
Colon	1.33	2.4	1.75	1.15	1.43	2.5	1.17	1.62
Esophagus	3.14	2.3	1.75	1.15	1.43	2.5	1.17	1.62
Leukemia	1.31	1.2	1.75	1.00	1.43	2.5	1.17	1.62
Liver	1.28	2.6	1.75	1.15	1.43	2.5	1.17	1.62
Lung	1.28	2.2	1.75	1.15	1.43	2.5	1.17	1.62
Pancreas	1.83	1.9	1.75	1.15	1.43	2.5	1.17	1.62
Stomach	1.33	1.9	1.75	1.15	1.43	2.5	1.17	1.62
Thyroid	1.08	2.7	1.75	1.15	1.00	1.0	1.00	1.00
Urinary (kidney/bladder)	1.43	4.1	1.75	1.15	1.43	2.5	1.17	1.62

S(1): GSD for statistical uncertainty in risk coefficient
B(2): Bias for baseline values (For screening purposes, it is assumed that all claimants have very low baseline risks)
S(3): GSD for age at exposure
S(4): GSD for time response
S(5): GSD for dose response relationship
B(5): Bias for dose response relationship

Note: S(5) and B(5) are not applied simultaneously, but rather as described in this Appendix, section "Treatment of Uncertainties," subsection d.

S(6): GSD for Japanese dosimetry
B(6): Bias for Japanese dosimetry

Table B. GSDs for Risk Coefficients for Each Cancer Type.

Cancer Type	GSD	----------Source of GSD----------
Leukemia	1.31	BEIR III, p. 233, Table V-8
Esophagus	3.14	A-Bomb survivor mortality data, Land 1986
Stomach	1.33	A-bomb survivor mortality data, Land 1986
Colon	1.33	A-bomb survivor mortality data, Land 1986
Liver	1.28	Combined Hiroshima and Nagasaki tumor registries, NIH Report, p.218
Pancreas	1.83	Combined Nagasaki tumor registry and British ankylosing spondylitis data, Land 1986
Lung	1.28	A-bomb survivor mortality data, Kato and Schull 1982
Urinary (kidney/bladder)	1.43	A-bomb survivor mortality data, Land 1986
Female Breast	1.15	A-bomb survivor incidence data, Tokunaga et al. 1984
Thyroid	1.08	Thymus irradiated patients, Shore 1980

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