May 17, 1996

FOR: The Commissioners

FROM: James M. Taylor
Executive Director for Operations

SUBJECT: COMPLETION OF RESPONSE TO THE STAFF REQUIREMENTS MEMORANDUM, FOR SECY-95-249, ON RISK HARMONIZATION WHITE PAPER AND RECOMMENDATIONS BY THE INTERAGENCY STEERING COMMITTEE ON RADIATION STANDARDS

PURPOSE:

To respond to Commission direction concerning risk harmonization between the U.S. Nuclear Regulatory Commission and the U.S. Environmental Protection Agency (EPA EXIT) and to obtain Commission approval of a staff recommendation in response to this direction.

BACKGROUND:

On October 3, 1995, NRC staff forwarded SECY-95-249 to the Commission to obtain approval of: (1) the joint NRC-EPA "White Paper on Risk Harmonization" (White Paper); and (2) Risk Harmonization Recommendations of the Interagency Steering Committee on Radiation Standards (ISCORS)." The Commission responded in a Staff Requirements Memorandum (SRM), dated November 29, 1995. This memorandum responds to the issues raised in that SRM.

DISCUSSION:

The Commission directed the staff to amend the White Paper to clarify whether EPA applies its 10^{-4}-10^{-6} lifetime risk on a similar basis to NRC, or whether it instead applies its limit to individual carcinogens, and also to discuss the significance of any difference that may exist. Attachment 1, "Application of U.S. Environmental Protection Agency's Lifetime Risk Range," explains that EPA sometimes applies its risk range on a similar basis to NRC, and sometimes it does not. The significance of the difference between EPA and NRC is unclear because there are differences within EPA as to how the risk range is applied. Therefore, the answer to the Commission's questions is complex and difficult, and the attempt to introduce the material in Attachment 1 into the White Paper would require a major commitment of resources by NRC, EPA, and the other ISCORS agencies. This effort would detract from ISCORS' efforts to implement the risk harmonization recommendations. Therefore, the staff recommends not attempting to revise the White Paper to incorporate Attachment 1. In lieu of that approach, the staff recommends distribution of Attachment 1 to the other ISCORS agencies and other interested parties.

The Commission directed that the "ISCORS Risk Harmonization Recommendations" be revised to clarify that agency implementation of the recommendations must be consistent with the authority, responsibility, and procedures of the agency and that final resolution may not follow the ISCORS consensus. At its January 17, 1996, meeting, the ISCORS Risk Harmonization Subcommittee modified the ISCORS recommendations by adding a preface that incorporates the Commission's requests (Attachment 2). The first paragraph of the preface was added in response to this specific Commission comment.

The Commission also directed that the ISCORS recommendations regarding the use and calculation of population risk should note the potential need for reconsideration after completion of the Committee on the Biological Effects of Ionizing Radiation (BEIR) VII review. At the January 17, 1996, ISCORS Risk Harmonization Subcommittee meeting, NRC staff proposed adding language to the "Recommendations" about the potential need for reconsideration of truncation after the completion of the BEIR VII review. The ISCORS Subcommittee agreed that BEIR VII could affect truncation. However, the Subcommittee concluded that the BEIR VII review, as well as other new scientific information, could affect not only the ISCORS recommendation on population risk, but also all the other ISCORS recommendations on Federal Guidance. Thus the subcommittee agreed to add language to this effect in the second paragraph of the new preface to the ISCORS Risk Harmonization Recommendations (Attachment 2).

The Commission further directed that, before formalizing the BEIR VII effort, the staff should provide the Commission with an explanation of how the results of the BEIR VII study will be factored into the risk harmonization effort and, in particular, into the Federal Guidance document. The staff responded to this direction in a separate memorandum to the Commission, dated March 11, 1996. The staff was informed of the Commission's approval of this response in an SRM dated April 2, 1996.

In addition, the Commission directed the staff to pursue with EPA the question of whether there is a background of chemical carcinogens that is analogous to background radiation, and explore with EPA the risk management implications of similarities and differences between any such chemical background and background radiation. The staff explored this question with EPA staff and shared a draft paper with EPA for review and comment. Attachment 3, "Chemical and Radiation Risks," reflects EPA staff comments and concludes that there is a background of chemical carcinogens that is analogous to background radiation. However, the implications of this conclusion for risk management are unclear because there is no consensus as to how background levels should be taken into account in setting risk management objectives.

Finally, the Commission directed the staff to brief the Commission on the progress and status of the risk harmonization effort in mid-1996 and keep the Commission fully apprised of the progress of the project and any significant agreements tentatively reached between the parties. The staff has been informing the Commission of these activities through memoranda, Assistants' briefings, and weekly items of interest and plans to continue to do so. In addition, the staffs of NRC and EPA plan to jointly brief the Commission in June 1996.

RECOMMENDATION:

That the Commission approve the staff's recommendation not to amend the White Paper to include a discussion about

the application of EPA's 10^{-4} -10^{-6} risk limits, but rather to approve distribution of Attachment 1 to the other ISCORS participants and other interested parties.

COORDINATION:

The Office of the General Counsel has reviewed this paper and has no legal objection.

Original signed by:

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Attachments:
1. Application of U.S. Environmental Protection Agency's Lifetime Risk Range
2. ISCORS Risk Harmonization Recommendations - Preface
3. Chemical and Radiation Risks

ATTACHMENT 1

APPLICATION OF U.S. ENVIRONMENTAL PROTECTION AGENCY'S LIFETIME RISK RANGE

1. INTRODUCTION

In the Staff Requirements Memorandum resulting from SECY 95-249, dated November 29, 1995, the Commission stated:

> NRC applies its 100 millirem/year (3.5×10^{-3} lifetime risk) limit on a per licensee (i.e., facility or activity) basis. The (White) paper should clarify whether EPA applies its 10^{-4}-10^{-6} lifetime risk on a similar basis or whether it instead applies its limit to individual carcinogens. The Paper should discuss the significance of any difference that may exist.

As explained below, the U.S. Environmental Protection Agency (EPA) sometimes applies its risk range on a similar basis to the U.S. Nuclear Regulatory Commission, and sometimes it does not. The significance of the difference between EPA and NRC is unclear because there are differences within EPA as to how the risk range is applied.

2. DISCUSSION

For radionuclides, EPA generally applies a 10^{-4} to 10^{-6} lifetime risk limit of cancer mortality (or cancer incidence,(1) in the Superfund program) to environmental exposures to humans. (For pollutants other than radionuclides, the numerical risk range in most EPA programs is applied to incidence, not to mortality.) EPA has adopted this risk range as a matter of policy under the Safe Drinking Water Act (SDWA), Clean Air Act (CAA), Resource Conservation and Recovery Act (RCRA), Atomic Energy Act (AEA), and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Congress has reinforced this adoption in statutory law and Committee reports on the CAA and CERCLA. Under SDWA and CAA, this risk limit is typically applied to each contaminant. Under CERCLA, the limit is typically applied to the total risk from all contaminants. The risk limit is used in deriving regulatory concentration limits in environmental media.

In many cases, the risk from environmental contaminants is dominated by a single contaminant. For example, benzene may be the dominant carcinogen in air effluents from petroleum refineries. Consequently, limiting the risk from the dominant contaminant often provides sufficient protection of the public and the environment by constraining the risk from the dominant contaminant, as well as other contaminants that may also be present.

Under CERCLA in general, and under the CAA in situations where risk is not clearly dominated by a single contaminant, EPA has considered the "additive risk" by summing the risks from each contaminant for comparison with the 10^{-4} risk discriminator. In these cases, the contaminants must yield similar health effects, such as fatal cancers. Other contaminants not yielding similar effects would be considered independently, unless information exists that suggests a synergistic effect of one contaminant on the health effects from another. EPA had provided policy guidance on such additive effects in setting alternate concentration limits under RCRA and in conducting risk assessments in support of remediation under CERCLA.

More recently, pursuant to Section 112 of the 1990 CAA Amendments, EPA has adopted an approach, when appropriate, of assessing the risks of multiple hazardous air pollutants emitted from an emission source category. This assessment is used, for example, in determining whether a source category should be regulated.

Under the Atomic Energy Act, EPA has typically applied the 10^{-4} lifetime risk limit to all contaminants collectively (except radon) by limiting the risk from exposure to ionizing radiation. Instead of deriving a concentration limit for each contaminant based on the 10^{-4} lifetime risk level, EPA constrains the dose from all radionuclides to a dose level that approximates the 10^{-4} lifetime risk (e.g., 3 to 15 mrem/yr). Radon is given special treatment because of its ubiquitous nature in the environment and its high relative radiotoxicity (small exposure yields a high dose). A similar approach is applied under CERCLA in conducting a health risk assessment for exposure to radionuclides or radiation.

The AEA and CERCLA approach is different from the approach employed in the SDWA program, in which the risks from some radionuclides may be added to the risks of other radionuclides. Under the primary drinking water standards in 40 CFR Part 141, the risks from three separate radionuclides or radionuclide groups are independently limited as described in the table on the following page. The following table is based on EPA's currently applicable maximum contaminant levels (MCLs), but uses NRC's more recent dose methodology (i.e., dose and risk are calculated using an effective dose equivalent approach consistent with 10 CFR Part 20).

Radionuclide Group	Dose (Effective Dose Equivalent [EDE]) (mrem/yr)	Risk (Lifetime risk of fatal cancer)
^{226}Radium + ^{228}Radium	4.8 to 5.2	1.8×10^{-4}
Gross Alpha (less Uranium and Radon)	0.05 to 25.8	1.8×10^{-6} to 9.0×10^{-4}
Artificial Beta and Photon Emitters(2)	0.01 to 35	3.5×10^{-7} to 1.1×10^{-3}

EPA's drinking water standards are applied independently. Consequently, it is possible (although unlikely) that an individual could receive a risk in excess of about 10^{-4} if drinking water that contained all three radionuclide groups were ingested on a continuing basis. In addition, two other radionuclides are specifically excluded from the existing standards (uranium and radon). Consequently, any dose and risk from the latter two radionuclides would be added to the dose and risk from ingesting drinking water at the limits. Although EPA proposed new standards, in 1991, to rectify these concerns, the proposal drew sharp criticism from Congress and water suppliers. EPA is currently considering whether there is sufficient need to promulgate drinking water standards for uranium and radon.

3. SUMMARY

EPA generally applies its 10^{-4} lifetime risk limit to individual contaminants in SDWA and CAA non-radiological environmental programs, but may sum the risks for comparison with the limit in situations where exposure to multiple contaminants could significantly increase human risk. For CERCLA, the sum of the risks from all contaminants is compared to the risk limit. For radionuclides, this additive approach is intrinsic with the use of limits on the EDE, in which doses from all radionuclides and all routes of exposure are summed to develop a total dose or risk. The drinking water program represents something of a hybrid between the conventional approaches employed under the CAA and CERCLA.

ATTACHMENT 2

ISCORS RISK HARMONIZATION RECOMMENDATIONS

PREFACE

According to the ISCORS charter, ISCORS has not been delegated any authorities established by law, regulation, Executive Order, or other administrative mechanism to act in lieu of formal agency action. Thus, agency implementation of the recommendations must be consistent with the authority, responsibility, and procedures of each respective agency. It is expected that agency legal and policy obligations and concerns would be directly factored into the discussion of any proposed ISCORS recommendations before they are adopted. Therefore, ISCORS does not expect there to be a conflict for any federal agency between the risk harmonization recommendations and any agency's authority, responsibility, and procedures. However, if such a conflict were to arise, the agency's legal obligations, not the ISCORS recommendations, would govern the outcome.

As part of the ISCORS process, the Agencies have agreed to develop Federal guidance on a number of risk assessment and risk management issues. The Agencies recognize that this guidance will be revised if continuing scientific developments and review, such as BEIR VII, indicate that changes are needed.

ATTACHMENT 3

CHEMICAL AND RADIATION RISKS

1. INTRODUCTION

In the Staff Requirements Memorandum responding to SECY-95-249, dated November 29, 1995, the Commission stated:

> The staff should pursue with EPA the question of whether there is a background of chemical carcinogens that is analogous to background radiation. The staff should also explore with EPA the risk management implications of similarities and differences between any such chemical background and background radiation.

The staff has pursued these questions with the U.S. Environmental Protection Agency (EPA) and has reviewed some recent literature on this subject. The responses are presented below. After a brief summary, this attachment: (1)

describes how background radiation and background chemical carcinogens are similar, first in terms of exposure, and then in terms of the relationship between dose and response; (2) describes how background radiation and background chemical carcinogens are different, first in terms of exposure, and then in terms of the relationship between dose and response; (3) provides some illustrative numerical risk comparisons, with important caveats; and (4) discusses the implications for risk management from a variety of perspectives.

2. SUMMARY

There is a background of chemical carcinogens that is analogous to background radiation. However, it is difficult to draw conclusions about the relative magnitudes of chemical background risk vs. radiation background risk because chemical risk assessments are so much more uncertain than radiation risk assessments. Based on the work of Bruce Ames and Lois Swirsky Gold (of the Division of Biochemistry and Molecular Biology, University of California at Berkeley), it appears that: (1) 99.99 percent of the chemicals to which people are exposed are naturally occurring; (2) as is the case for synthetic chemicals, about half the natural chemicals that have been tested have been classified as possible or probable human carcinogens because they cause cancer in laboratory rodents at very high doses; and (3) assuming the positivity rate for untested natural chemicals is the same as that for untested synthetic chemicals, natural rodent carcinogens in the human diet are much more important contributors to cancer risk than pesticide residues and water pollutants.(3)

As for radiation exposure and relative risk, total natural background radiation (average U.S. individual dose of 300 mrem/year) is about one order of magnitude greater than total man-made radiation (average individual dose of 60 mrem/year, mostly from medical uses); about two orders of magnitude greater than radiation from consumer products (average individual dose of 10 mrem); and about four orders of magnitude greater than radiation from industrial sources (about 0.1 mrem/year).(4) Background exposure to chemical carcinogens in the diet is potentially much more important--in terms of risk, to overall chemical exposure than background radiation exposure is to overall radiation exposure, but the uncertainties in risk assessment preclude a definitive quantitative comparison.

The implications of this information for risk management are unclear. Certainly if background levels are important for radiation, they are also important for chemicals. EPA has not considered total natural background levels for chemicals or radiation in establishing its acceptable risk range (i.e., it is only the incremental risk from the regulated activity that is relevant). However, EPA has taken natural background levels of certain pollutants in particular media into account when regulating those pollutants in those media (e.g., lead, dioxin, manganese, and mercury), but there are no general implications for risk management that can be drawn from those cases.

3. HOW BACKGROUND RADIATION AND BACKGROUND CHEMICAL CARCINOGENS ARE SIMILAR

3.1 Exposure

We are constantly bathed in a sea of naturally occurring radiation. This includes radon and radon daughters in indoor air, cosmic rays, cosmogenic radiation, terrestrial radiation, and internal radiation. Similarly, through the food we eat, we are constantly exposed to naturally occurring chemical carcinogens. Lettuce, celery, and beets contain caffeic acid; peanuts, corn, and milk can contain mold toxins (including aflatoxin and sterigmatocystin); and eggs contain benzene. The dose we receive from natural background radiation is generally an order of magnitude higher than the dose we receive from man-made sources of radiation. Similarly, natural chemicals make up the vast majority of the chemicals to which humans are exposed. Although most chemicals have never been tested, 50 percent of all chemicals that have been tested cause cancer in laboratory rodents. The positivity rate for tested synthetic chemicals is the same as for tested natural chemicals. If one assumes that the positivity rate for untested synthetic chemicals is the same as that for untested naturally occurring chemicals, natural chemical carcinogens make up the majority of the chemical carcinogens to which humans are exposed.(5)

3.2 Dose-Response Relationship

For low doses and dose rates of both chemical carcinogens and radiation, risk assessors generally assume that the dose-response relationship is linear, and that there is no threshold below which effects disappear. For both chemical carcinogens and radiation, there is uncertainty about this assumption. Analyses of both of these categories of carcinogens are almost always based on linear extrapolations (that may or may not be valid) from effects at high doses.

4. HOW BACKGROUND RADIATION AND BACKGROUND CHEMICAL CARCINOGENS ARE DIFFERENT

Carcinogenic risk assessments for chemicals generally involve greater uncertainty than do carcinogenic risk assessments for radiation.(6) The uncertainties are greater in estimating both exposure and the dose-response relationship.

4.1 Exposure

Radiation. The National Council on Radiation Protection and Measurement (NCRP) states, based on studies conducted over the last four decades, that the average dose to an individual from natural sources of radiation is about 300 mrem/year.(7) However, there is considerable variability in background exposure to radiation. Background radiation levels generally vary from 100 to 1000 mrem/year in the United States, with most levels between 200 and 400 mrem/yr. There are some isolated areas where background exposures are as much as two orders of magnitude higher than the national average. These highest exposures are dominated by large exposures to radon gas and its decay products, in indoor air.

Chemical Carcinogens. It is currently infeasible to derive a similar quantitative exposure estimate for natural chemical carcinogens. First of all, we simply don't know how many of the 6 million natural chemicals (60,000 in commerce) are actually carcinogens.(8) The few chemicals that have been observed to cause cancer in humans, and the hundreds of chemicals which cause cancer in laboratory animals at high doses, include compounds of such widely diverse structures that it is impossible to make general conclusions about the carcinogenicity of the untested chemicals.(9)

Thus we cannot measure exposure because we don't know what to measure exposure to. Naturally occurring chemicals have not been the focus of testing. Ames and Gold have pointed out that for both the many synthetic and the few natural chemicals that have been tested, about 50 percent caused cancer in laboratory rodents.(10) Because 99.99 percent of the chemicals we ingest are naturally occurring, if one assumes (1) that the positivity rate for all untested chemicals is significant (i.e., greater than one percent) and (2) that the positivity rate for untested natural chemicals is the same as the positivity rate for untested synthetic chemicals, exposure to natural chemical carcinogens overwhelms exposure to synthetic chemical carcinogens.(11) Although this may be a

reasonable extrapolation, it is not really comparable to the exposure data we have for radiation.

But even for known rodent carcinogens, exposure assessment is difficult. Whereas radioactive materials decay with well-defined half-lives, the fates of chemicals are much more diverse. Measurement of dietary intake of chemicals is expensive and rarely done. Whereas human beings are exposed to a relatively uniform level of radiation, exposure to chemicals occurs largely through diet, which varies greatly from person to person and from society to society. Estimates of the daily intake of known chemical carcinogens vary over an enormous range, and can be in error by several orders of magnitude.(12)

Further, it is more difficult to measure the concentrations of rodent chemical carcinogens in diet, air, and water than the radionuclides. The minimum detectable concentrations of many of the chemical measurement methods are often close to or above commonly occurring exposure levels (i.e., 1 part per billion).

4.2 Dose-Response Relationship

Radiation. Risk assessors estimate, based on extrapolation from cancer incidence in atomic bomb survivors, that the risk of cancer death because of natural background radiation is approximately 1×10^{-2} over a person's lifetime. (0.3 rem/year x 70 years x 5×10^{-4} cancer death per person-rem.)(13)

There is controversy as to whether the high doses received by the Hiroshima and Nagasaki survivors can be reasonably extrapolated down to levels commonly experienced as background. In addition, there are some who believe that background radiation is actually beneficial (i.e., hormesis). Although there is some evidence from mechanistic studies that radiation at low doses has beneficial effects, there is not enough information on the actual effects of low doses of radiation to determine whether the beneficial effects are larger or smaller than the detrimental effects. The above-cited quantitative estimate of the risk from background radiation is generally accepted as a conservative estimate by most experts, although its reasonableness is being questioned by the Health Physics Society and the French National Academy.

Chemical carcinogens. It is currently infeasible to come up with a similarly definitive quantitative risk estimate for exposure to natural background chemical carcinogens. For most chemicals, there are no dose-response data in humans. Thus, for the most part, the dose-response relationship is estimated by extrapolating effects occurring at extremely high doses in rodents to low doses to humans. About half the chemicals that have been tested on rodents in laboratories have produced tumors. This could mean (1) that half of all chemicals are carcinogenic; (2) that we have done an excellent job of selecting the most hazardous chemicals for testing; or (3) that there is something very wrong with the laboratory tests. Typical rodent studies of chemical carcinogenicity cost on the order of $2 million per study. To keep testing costs reasonable, the number of animals needs to be minimized. Thus the laboratory tests use tumor-sensitive animals and nearly toxic doses. Lois Gold and Bruce Ames have argued that testing at the maximum tolerated dose frequently can cause chronic cell killing and consequent cell replacement, both of which are risk factors for cancer, and neither of which would occur at low doses.(14)

About 30 percent of the chemicals that have been tested in both rats and mice are carcinogenic in one, but not the other. Since these are species that are more similar to one another than to humans, it would be reasonable to assume that not all chemicals that are carcinogenic in rodents are carcinogenic in humans. Yet EPA assumes that if a chemical produces tumors in either rats or mice at high dose, then it is a possible human carcinogen at low dose, and a candidate for regulation.(15)

For radiation, the dose-response relationship is an extrapolation based on nearly one million data points. The linear multistage model (the most commonly used mathematical technique for extrapolating effects at high doses to risks at low doses) for chemical carcinogens uses only a very small number of rodent data points (often only two) to obtain a 95 percent confidence upper bound estimate.(16)

Establishing the dose-response relationship for chemical carcinogens is much more difficult than for radiation. Chemical exposure is much more variable with chemicals than with radiation because of (1) different dietary intakes; (2) large differences among individuals in their ability to metabolize chemicals; and (3) the fact that repeated high doses cause physiological disturbances. Variations in radiation effects among different exposed tissues are not as great as the variations in chemical effects among different tissues, and are better understood. There are almost no data available concerning the pharmokinetics of chemical carcinogens in humans.(17) Whereas the radiation-induced ionization process is fairly well understood, for chemicals, numerous parameters interact--the type of chemical, whether the metabolites or the parent compound is the ultimate carcinogen, the dose, route of administration, duration of exposure, genetic differences in metabolism, route and rate of excretion, and the number of possible intermediate metabolic pathways.(18) The potential for synergistic effects, and absence of information on the mechanism of carcinogenesis, further complicate chemical risk assessment.

Finally, risk assessment for chemical carcinogens is complicated by the fact that many chemical carcinogens are also nutrients themselves, or are found in foods that also contain other chemicals that are nutrients, including nutrients (mostly anti-oxidants) that are believed to reduce the risk of cancer. However, route of exposure and chemical form are very important factors. For example, although inhaled chromium VI is considered carcinogenic, a small amount of ingested chromium III is considered an essential nutrient. No analogous beneficial relationship has been broadly accepted for ionizing radiation.

5. SOME ILLUSTRATIVE NUMERICAL RISK COMPARISONS (WITH IMPORTANT CAVEATS)

In a 1992 Science article, Lois Swirsky Gold, et al. used the HERP (human exposure/rodent potency) index to rank the possible hazards from human exposure to 80 rodent carcinogens, some of which are naturally occurring.(19) The HERP index is the ratio of the amount of a substance (in milligrams of the substance/kilogram body weight/day) that humans typically ingest to the amount of the substance (in mg/kg/day) that causes cancer in rodents, expressed as a percentage. HERP can be roughly converted into cancer risk estimates by multiplying by 0.1 for mouse studies and 0.0333 for rat studies. (This factor is derived from the linearized multistage model.) The HERP index and the conversion factors produce a risk factor that approximates the methods used by EPA and others for purposes of regulating synthetic chemicals.

Gold, et al. do not believe that it is possible to estimate low-dose risk from bioassay results without additional data on the carcinogenic mechanism. The authors did their analysis to demonstrate that if the methods now used in quantitative risk assessment for synthetic chemicals were applied to naturally occurring chemicals, the calculated risk from naturally occurring chemicals would overwhelm the risk from synthetic chemicals. Gold, et al. believe that the methods currently used to establish chemical carcinogenicity and dose-response relationships in humans are highly speculative. Their point is that, if these speculative methods are applied to naturally occurring chemicals, they would yield very high quantitative risk estimates that cast doubt on the plausibility of calculated hazards from synthetic chemical residues.

Thus the numbers that follow should be used only as points of comparison with EPA's quantitative risk estimates for chemicals. They are really not comparable, for example, with radiation risk estimates, because radiation risk estimates are derived from real human exposure data and human epidemiological studies, not upper bound estimates derived from animal data.

Gold, et al. hazard rankings indicate that if you eat one apple a day, the calculated lifetime cancer risk from the caffeic acid in the apple would be equivalent to 3×10^{-3}. One-eighth of a head of lettuce per day would yield a lifetime risk of 1×10^{-2} (also from caffeic acid); the risk from one mushroom per day would be equivalent to 1×10^{-2} (from hydrazines). A cup of coffee per day would imply a lifetime risk of 1×10^{-3} of cancer from caffeic acid. (Coffee contains 1000 natural chemicals, and only 26 have been tested. Of those that have been tested, 19 have produced cancer in laboratory animals. Of the chemicals that have been tested, caffeic acid yields the highest risk estimate.) The lifetime cancer risk from adding together the nitrosamines in 100 grams of bacon per day would be 4×10^{-4}. The lifetime cancer risk from drinking one 12 oz beer a day, based on rat bioassay data, would be 2.8×10^{-1}.

It is not clear whether it is appropriate to add the risks calculated for individual rodent carcinogens together--perhaps the substances neutralize each other, or perhaps they have synergistic effects. However, if one were to simply add these individual risks together, depending on one's diet, it is fairly easy to calculate hypothetical background chemical risk levels on the order of 10^{-1}, just based on what we know about human exposure to naturally occurring chemicals that cause cancer in rodents. And we only have information on a tiny fraction of natural chemicals.

One should probably not pay much attention to these absolute numbers because, despite the fact that fruit and vegetables are full of rodent carcinogens, it is fairly clear from epidemiological studies that fruit and vegetable consumption actually reduces the risk of cancer. However, these hypothetical risk estimates are very important in a relative sense. It is interesting to compare the 10^{-1} background risk to the 10^{-4} to 10^{-6} residual risk range that is the goal of EPA regulation. As Bruce Ames has pointed out, only 0.01 percent of the pesticides we take in every day are man-made (i.e., background chemical exposure levels are several orders of magnitude higher than synthetic chemical levels). If the fraction of natural chemicals that are carcinogenic is the same as the fraction of synthetic chemicals that are carcinogenic, then the calculated chemical background risk is actually much larger relative to calculated man-made chemical risk than radiation background risk is relative to man-made radiation. (Man-made radiation is on the order of 60 mrem per year, or 20 percent of background levels, if medical uses are included; or 10 mrem/year or 3 percent of background levels, if they are excluded.)

6. IMPLICATIONS FOR RISK MANAGEMENT

6.1 NCRP's View

According to NCRP:

> Although natural background radiation and its fluctuations--or the content of naturally occurring mutagens in foods--can be used as points of reference, they do not justify exposures from man-made sources.[20]

NCRP does not say how these points of reference are to be used in selecting standards for man-made sources that are justified.

6.2 EPA Science Advisory Board's View

On May 18, 1992, EPA's Science Advisory Board said,[21]

> To many radiation scientists, reducing excess exposures much below 100 mrem/yr seems unnecessary and in any case exceedingly difficult to monitor for compliance because it is within the natural variability of background...the prototype chemical carcinogens were synthetic substances with no or limited natural sources. In calculating excess risk from human sources of a chemical, background levels, if any, are therefore frequently seen as irrelevant, even though in actuality background levels from either natural sources or anthropogenic sources other than the one being considered often exist....
>
> ...The harmonization between chemical and radiation risks of different types could occur by clearly and explicitly taking into account the differences in risk-reduction criteria or strategies between hazards that have natural sources (rather than, or in addition to anthropogenic sources) and those that have only anthropogenic sources. For example, risk criteria for substances with no natural sources (including radionuclides such as plutonium or americium) could be different from those used for substances that have natural sources (including carcinogenic inorganic substances and organic materials with significant natural sources).

Although this suggested approach would address the variability issue for specific radionuclides and other chemicals to some extent, it does not address the general risk management implications of total background levels of radiation in the atmosphere and chemicals in the diet.

6.3 EPA Staff's View

EPA staff's view is that it is the incremental risk from a particular regulated activity that is important; not the relationship of that risk to overall background risk. Thus in EPA staff's view, there are no general implications of high levels of background chemical carcinogens for the risk management of man-made chemical carcinogens. However, in specific cases, EPA has taken background levels into account in its regulations.

Under the Safe Drinking Water Act, the maximum contaminant levels (MCLs) are set based on considerations of public health protection and the feasibility of water treatment. Natural background is simply not a consideration, because the regulatory program seeks to ensure that Americans have safe public drinking water (rather than to control sources of contamination that might increase the risk). In fact, in the case of the MCL for naturally occurring inorganic substances, natural background levels in public drinking water systems are sometimes higher than the MCLs. The regulations require that the contamination in public drinking water systems, whether from natural or man-made sources, be treated to meet the MCLs. Some small systems with relatively high natural background levels have had difficulty complying with this rule. However, the only natural background levels of interest are the levels in the water; natural background levels in other media (e.g., air) are not taken into account.

Under the Superfund law, background contaminant levels in soil or drinking water are taken into account in accordance with EPA guidance. EPA distinguishes natural background levels from man-made contamination, and only lists sites with man-made contamination on the National Priorities List. In selecting a cleanup level, EPA takes background levels into account. EPA would not list a site with high natural background levels unless there were significant man-

made contamination.

6.4 NRC Staff's View

NRC sometimes takes into account natural background levels of radioactivity in establishing its standards. NRC has sometimes stated that natural background levels are relevant to the determination of what is acceptable risk. NRC relied heavily on ICRP in selecting the public dose limit in 10 CFR Part 20. ICRP considers the public dose limit of 100 mrem/year to be acceptable, in part, because,(22)

> The second approach (to choosing a dose limit for public exposure) is to base the judgement on the variations in the existing level of dose from natural sources. This natural background may not be harmless, but it makes only a small contribution to the health detriment which society experiences. It may not be welcome, but the variations from place to place (excluding the large variations in the dose from radon in dwellings) can hardly be called unacceptable... Excluding the very variable exposures to radon, the annual effective dose from natural sources is about 1 mSv (100 mrem), with values at high altitudes above sea level and in some geological areas of at least twice this.

However, this was not the sole criterion used to select 100 mrem/year limit, and NRC has sometimes sided with NCRP regarding the relevance of natural background radiation. For example, in the VEPCO case, 11NRC405, the Commission stated that, for a specific worker population, a comparison of the number of cancer deaths from occupational radiation exposure to the number of cancer deaths from other causes (such as background radiation exposure), cannot alone be used as a measure of the significance of the occupational radiation risk itself.

NRC generally sets its limits on particular sources of radiation in terms of the man-made or technologically enhanced increment above natural background levels, and its regulations do not require reductions in natural background.

6.5 Other Views

Gold and Ames have pointed out that despite the presence of relatively large quantities of chemicals that cause cancer in rodents, high consumption of fruits and vegetables actually reduces the risk of cancer in humans. Gold and Ames believe that EPA's and other Federal agencies' focus on very small risks from synthetic chemicals in the environment is a distraction from what decades of mechanistic and epidemiological cancer research demonstrate are the major preventable causes of cancer--i.e., smoking, diet, lack of exercise, hormone levels, chronic infections, and occupational exposure to extremely high levels of synthetic chemicals. They conclude that:

> ...widespread exposures to naturally occurring rodent carcinogens may cast doubt on the relevance to human cancer of far lower exposures to synthetic rodent carcinogens...the concern with minuscule [pesticide] residues makes fruits and vegetables more expensive and thus serves to decrease consumption of foods that help to prevent cancer.(23)

Similarly, a number of health physicists have argued that exposure to man-made low-level ionizing radiation is not important relative to background levels. Certainly, if background radiation levels are relevant to the regulation of man-made sources of radiation, background chemical carcinogen levels are relevant to the regulation of chemicals. EPA staff has taken the position that neither is relevant; NRC has considered background radiation in establishing its radiation protection limits.

7. CONCLUSIONS:

a. There is a significant natural background cancer risk from chemicals. The background chemical risk is probably larger relative to man-made chemical risk, than natural background radiation risk is relative to man-made radiation risk. However, there is greater uncertainty with the chemical risk estimates than the radiation risk estimates.

b. The implications for risk management are unclear. Some have argued that EPA should treat radiation more leniently than chemicals because EPA's chemical risk goals are so low relative to natural background radiation. It turns out that EPA's chemical risk goals are also low relative to calculated natural chemical background risk.

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1. Incidence is the sum of fatal and non-fatal cancers.

2. EPA would define the dose from its MCL as 4 mrem/year, based on EPA's calculational methodology that is codified in EPA's existing drinking water standards. At the time the standards were promulgated, EPA employed NBS Handbook 69, which limits the dose either to the whole body or any critical organ. The range in this table reflects these doses, when converted to EDE, using contemporary dosimetry. EPA would calculate the risk from a 4 mrem/year EDE to be 1.4×10^{-4}.

3. Gold and Ames also concluded that, when ranked in terms of potency, for the chemicals that have been tested, natural rodent carcinogens in the human diet rank higher than pesticide residues and water pollutants. A recent Natural Research Council study, *Carcinogens and Anticarcinogens in the Human Diet* (National Academy Press, Washington, D.C.), did not agree with Gold and Ames' conclusions with regard to potency, but did agree with their conclusions regarding comparative exposure and positivity rates for carcinogenicity, and their implications for relative risk.

4. National Council on Radiation Protection and Measurement, "Ionizing Radiation Exposure of the Population of the United States," Report No. 93, Bethesda, MD, 1987. The dose from medical uses of radiation is probably not relevant for purposes of this paper, because medical uses of chemicals (i.e., drugs) are not considered.

5. L.S. Gold, et al.; "Rodent Carcinogens; Setting Priorities," *Science*, V. 258., October 9, 1992 p. 261.

6. National Council on Radiation Protection and Measurements, *Comparative Carcinogenicity of Ionizing Radiation and Chemicals*, NCRP Report No. 96, March 1, 1989, p. 128.

7. Ibid; p. 34.

8. Ibid; p. 24-25.

9. Ibid; p. 24.

10. L.S. Gold, et al.; op. cit.

11. Ibid.

12. NCRP Report No. 96, p. 33.

13. Committee on the Biological Effects of Ionizing Radiations, *Health Effects of Exposure to Low Levels of Ionizing Radiation, BEIR V*, National Academy Press, 1990, Washington, D.C.

14. L.S. Gold, et al., op. cit.

15. Executive Office of the President of the United States, *Regulatory Program of the United States Government*, April 1, 1990 to March 31, 1991, p. 18.

16. Ibid; p. 19.

17. NCRP Report No. 96, op. cit.; p. 36.

18. National Council on Radiation Protection and Measurements, op. cit.; p. 46.

19. L.S. Gold, et al.; op. cit.

20. National Council on Radiation Protection, op. cit., p. 125.

21. Letter from Raymond Loehr and Oddvar Nygaard, EPA Science Advisory Board to William Reilly, Administrator, EPA, May 18, 1992, regarding commentary on harmonizing chemical and radiation risk-reduction strategies.

22. International Commission on Radiological Protection, *ICRP Publication 60*, Annals of the ICRP, 1990 Recommendations, Pergamon Press, 1990; p. 45.

23. Lois Swirsky Gold, et al., op. cit.