Implementing New Approaches to Assess Health Risks: Age-Dependent Factors - 9351

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ABSTRACT

A standard process is applied to assess health risks at contaminated sites to help guide cleanup decisions. Recent scientific advances have improved our understanding of biokinetic and dynamic process that can lead to adverse health effects following human exposures to environmental contaminants. These advances include information that allows better estimates of risks to children from exposures to carcinogens. Agency guidance for conducting health risk assessments typically lags years behind new scientific information. This delay reflects the time it takes for extensive Agency reviews of the new information and the preparation and review of the updated guidance documents themselves. Meanwhile, risk assessments must continue to be prepared in accordance with extant guidance. Therefore, approaches are needed to bridge the procedural-scientific gap so current knowledge can be reflected in the risk assessments and the cleanup decisions they are intended to inform. Such an approach has been developed for a radioactively contaminated site, with the newer scientific information presented as context within the uncertainty characterization discussion of the risk assessment.

INTRODUCTION

Potential health risks are assessed for contaminated sites as part of the integrated evaluation conducted to guide cleanup decisions. The standard approach established by the U.S. Environmental Protection Agency (EPA) involves calculating incremental cancer risk by estimating exposures under reasonable scenarios and then applying contaminant- and route-specific risk estimators [1]. (The potential for noncancer effects is also assessed as part of the standard process for contaminated sites; this paper focuses on the cancer risk.)

Peer-reviewed reference toxicity values established by EPA are used to assess the increased probability above a background rate that an individual will develop cancer over a lifetime as a result of chronic exposures. Also referred to as excess lifetime risk, this estimate is based on population statistics. The risk estimator can be a slope factor that indicates risk per dose (e.g., for oral exposure) or a unit risk estimator, which is simply risk per unit measure. The latter is illustrated by a radiological risk coefficient given in units of risk per picocurie (pCi), or for chemicals: an inhalation unit risk as risk per microgram/cubic meter ($\mu g/m^3$) or drinking water unit risk as risk per milligram/liter (mg/L). Note the specific activity of an isotope (generally given as Ci/g) can be used to convert from activity to mass (e.g., pCi to pg). Cancer is considered a stochastic endpoint and is assumed to have no threshold dose, i.e., the probability of occurrence not the severity of effect increases with the absorbed dose, and it is assumed that there is no dose level below which the risk is zero.

Recent advances in our understanding of biokinetics and the biophysical and biochemical processes that can lead to adverse effects following exposure to radioactive and nonradioactive chemicals have led to updates in the methods used to assess health risks. Overviews of the basic concepts and new information being developed to support radiological and chemical risk assessments are presented in the following section.

APPROACH

Radiological Risk Assessment

Radionuclides associated with contaminated sites can generally be characterized as low-level ionizing radiation, and the hypothetical individuals evaluated in risk assessments reflect chronic (lifetime) exposures. Ionizing radiation is a known human carcinogen, and the relationship between radiation dose and health effects is relatively well characterized for high doses of most types of radiation. Ionizing radiation causes biological damage only when the energy released during radioactive decay is absorbed in tissue. This absorbed dose is typically expressed in units of rad (radiation absorbed dose), and represents the amount of energy deposited per unit of tissue. Chronic doses of low-level radiation have not directly been shown to cause cancer, although this has been assumed, to be protective. Evidence linking radiation exposure to observable biological effects has only been found at doses above 25 rads delivered over a short time, so in translating to chronic doses far below that level, it is difficult to establish a dose-response relationship. Although information indicates a threshold exists below which adverse effects are not distinguishable, to be conservative it is commonly assumed that the dose-response relationship is linear.

Ionizing radiation causes injury by breaking molecules into electrically charged fragments (ion pairs), producing chemical rearrangements that can lead to permanent cellular damage. The degree of biological damage caused by different types of radiation varies according to how spatially close the ionizations are. For example, alpha particles produce high-density regions of ionization, while gamma rays and beta particles produce a lower-density pattern. Equal absorbed doses (in rads) of radiation from alpha particles result in much greater harm than that from gamma rays and beta particles due to the higher density of ionizations. The dose equivalent approach was developed to normalize the unequal biological effects produced by different types of radiation. The dose equivalent is the product of the absorbed dose and a quality factor that accounts for the relative biological effectiveness of the radiation. The dose equivalent is typically expressed in the units of rem (Roentgen equivalent man) or millirem (mrem, one-thousandth of a rem). The biological damage caused by ionizing radiation can result in cancer induction. On average, the EPA estimates that about half of all cancers that can be induced by radiation are fatal. The fraction of cancers that are fatal ranges from about 10% for thyroid cancer up to essentially 100% for liver cancer.

Biokinetics plays an important role for both radionuclides and chemicals. Upon intake, radionuclides constantly emit radiation at a rate proportional to their specific activity as they pass through the body irradiating various organs. Some quickly deposit in one or two organs; others deposit more slowly throughout the entire body. Various models and computer codes have been developed by the International Commission on Radiological Protection (ICRP), EPA, and others to calculate internal radiation doses and risks from estimated intakes, such as those reflected in Federal Guidance Report 13 [2]. Similarly, physiologically based pharmacokinetic models are being developed for an increasing number of chemicals, to estimate internal doses and address absorption, distribution, metabolism, and elimination.

Although a linear dose-response relationship has traditionally been assumed for both radionuclides and chemicals, this situation is changing as recent dosimetry and mechanistic modeling and guidance updates aim to keep pace with updated scientific understanding. Most radiation toxicity studies describe effects in terms of the absorbed doses (in rads) or dose rates delivered. Note that the relationship between the absorbed dose and cancer risk calculated using standard EPA methodology is not linear but depends on the type of radiation (alpha, beta, or gamma), the exposure route (external gamma irradiation, ingestion, inhalation, or dermal), and the organs being irradiated by the given radionuclide. Other agencies, including the U.S. Department of Energy (DOE), also estimate the dose equivalent as part of evaluating

health protection for specific programs. These doses (mrem or mrem/yr) are estimated using standard dose conversion factors (DCFs) developed by the EPA. To provide a fuller set of information for a given site risk assessment, both dose equivalents (in mrem) and cancer risk estimates are often developed to support a dual evaluation of radiological health endpoints.

The standard DCFs used to calculate the radiation dose equivalents are given in two Federal Guidance Reports (FGRs) issued by the EPA. The DCFs for inhalation and ingestion are given in FGR 11 [3], and the DCFs for external gamma irradiation are given in FGR 12 [4]. No values have been developed for dermal exposures because it is generally not a significant exposure pathway for radionuclides. The DCFs are based on the metabolic and anatomical model of an adult male, representing the ICRP reference man, weighing 70 kg (which is roughly 150 pounds). The DCFs have been used in many radiological risk assessments; the limitation that these values do not reflect conversion factors for other (younger) receptors is generally acknowledged and addressed qualitatively as part of the uncertainty discussion within these assessments.

The ICRP recently published age-dependent DCFs, which consider that children are more susceptible to cancer risk from radiation exposure than adults [5]. These coefficients address five age groups ranging from 3 months to 15 years old. These DCFs have not yet received general approval by many federal agencies, including the EPA, and the values in FGR 11 and 12 still represent current EPA guidance.

Chemical Risk Assessment

As described for radionuclides, age-specific information is also being incorporated into the risk assessment approach for chemicals. Following years of extensive analyses, EPA updated its cancer guidelines in 2005 to move away from the classical cancer designations used by the International Agency for Research on Cancer and others, in favor of a more descriptive narrative of the evidence of carcinogenicity [6-7]. Part of this description includes a consideration of whether the mode of action (MOA) for carcinogenicity is mutagenic or whether a threshold exists, e.g., the cancer results from cytotoxicity. For the latter case, the linear-no-threshold dose-response relationship is not used to characterize cancer risk – rather a reference dose/concentration process can be applied. For certain carcinogens, cancer may result from direct damage to the genetic material, deoxyribonucleic acid (DNA), while for others cancer may result from indirect damage (e.g., interference with DNA repair mechanisms). When a chemical is considered to cause cancer via a mutagenic MOA, i.e., by directly affecting genetic material, additional consideration must be given to those who are more susceptible to that damage – notably children.

To address differential susceptibility, EPA expanded its basic cancer guidelines with supplemental guidance for children [6-7]. Reflecting the same increased susceptibility to harm from early-life exposures addressed by the ICRP DCFs, EPA identified age-dependent adjustment factors (ADAFs), which are also captured in related 2008 Navy guidance for human health risk assessments. In only limited cases are chemical-specific data available for deriving a cancer potency factor that distinguishes between children and adults (e.g., vinyl chloride). When a chemical is determined to cause cancer via a mutagenic MOA but data are unavailable to derive a specific value for children, default ADAFs are applied to the standard risk estimator for chronic exposures available via EPA's Integrated Risk Information System (IRIS) [8]. For children 0 to 2 years old, the default factor is 10; for those 2 to16 years old, the default factor is 3. Carcinogenic polycyclic aromatic hydrocarbons (PAHs) such as benz(a)anthracene, benzo(a)pyrene, and chrysene are among roughly a dozen chemicals considered to be carcinogenic via a mutagenic MOA, for which the default adjustments are applied in assessing children's risks.

RESULTS: EXAMPLE RADIOLOGICAL RISK APPLICATION

An approach for incorporating updated scientific information in a radiological risk assessment was recently developed for the Harshaw Site. This contaminated site is being addressed by the U.S. Army Corps of Engineers under the Fomerly Utilized Sites Remedial Action Program (FUSRAP). In the risk assessment conducted to support ongoing environmental management evaluations, radiation doses and radiological cancer risks were calculated using the current standard EPA FGR values. The effect of using the age-dependent values was then described in the uncertainty characterization discussion. In that section, differences in the DCFs for the five age groups were compared to those given in ICRP 72. Under this approach, a separate set of age-dependent doses was not calculated, which avoided confusing various parties interested in the risk evaluations regarding which estimates would serve as the basis for site decisions.

For this risk assessment, the age-dependent DCFs from ICRP 72 to those for reference man from FGR 11 were compared for inhalation and ingestion of uranium, the main radioactive contaminant at the site. The uranium inhalation DCFs from FGR 11 were slightly higher than the ICRP age-dependent factors, even for the youngest age group (infant). This finding reflects improvements in the respiratory tract model that was used to develop the ICRP values, compared to the conservative model underlying FGR 11 values. These improvements allow more realistic estimates of the radiation dose from inhaled radionuclides, because some of the conservatism associated with the original model was removed. (Note the National Institute for Occupational Safety and Health has also applied the updated lung model for current evaluations.)

Similarly, for the ingestion calculations, the DCFs for children 10 to 15 years old are lower than those for the reference man, due to improved methodology for calculating ingestion doses. However, the ICRP age-dependent ingestion DCFs for infants and 1- to 5-year-old children are higher than those from the (earlier) FGR 11, by factors of 4.8, 1.8, and 1.2, respectively. Thus, using the current default values in FGR 11 for short-term exposures to children up to a few years old could underestimate the doses incurred by these individuals (e.g., in a risk assessment conducted for the cleanup period of a given site). However, as age increases beyond the first year, the ICRP DCFs quickly approach those identified in FGR 11 and are smaller than those EPA values for children age 10 and older. This means that for the chronic exposure scenarios routinely assessed at contaminated sites, the FGR 11 values will result in conservative risk estimates overall. Therefore, in developing land use assumptions it is important to consider who could be exposed to site contaminants over what time frame, with residential scenarios often extending from infancy through adulthood. Note that although the updated DCFs are higher for children than adults in terms of dose per pCi, the intakes of children are generally lower, which tends to offset the difference.

CONCLUSIONS

Scientific studies continue to improve our understanding of biokinetics and mechanisms of toxicity for contaminants being assessed as part of ongoing analyses for cleanup programs. The process for Agencies to incorporate these new data into their assessment guidance involves extensive procedural reviews, so formal methodology updates typically lag years behind the peer-reviewed scientific data themselves. During this time, risk assessments must still be prepared, and it is important that they reflect current scientific information in order to be most useful for the practical cleanup decisions these assessments are intended to inform.

An approach was developed for a radioactively contaminated site to meet both conditions: adhere to extant guidance and reflect current scientific understanding. The risk assessment for this illustrative site reflects extant DCFs from the EPA FGR for the basic risk calculations, while presenting quantitative

context regarding current scientific knowledge within the uncertainty discussion. This further context allows interested parties to appreciate the relative significance of exposures to younger receptors, which can then be factored into the risk management approach. Incorporating this current knowledge can be particularly useful for sites where children exposures are a factor, such as due to proximity of daycare centers or schools.

As a technical note, it is important to account for the different intakes of children when using age-dependent DCFs and ADAFs in quantitative dose/intake and risk calculations. For the radiological risk example, differences in the risk estimates were observed for relatively short exposure scenarios. But as durations increase into the long term (as commonly assessed for cleanup sites) this difference disappears. Thus, per realistic land use assumptions, "chronic lifetime exposures" that extend from infancy to 70 years old would offset short-term differences.

The illustrative example described here illustrates one approach for integrating new scientific data into the standard risk assessment process. Other approaches can also be applied, the important point is to assure that appropriate information is available in the risk assessment to help inform sound risk management decisions.

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