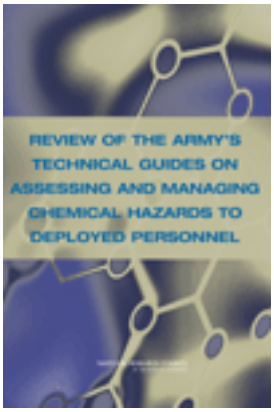

Review of the Army's Technical Guides on Assessing and Managing Chemical Hazards to Deployed Personnel

Subcommittee on the Toxicological Risks to Deployed Military Personnel, Committee on Toxicology, National Research Council

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Appendix B

Review of Acceptable Cancer Risk Levels

ORGANIZATIONAL USE OF ACCEPTABLE RISK LEVELS

Federal Agencies

In an evaluation of regulated chemicals, Travis and Hattemeyer-Frey (1988) found that 70% of chemical carcinogens have a post-regulatory added lifetime estimated risk greater than 1×10^{-6}, and 30% have a post-regulatory added lifetime estimated risk greater than 1×10^{-4}. They concluded that past regulatory decisions explicitly acknowledge that some risks, in the range of 1×10^{-6} to 1×10^{-3}, are acceptable in modern society. In the case of benzene, high estimates of maximum individual risk (1×10^{-3}) are considered tolerable when the aggregate population risk (extra cancers per year in the population) is insignificant. Similar levels of risk are accepted for emissions from zinc-oxide plants (3×10^{-3}), secondary lead smelters (3×10^{-3}), elemental phosphorus plants (1×10^{-3}), vinylidine chloride facilities (8×10^{-4}), DOE facilities emitting radionuclides (7×10^{-4}), and uranium mill tailings emitting radon (5×10^{-4}) (EPA 48 Fed. Reg. 33112 [1983]; 50 Fed. Reg. 5190 [1985]; 50 Fed. Reg. 32632 [1985]; 51 Fed. Reg. 6382 [1986]; Rodricks et al. 1987; Travis and Hattemeyer-Frey 1988).

Occupational Safety and Health Administration

In deciding on a level of acceptable risk associated with the workplace,

the Occupational Safety and Health Administration (OSHA) used an approach similar to that of the U.S. Food and Drug Administration (FDA) by not defining "safe" as the equivalent of risk-free, because many activities considered safe by most people entail some risk of accident or health damage. Workplace activities or exposures are not considered unsafe unless a significant risk of harm exists. In addition, because of the benefits accrued from employment (e.g., income), workers are presumed to be willing to accept higher levels of risk than would someone to whom little or no benefit accrues from accepting risk. Some studies have shown that salary is commensurate with the level of risk inherent in an occupation (Starr 1969; Whipple 1988).

Supreme Court action (*Industrial Union Department, AFL-CIO v. American Petroleum Institute et al.* 448 U.S. 607 [1980]) was instrumental in defining acceptable occupational risk for OSHA. The court suggests that significant occupational risk be determined by comparing the risk in question with other common occupational risks levels. The court suggested that an occupational lifetime cancer risk of 1×10^{-3} is significant. On the basis of actuarial data from 1984, the average lifetime (i.e., 45 years) risk of work-related death in a private company with 11 or more employees was 2.9 per 1,000. Risks in high-hazard occupations, like mining, range between 7.6 and 18.6 per 1,000, and risks in low-hazard workplaces, like the service industry, range between 0.9 and 1.8 per 1,000 (Cotter 1986; Rodricks et al. 1987). These rates are measured, not estimated risks, and show little variation from year to year.

OSHA as well as the U.S. Environmental Protection Agency (EPA) and the Nuclear Regulatory Commission have used those lifetime risk values as benchmarks to develop occupational acceptable risk levels. In developing radiation protection guidelines, EPA selected 3×10^{-3} because it was comparable to the working lifetime risk of accidental death in the least hazardous occupations (EPA 46 Fed. Reg. 7836 [1981]; Rodricks et al. 1987). The Nuclear Regulatory Commission stated that the average annual mortality rate in "safe industries" does not exceed 1×10^{-4}, which translates to a worker 45-year lifetime risk of approximately 4×10^{-3}. Like EPA, the commission proposed occupational standards on the basis of the assumption that worker risks due to radiation are acceptable if kept at or below the "safe industry" risk level (Nuclear Regulatory Commission 1986; Rodricks et al. 1987).

For other workplace carcinogens, OSHA has not regulated below 1×10^{-3}, largely because of technical feasibility. Residual lifetime occupational risks associated with permissible exposure levels (PELs) revised in the

1980s range from a low of 0.2 per 1,000 to 6 per 1,000 for ethylene dibromide and 39 per 1,000 for acrylonitrile (Table B-1). As with other federal agencies, OSHA has not claimed that those health risks are insignificant, but rather that they are "acceptable" (Rodricks et al. 1987).

National Institute for Occupational Safety and Health

Unlike OSHA, the National Institute for Occupational Safety and Health (NIOSH) is not a regulatory agency, but it is engaged in research on and interpretation of occupational health and safety issues. Its policy on acceptable cancer risk is qualitative, as first stated in 1976, calling for "no detectable exposure levels for proven carcinogens" (Fairchild 1976; NIOSH 2002). That statement represents a zero-risk policy similar to FDA's Delaney Clause of 1958 and the treatment of Category I potential carcinogens in the generic OSHA rulemaking on carcinogens (29 CFR 1990). Under the policy, when carcinogen thresholds that would protect 100% of the population have not been identified, nonquantitative recommended exposure levels (RELs) labeled "lowest feasible concentrations" (LFCs) are adopted for most carcinogens. The few quantitative RELs for carcinogens (e.g., for asbestos, formaldehyde, benzene, and ethylene oxide) were set based on limits of detection or technological feasibility. NIOSH also adopted several quantitative RELs from OSHA's 1989 PEL update (implying an acceptable risk limit consistent with that used by OSHA for category II potential carcinogens).

TABLE B-1 Risk Considered Acceptable within OSHA Permissible Exposure Limits

Chemical	Residual Risk at PELs
Arsenic	8×10^{-3}
Ethylene oxide	$1\text{-}2 \times 10^{-3}$
Ethylene dibromide	$0.2\text{-}6 \times 10^{-3}$
Benzene	$5\text{-}16 \times 10^{-3}$
Acrylonitrile	39×10^{-3}
Dibromochloropropane	2×10^{-3}
Asbestos	6.7×10^{-3}

Source: Adapted from Rodricks et al. 1987.

In the 20 years since NIOSH first set its policy, science and risk-assessment techniques and management techniques have advanced to the point that NIOSH has adopted a more inclusive attitude. NIOSH projects both no-effect exposure levels for chemical or physical agents as well exposure levels at which residual risks for all workplace hazards, including carcinogens, might be present. This approach is consistent with the 1970 OSH Act (P.L. 91-596 Section 20(a)(3)) that charged NIOSH to "describe exposure levels that are safe for various periods of employment, including but not limited to the exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience." However, no single acceptable risk level or range of values has been set forth in policy to date.

U.S. Environmental Protection Agency

EPA has been at the forefront of the issue of acceptable risk in virtually all of its programmatic areas, primarily as the result of court challenges to its regulations. In response to the 1987 Section 112 Clean Air Act decision (*Natural Resources Defense Council v. U.S. Environmental Protection Agency* 824 F. 2nd 1146 [1987]), EPA decided it would base its regulatory decisions on quantitative risk assessments using the general policy that a lifetime added cancer risk for the most exposed person of 1 in 10,000 (1×10^{-4}) might constitute acceptable risk and that the margin of safety required by statute and reinforced by the court should reduce the risk for the greatest number of persons to an added lifetime risk of no more than 1 in 1 million (1×10^{-6}). However, EPA (along with the courts) has not viewed "safe" as the equivalent of risk-free and has determined that standards should protect against significant public health risks (EPA 49 Fed. Reg. 8386 [1984]; Rodricks et al. 1987; *Industrial Union Department, AFL-CIO v. American Petroleum Institute et al.* 448 U.S. 607 [1980]). EPA has repeatedly rejected the opinion that it can establish a universal (i.e., brightline) acceptable risk that should never be exceeded under any circumstances, and they maintain that guidance provided under one statute might have little relevance to others because of differing program goals. In practical terms, EPA almost never regulates at a theoretical risk below 1×10^{-6} (*de minimis*) and almost always regulates at a theoretical risk below 1×10^{-4} (*de manifestis*).

U.S. Food and Drug Administration

The U. S. Food and Drug Administration (FDA) was the first federal agency known to have encountered the issue of acceptable risk with the adoption of the Delaney Clause in 1958. The clause states that no additive that is deliberately included in food products during or after processing is allowed to be in use if it causes cancer in animals (Federal Food, Drug, and Cosmetic Act Sec. 409.[348](c)(3)(A); Sec. 512.[360b](d)(1)(I); and Sec. 721.[379e](b)(5)(B)). At the time, this zero-risk policy was based on the presumption that no safe human exposures to animal (nonthreshold) carcinogens could be identified the way that safe levels of compounds acting through threshold mechanisms could (NRC 1994).

In 1973, FDA employed quantitative risk assessment using the Mantel-Bryan methodology for estimating cancer risks (Mantel and Bryan 1961; Rodricks et al. 1987) and defined the risks associated with the residues of carcinogenic drugs used in food animals. The acceptable risk level proposed at the time was 1×10^{-8}, as suggested by Mantel and Bryan (Mantel and Bryan 1961; FDA 38 Fed. Reg. 19226 [1973]; Rodricks et al. 1987). The risk-assessment methodology was later modified to a linear-proportional form, and the acceptable risk level changed to 1×10^{-6} in response to public comment, the idea of risk assessment having become firmly entrenched by 1979 (FDA 44 Fed. Reg. 17070 [1979]; Rodricks et al. 1987). FDA has since employed this technique for other substances regulated under the federal Food, Drug, and Cosmetic (FD&C) Act. D&C Green No. 5 was listed with an estimated upper limit risk of 3×10^{-7}, and lead acetate also received approval as a colorant with a lifetime added risk of between 5×10^{-6} and 1.9×10^{-7} (FDA 45 Fed. Reg. 72112 [1980]; 47 Fed. Reg. 24278 [1982]; Rodricks et al. 1987). In neither instance was 1×10^{-6} declared an agency-significant risk criterion, but the above risks were considered insignificant in terms of the public health as applied to food additives.

The same risk-assessment tools have been used to address the zero-risk requirements of the Delaney Clause. In those cases, FDA has interpreted "safe" in the context of food law to be defined as "reasonable [but not absolute] certainty of no harm," although at the same time, the benefits of an additive cannot be considered in its decisions. The FDA position is that a carcinogen is considered safe as long as exposure to it is restricted to levels posing insignificant risks. Insignificant risk has been defined as 1×10^{-6} or less in several agency decisions.

Even though 1×10^{-6} has been used as the *de facto* brightline acceptable risk level in several cases, FDA has also found that cancer risks above 1×10^{-6} are acceptable for certain classes of contaminants (e.g., PCBs, dioxins, and aflatoxins) given the technical difficulties and costs associated with reducing exposure. In the case of fish contaminated with PCBs, FDA considered that an estimated risk of 1×10^{-4} provided adequate protection to the public health on the basis of their PCB residue tolerance of 2 ppm. This conclusion considered the ubiquity of the contaminant and the presumed benefit from consuming fish proteins. FDA stopped short of labeling estimated risks greater than 1×10^{-6} as insignificant (Rodricks et al. 1987).

Other Authoritative Sources

American Conference of Governmental Industrial Hygienists

The American Conference of Governmental Industrial Hygienists (ACGIH), like NIOSH, develops recommended occupational exposure limits to protect workers from injury. Their Threshold Limit Values (TLVs) are not enforceable because ACGIH is a nongovernmental organization. The TLVs are based on threshold toxicity events and include a designation for the weight-of-evidence for carcinogenicity and other forms of toxicity similar to that used by IARC and EPA. ACGIH has not to date identified an acceptable risk for any carcinogen in the workplace, stating instead that exposure to carcinogens must be kept to a minimum (ACGIH 2001). Workers exposed to known human carcinogens that do not have a TLV should be properly equipped to eliminate exposures to those carcinogens to the fullest extent possible. For known human carcinogens that have a TLV or suspected human carcinogens, worker exposures by all routes should be carefully controlled to levels as low as possible below the TLV.

National Commission on Radiologic Protection

The National Commission on Radiologic Protection (NRCP) proposed an average cancer risk of 1×10^{-5} per year (not per worker lifetime or full lifetime) for members of the public exposed continuously or repeatedly to radiation sources other than medical and background. This translates to a lifetime cancer risk of 7×10^{-4} and may be considered the *de manifestis* risk. A negligible 1% of that risk (7×10^{-6}) was suggested by Schiager et al. (1986).

World Health Organization

In developing drinking water guidelines, the World Health Organization (WHO) employed an acceptable risk level of 1×10^{-5} (WHO 1996; Fiori and Meyerhoff 2002) but did not indicate how that level of health protection was selected. For its air quality guidelines, WHO provides only qualitative guidance by specifying that the "acceptability of the risk and, therefore, the standards selected, depends on the expected incidence and severity of the potential effects, the size of the population at risk, the perception of the related risk and the degree of scientific uncertainty that the effects will occur at a specific level of air pollution" (WHO 2000).

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