THE MYTH OF 10^{-6} AS A DEFINITION OF ACCEPTABLE RISK

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ABSTRACT

The concept of 10^{-6} (or one-in-a-million risk of developing cancer) has had a major economic effect in environmental hazard mitigation and pollution control. For example, in hazardous waste site cleanups, 10^{-6} is a common standard adopted by many authorities and countries as a designation of "acceptable" risk. This paper discusses the origins of 10^{-6} as a standard of "acceptable risk" and its widespread use today. The article concludes that despite its widespread use: no agencies we contacted could provide documentation on the origins of 10^{-6}; its origin was determined to be a completely arbitrary figure adopted by the FDA as an "essentially zero" level of risk for residues of animal drugs; there was virtually no public debate on the appropriateness of this level despite requests by the FDA; this legislation stated that 10^{-6} was specifically not intended to be used as a definition of acceptable risk; 10^{-6} is almost exclusively applied to contaminants perceived to be of great risk (hazardous waste sites, pesticides); and 10^{-6} as a single criterion of "acceptable risk" is not and has never been in any EPA legislation or guidance documents. In light of the billions of dollars that have been spent or committed to reaching this goal, it would seem appropriate to revisit the scientific, social, and economic basis of 10^{-6} as a criterion of "acceptable" risk.

INTRODUCTION

It is difficult to imagine a criterion in wider use in U.S. environmental legislation than 10^{-6}. This number guides the use of pesticides and food additives; it defines our allowable exposure to groundwater contamination and incinerators. It is the most influential determinant we have in deciding what emissions should be allowed from stacks, how a hazardous waste site should be cleaned up, and how much Alar to leave on apples.

In the context of human health risks, 10^{-6} is a shorthand description for an increased lifetime chance of 0.000001 in 1 (or one chance in a million) of developing cancer due to lifetime exposure to a substance. The number 10^{-5} represents 1 chance in 100,000, and so on. Lifetime exposure to a substance associated

with a risk of 10^{-6} would increase our current chances of developing cancer from all causes (which are 1 in 3, or 3.33×10^{-1}) by a mere 0.0003%.

The risk of developing cancer associated with background levels of exposure to environmental contaminants is estimated at 10^{-3} to 10^{-2}.[1] The vast majority of our exposure to carcinogens is thought to be due to those that occur naturally in our foods.[2] The risk level 10^{-6} is less than our current risk of background exposure to environmental contaminants or developing cancer from all causes by a factor of 1,000 to 100,000. As 10^{-6} is an upper-bound estimate of risk, not an absolute or average value, the relative difference may actually be much greater.

The past, present, and future costs of achieving compliance with such a stringent criterion are virtually incalculable; certainly many billions of dollars have been spent in attempting to achieve this goal for cleanups at hazardous waste sites in the U.S. As a result, the origins of 10^{-6} is of considerable social, scientific, and economic interest.

This paper reveals that there is apparently no sound scientific, social, economic, or other basis for the selection of 10^{-6} as a cleanup goal for hazardous waste sites. Remarkably, this criterion, which has cost society billions of dollars, has never received widespread debate or even thorough regulatory or scientific review. It is an arbitrary level proposed 30 years ago for completely different regulations (animal drug residues), the circumstances of which do not apply to hazardous waste site regulation. As a result, implementing it consistently has frequently been socially, politically, technically, and economically unfeasible. Although the benefits of 10^{-6} generally have not been shown to outweigh the significant costs of attaining this goal, many federal and state cleanup guidelines still advocate or require the use of 10^{-6}.

Under these circumstances, communicating the meaning of 10^{-6} and the definition of "acceptable risk" poses considerable challenges to those responsible for explaining risk. The origin of 10^{-6} relative to its use as a criterion of "acceptable risk" is explored below.

THE SURPRISING ORIGINS OF 10^{-6}

In 1991, we conducted an extensive review to determine the origin of 10^{-6} as a criterion of "acceptable risk." We began with an informal telephone survey of affected agencies and an extensive literature search. The conclusions of this survey include the following:

1. *None of the officials contacted at any federal or state agency currently using 10^{-6} as a criterion knew the basis of this criterion, nor is there any readily available documentation that specifically describes the origin of 10^{-6}.*

The extensive literature search included numerous toxicological, medical, regulatory, pollution, environmental, and governmental databases that were queried back to the origin of each database (usually the mid-1970s). Not finding any written documentation, the authors began calling a "Who's Who" of the environmental industry. The contacts included the following:

- The White House
- The U.S. Environmental Protection Agency (EPA)
- The EPA's Science Advisory Board
- The EPA's Risk Assessment Forum
- The U.S. Food and Drug Administration (FDA)
- The U.S. Department of Agriculture

- The U.S. Conference of Mayors
- Oak Ridge National Laboratories
- The Congressional Office of Technology Assessment
- The Natural Resources Defense Council
- Citizen's Clearinghouse for Hazardous Waste
- Greenpeace
- Two former EPA Administrators
- A former state environmental commissioner
- Rockefeller University
- Environmental divisions of major law firms
- Staff members of several Congressmen
- And many other contacts in government and industry.

Despite widespread use of this criterion, none of the agencies could cite the source of 10^{-6}, although there was almost universal surprise that the origin of 10^{-6} was not readily available. We were offered many good theories, but no written documentation. A sample of the responses:

- "My mind is a complete blank."
- "My, what an interesting question!"
- "I think it came from pesticides legislation or the Delaney Clause."
- "It came from the FDA in the 1950s."
- "It was derived from the Virtually Safe Dose used in the Safe Drinking Water Act."
- "It's an economic criterion."
- "It's based on the chance of being hit by lightning, which is one in a million."
- "I just assumed it was because one-in-a-million sounded like such a nice phrase."
- "It was selected because it was 'doable.' Or at least that's what we thought at the time."
- "It was a purely political decision made by several of the major agencies behind closed doors in the 1970s. I doubt very much you'll get anyone to talk to you about it."
- And our favorite, "You really shouldn't be asking these questions" (this from one of the federal agencies).

2. *The concept of 10^{-6} was originally an arbitrary number, finalized by the U.S. Food and Drug Administration 14 years ago as a screening level of "essentially zero" or de minimus risk. This concept was traced back to a 1961 proposal by two scientists from the National Cancer Institute (NCI) regarding methods to determine "safety" levels in carcinogenicity testing.*

The proposal for *de minimus* risk was contained in a 1973 notice in the Federal Register entitled "Compounds Used in Food-Processing Animals: Procedures for Determining Acceptability of Assay Methods Used for Assuring the Absence of Residues in Edible Products of Such Animals," commonly called the "Sensitivity of Method" regulations.[3] The term *de minimus* is an abbreviation of the legal concept, "*de minimus non curat lex*: the law does not concern itself with trifles." In other words, 10^{-6} was developed as a level of risk below which was considered a "trifle" and not of regulatory concern.

The purpose of these proposed rules was to set forth guidelines for assay methods for carcinogenic animal drugs "which may be administered to food-producing animals, but for which no residue is permitted in human food" under the Delaney Clause of 1958. The rules were specifically prompted by the use of diethylstilbestrol (DES) as a growth promoter in cattle.

In adopting a threshold of safety, the FDA referred to a 1961 article by Nathan Mantel and Ray Bryan, originators of the well-known Mantel-Bryan equation, on the subject of safety testing in animal studies. Mantel, a biostatistician at the National Cancer Institute, had been asked by the Director of the institute to develop guidelines for the number of laboratory animals required to establish the safety of a substance. This in turn was in response to a request made after the Thanksgiving cranberry scare of 1959 by the Secretary of the Department of Health, Education and Welfare (HEW) to the NCI. (Trace residues of a cancer-causing herbicide were found in supplies of cranberries shortly before the holiday, prompting the Secretary to recommend against buying cranberries that year. This in turn set off a mild panic which nearly devastated the cranberry industry.) HEW wanted NCI to help establish which cancer-causing substances were "safe" and at what levels.

In their 1961 article, Mantel and Bryan reasonably pointed out that to define the parameters of safety testing, one must first come up with a definition of safety. For the purposes of discussion, they said, we'll assume "safe" is equal to 1 chance in 100,000,000 of developing cancer. Asked how he chose the number of one in one hundred million, Mantel replied, "We just pulled it out of a hat." After all, defining "safe" was not the focus of their article. But this is the ultimate origin of 10^{-6}.

FDA initially adopted this "1 in 100,000,000" in their 1973 notice in the Federal Register, but changed this value to 1 in 1,000,000 by the time the final rule was issued in 1977. "One in one million" was thus established as the "maximum lifetime risk that is essentially zero," or the level below which no further regulatory consideration would be given regarding the safety of residues of a carcinogenic animal drug. Only two comments were received on these proposed rules, despite a specific request from the FDA Commissioner for public comment on the setting of one-in-a-million risk as a threshold of "essentially zero" risk.

3. *In the FDA legislation, the regulators specifically stated that this level of "essentially zero" was not to be interpreted as equal to an acceptable level of residues in meat products.*[4]

Nevertheless, many current regulations and guidance documents have done exactly that: interpreted this "essentially zero" level developed by the FDA, a level below which there would be no regulatory consideration given regarding safety, as a maximum "acceptable" level of risk.

An analogy to automobiles is that if we could not measure when a car were standing completely still, the FDA might consider one mile per hour a "virtually safe" rate of speed. Below this rate either speed is unmeasurable, or the costs of such measurements outweigh the benefits of the information gained.

In a sense, this criterion of one mile per hour has been misinterpreted to be a maximum "acceptable" rate of speed for driving a car on the highway without risk of dying in a car crash. The former is a *screening* level below which no regulatory consideration would be given to risks; the latter is a *safety* decision that takes into account cost-benefit considerations of highway safety, the road conditions, type and weight of automobile, etc.

Cleaning up all hazardous waste sites to a 10^{-6} level of "essentially zero" risk is therefore comparable to limiting highway traffic to 1 mph. The cost-benefit tradeoffs need to be evaluated more carefully in selecting a final cleanup number, using 10^{-6} as a starting point instead of a goal.

HOW IS 10^{-6} USED?

A review of the evolution of 10^{-6} reveals that *perception* of risk is a major determinant of the circumstances under which this criterion is used.

1. *The risk level 10^{-6} is not consistently applied to all environmental legislation. Rather, it seems to be applied according to the general perception of the risk associated with the source being regulated. Specifically, 10^{-6} has been applied almost exclusively to hazardous waste sites, pesticides, and selected carcinogens, but not to air, drinking water, or other sources perceived to be of less risk.*

Cleanup levels for a given contaminant are not consistent from site to site and vary by orders of magnitude. From these past site cleanup decisions, we can see that "acceptable" is not a set value; the threshold of "acceptability" varies among countries, among states, and among different cities of the same state. Furthermore, the lack of consistent quality among risk assessments has resulted in widely differing cleanup levels at similar sites, all of which are claimed to have been cleaned up to 10^{-6}.

Less well known are the extreme differences even among various divisions of the same agency for the same substance. For example, there are six orders of magnitude (one million-fold) difference in target risk within different EPA regulations for arsenic.[5] The differences may be partly due to the *perception* of risk associated with the particular regulatory decision: the greater the perceived risk, the narrower the gap between "essentially zero" and what the public will allow as "acceptable risk." As a result, some sources that actually pose a higher risk to society, such as automobile emissions, are regulated less stringently simply because they are *perceived* to pose less risk than such sources as hazardous waste management facilities, whether or not the data support that assumption.

2. *Although it has been in widespread use for hazardous waste sites for many years, the concept of 10^{-6} as a criterion of acceptable risk has never been mandated in any EPA regulations. In fact, the target range of 10^{-6} to 10^{-4} as a range of "generally acceptable risk" was not actually codified into EPA Superfund legislation until 1990 with the passage of the revised National Contingency Plan (NCP).*

How did the misconception arise that 10^{-6} was a legislative requirement? As the concept of risk assessment was broadened over two decades from carcinogenic animal drugs at the FDA to a host of other decisions and agencies (including food, water, air, hazardous waste, and others), the 10^{-6} concept was carried along as well. In the opinion of a former FDA counsel, the concept of 10^{-6} was repeated so often that it took on the stature of a firm regulatory policy, although the record clearly indicates otherwise. The original intent of 10^{-6} as a screening level was lost, and still is not recognized today.

No reference to 10^{-6} as a criterion for "acceptable risk" could be found in any published EPA regulation or guidelines. The guidance published in 1984 by the Office of Science and Technology Policy[6] made no mention whatsoever of any target risk with which to compare results of health risk assessments, nor did EPA's proposed or final Guidelines for Carcinogenic Risk Assessment.[7,8]

The first use of "acceptable risk" in any environmental guidance appears to have been a part of the Superfund Public Health Evaluation Manual, issued in 1986 and now superseded by the 1990 National Contingency Plan.[9] The original Superfund guidelines stated: "... remedies considered should reduce ambient chemical concentrations to levels associated with a carcinogenic risk range of 10^{-4} to 10^{-7}." This range was modified to 10^{-4} to 10^{-6} in the final NCP.

3. *In codifying 10^{-6} for the first time in hazardous waste site rules, the National Contingency Plan specifically designates 10^{-6} as a starting point for discussion of acceptable target risk at a site or as a "point of departure," not the ultimate goal.[9] This designation is consistent with the original intent of the use of 10^{-6} as a level below which regulatory consideration was not warranted, i.e., as a starting point for discussion.*

The plan specifically states that 10^{-6} should not be presumed to be the final target risk for hazardous waste sites, but instead a "point of departure" for deciding an appropriate target level. Levels of 10^{-6} to 10^{-4} are given as a range of "generally acceptable risk," with the option that even 10^{-4} may be exceeded in some circumstances.

Because no two sites are alike, the NCP guidance then lists several site-specific or remedy-specific factors that can be used to assist in the selection of a final risk level. This approach is consistent with EPA's requirement to develop protective strategies for hazardous waste sites, not eliminate risk.

4. *A single value of "acceptable risk" has never been used in EPA hazardous waste site regulation -- only a range of values.*

In an analysis of the final NCP by one of the EPA attorneys who drafted the rule, the attorney states:

> "The use of a *range* of acceptable risk is general practice for most government programs...[It] affords the Agency the flexibility to take into account different situations, different kinds of threats, and different kinds of technical remedies. If a single risk level had been adopted (e.g., at the more stringent end of the risk range), fewer alternatives would be expected to pass the protectiveness threshold and qualify for consideration in the balancing phase of the remedy selection process."[10]

The use of 10^{-6} as a definition of acceptable risk thus has no scientific or regulatory basis. Its use appears to be arbitrary and generally applied where risks are perceived to be high relative to other risks, regardless of the available data.

SO WHAT IS AN ACCEPTABLE LEVEL OF RISK?

Much has been written about determining the acceptability of risk. The general consensus in the literature is that "acceptability" of a risk is a judgment decision properly made by those exposed to the hazard or their designated health officials. It is not a scientifically derived value or a decision made by outsiders to the process. Acceptability is based on many factors, such as the number of people exposed, the consequences of the risk, the degree of control over exposure, and 40 or so other factors. The degree of risk acceptable at hazardous waste sites has never been formally quantified, but it does vary with each site, and the public tolerates a very low threshold of acceptable risk at hazardous waste sites in part because hazardous waste ranks very high with many of these factors.

Travis *et al.* attempted to answer the question of what is acceptable risk indirectly by quantifying the risk levels associated with 132 federal regulatory decisions, and thus determine a *de facto* level of acceptable risk.[5] If a consistent threshold of risk could be shown in other federal health and safety decisions, that threshold could provide guidance for comparable protection at hazardous waste sites. From this effort, they rather convincingly concluded that the *de facto* level of acceptable risk in federal regulatory decisions is approximately 10^{-4}.

This level, which is 100 times greater than 10^{-6}, is likely due to several factors. Chief among those reasons is that *perception* of risk may largely drive the regulatory decision on what constitutes the level of "acceptable" risk. This notion is supported by findings of the U.S. EPA Science Advisory Board (SAB).[11] The SAB ranks hazardous waste near the bottom of its list of actual risks to the public but near the top of the agency's priorities, which in turn are dictated by public perceptions and Congressional funding. In response to these findings, former U.S. EPA Administrator Reilly undertook a major reorganization of the EPA to refocus its efforts on the major sources of actual risk and their reduction, apparently without success.[12]

A second reason 10^{-6} has probably been so widely applied to hazardous waste sites is that unlike decisions about air contamination, pesticides, and other agency reviews made at the federal level, hazardous waste site cleanup decisions are made on a very local and site-specific basis. What seems "doable" at the local level, such as spending a million dollars for cleaning up a site in return for virtual elimination of risk, often does not seem "doable" on a larger scale — thousands of sites at perhaps several million dollars per site to reduce risk to levels well below those considered "acceptable" by other public health standards. Indeed, current estimates for cleaning up all currently designated U.S. hazardous waste sites range up to one trillion dollars.

What does this mean for current and pending state environmental policy? One possible outcome is that agencies will begin to adopt policies such as that established by the New Jersey Department of Environmental Protection, Division of Environmental Quality (DEQ), in their guidance for risk assessments for municipal solid waste incineration facilities. This policy quite succinctly states:

> "Incremental risks from a new source which are less than one in a million are considered by the DEQ to be negligible. Incremental risks greater than one in ten thousand are deemed unacceptable. Risks between these two limits are judged on a case-by-case basis."[13]

SUMMARY AND CONCLUSIONS

It has been over two decades since the FDA introduced the concept of risk assessment in its efforts to deal with DES as a growth promoter in cattle. As part of this effort, the threshold of one-in-a-million risk of developing cancer was established as a screening level to determine what carcinogenic animal drug residues merited further regulatory consideration.

Since then, the use of risk assessment and 10^{-6} (or variations thereof) have been greatly expanded to almost all areas of chemical regulation, to the point where today clearly one-in-a-million risk means different things to different agencies. What the FDA intended to be a *lower* regulatory level of "zero risk" below which no consideration would be given as to risk to human health, many federal and state agency decisions somehow came to consider a *maximum* or *target* level of "acceptable" risk.

As 10^{-6} seemed like a reasonably conservative level (or "doable," according to many), it was adopted first for a few chemicals and exposure pathways, then more chemicals and exposure pathways, and so forth. Not until the rule came into widespread use -- or until everyone was limited to one mile per hour on the freeway, so to speak, and it was costing billions of dollars to eliminate risk -- did it become readily apparent that the "zero risk" screening criterion was not intended to be interpreted as "acceptable risk." Accordingly, the benefits of the 10^{-6} criterion applied to hazardous waste sites will rarely exceed the risks and costs, and the criterion is thus unsuitable for regular implementation or enforcement.

Furthermore, 10^{-6} as a criterion for "acceptable risk" has not been applied to other sources of exposure that pose considerably more risk to public health than hazardous waste, such as automobile emissions,

radon, or sources of benzene. The primary reason for the inconsistent application of this criterion appears to be that public perception of risk has driven the regulatory management of these sites to a greater degree than supported by the actual data. Reorganizing the EPA's priorities towards issues of actual rather than perceived risk was a major goal of former EPA Administrator Reilly.

Lack of a sound basis for extrapolating the use of 10^{-6} from its very specific origins to a wide variety of other non-related applications partly explains the extreme difficulty agencies have had in implementing 10^{-6} as a goal. Such extrapolations face costs and benefits that are often not in balance (e.g., the Office of Management and Budget's unwillingness to approve proposed hazardous waste incineration rules because of EPA's inability to fully account for and justify the costs of implementing these rules -- i.e., $288 million dollars per case of cancer avoided).[14]

The discovery of a lack of a sound basis for the choice of 10^{-6} offers opportunities for introducing health-based considerations into the discussion of how to clean up hazardous waste sites, particularly when so many sites demand attention for cleanup and funds are limited. This is particularly urgent considering the Agency for Toxic Substances and Disease Registry announced in 1990 that only 11.5% of all Superfund sites pose an actual or current risk to human health or the environment.[15] Revisiting the issue of 10^{-6} as a Holy Grail that is frequently sought but rarely found allows us the opportunity to create cleanup criteria with a more scientific basis, rather than to present a continued obstacle to further informed decision-making regarding important health and environmental matters. Efforts by the 104th Congress to implement just such risk reform legislation, which would require the agencies to demonstrate the costs of proposed regulations were commensurate with their benefits, were ultimately unsuccessful.[16]

The solution to developing better criteria for environmental contaminants is not to adopt arbitrary thresholds of "acceptable risk" in an attempt to manage the public's perception of risk, or develop oversimplified tools for enforcement or risk assessment. Rather, the solution is to standardize the *process* by which risks are assessed, and to undertake efforts to narrow the gap between the public's understanding of actual vs. perceived risk. A more educated public with regard to the actual sources of known risks to health, environmental or otherwise, will greatly facilitate the regulatory agencies' ability to prioritize their efforts and standards to reduce overall risks to public health.

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