REYNOLDS ALUMINUM

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Docket Office
Occupational Safety & Health
Administration, Room S6212
U.S. Department of Labor
200 Constitution Avenue, N.W.
Washington, D.C. 20210

file H92

Re: OSHA Cancer Policy
Docket No. H090C

Gentlemen:

I have enclosed a copy of Reynolds Metals Company's comments on the reevaluation of the OSHA Cancer Policy. These comments are submitted within the three-day extended period for filing, which I requested in my letter of 1982 March 31. They are the work product of a committee comprised of: Harry L. Skalsky, Ph.D., Corporate Toxicologist; Ronald E. Benton, Corporate Industrial Hygienist; David B. Mortimer, Corporate Engineer; and the undersigned. All the committee members can be contacted at Reynolds Corporate Headquarters in Richmond, Virginia, at (804)281-2000.

Very truly yours,

Patrick R. Laden

Patrick R. Laden

brm
Enclosure

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UNITED STATES OF AMERICA
BEFORE THE OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION

In The Matter Of:	)	
	)	Docket No. H090C
REASSESSMENT OF THE OSHA CANCER POLICY	)	

COMMENTS OF
REYNOLDS METALS COMPANY

I STATEMENT OF POSITION:

On 1982 January 05, the Occupational Safety and Health Administration (OSHA) published a notice which solicited comments on the reevaluation of certain provisions of the OSHA cancer policy (47 Fed. Reg. 197).[1] OSHA cited five reasons as grounds for this reevaluation:

1. To assure the cancer policy's consistency with the Supreme Court's decisions in the Benzene and Cotton Dust cases;[2]
2. To respond to the requirements of Executive Order 12291;
3. To consider amendments that will make the cancer policy more cost effective;

1 The OSHA cancer policy refers to the generic carcinogen standard, i.e., the generic standard for Identification, Classification and Regulation of Potential Occupational Carcinogens, 29 C.F.R. § 1990 (1978).

2 Industrial Union v. American Petroleum, 100 S.Ct. 2844 (1980) (benzene); American Textile Mfr. Inst., Inc. v. Donovan, 101 S.Ct. 2478 (1981) (cotton dust).

4. To consider modifications based upon experience with the cancer policy to date; and

5. To consider relevant advances in science, including advances in quantitative risk assessment.

On behalf of Reynolds Metals Company, I would like to offer some general comments on the cancer policy and three specific recommendations.

The cancer policy was initially intended as a loose framework to organize the regulation of carcinogens. Unfortunately, as a result of regulatory exuberance, the loose framework was transformed into a rigid code with little flexibility. Because this code deals with carcinogens, it must also address the sciences related to carcinogens. Science, however, cannot be frozen in time or confined to a rigid code. Instead, science is in a constant state of flux as a result of innovation and new discoveries.

If the cancer policy is to be tranformed into a useful regulatory tool, it must return to its original format as a loose framework. The rigid inflexible aspects of the policy must be deleted and replaced by provisions that will accommodate the growth of scientific knowledge. To accomplish this task, Reynolds suggests the adoption of the following three proposals:

1. The formal carcinogen classification system should be deleted and replaced with a more scientific approach to ranking carcinogens.

2. A method of quantitative risk assessment should be adopted to assist OSHA in developing permissible exposure levels.

3. The cancer policy's strong preference for engineering controls should be deleted to allow the issue of controls to be addressed on a case by case basis.

II ARGUMENT

A. THE PRESENT METHOD FOR CLASSIFYING CARCINOGENS SHOULD BE REPLACED WITH A MORE SCIENTIFIC RANKING SYSTEM

The OSHA cancer policy presently classifies all carcinogens as either Category I or Category II potential carcinogens. Category I carcinogens include all substances that show evidence of increasing the incidence of benign or malignant neoplasms or reducing the latency period between exposure and the onset of neoplasms. Category II is comprised of those substances where the data is only suggestive of increasing the incidence of neoplasms.

The evidence needed to classify a substance in either category is minimal. Positive results from one epidemeologic study on humans or one experimental study on mammals is sufficient. Studies with negative results are barred from consideration unless they meet strict criteria that do not apply to positive studies. Moreover, certain grounds for criticizing positive studies, e.g., an argument that a substance only produces benign tumors, are also barred from consideration unless rigid criteria are met. The standard also prohibits any inquiry as to whether there may be safe threshold levels for some carcinogens.

The cancer policy is not yet two years old, but there are already developments that reveal significant errors in OSHA's classification system. For example, by assuming there are no safe threshold levels for carcinogens, OSHA has been forced to ignore a growing school of thought about the distinction between genotoxic and nongenotoxic carcinogens. The integrative theory of carcinogenesis, as proposed by Tresko and Chang,[3] is rapidly gaining general acceptance. This theory asserts that some neoplasms may arise as a result of a mutagenic event in a regulatory locus of the DNA, i.e., as a result of a chemical reacting directly with the DNA molecule. Other neoplasms, however, may be caused by the abnormal derepression of genes during a critical stage of development, i.e., through indirect chemical action. Because chemicals may produce tumors via several different mechanisms, Weisburger and Williams have proposed that carcinogenic substances be divided into two general classifications:[4]

1. Genotoxic carcinogens, which are primary and act directly as a result of their mutagenicity; and
2. Nongenotoxic carcinogens, which work indirectly, e.g., solid state carcinogens, hormones and immunosuppressive agents.

3 Tresko & Chang, Integrative Theory of Carcinogenesis, 28 Photochemistry & Photobiology 157 (1978).

4 T. Weisburger & G. Williams, Toxicology: Basic Science of Poisons 84-138 (1980).

This distinction between genotoxic and nongenotoxic mechanisms is of great significance in carcinogenic risk assessment. Genotoxic carcinogens may cause an irreversible initiation of tumors at less than toxic dosages. As a result, even low dosages of genotoxic substances, i.e., aflatoxin or dimethylnitrosamine, always involve some element of risk. Nongenotoxic carcinogens, however, exhibit characteristics of safe thresholds because the cellular responses they evoke are often reversible. Moreover, nongenotoxic responses are usually observed only after repeated administration of high, metabolically-saturated dosages. Accordingly, chemicals like chloroform appear to have safe threshold levels and, therefore, should be classified as nongenotoxic carcinogens.[5]

5 Many theories have been proposed to explain the mechanics of nongenotoxic (epigenetic) carcinogens. Among them, the cytotoxic (cell death) theory appears to be the most plausible. Regenerative cellular proliferation in response to chemical cytotoxicity is the cornerstone of the irritation theory of carcinogenesis (Berenblum, Irritation and Carginogenesis, 38 Archives of Pathology 233 (1944). While the cytotoxic theory does not provide a complete explanation of nongenotoxic carcinogenesis, it appears to explain the promoting effects of phorbal esters and the production of tumors by repeated tissue injury (Berenblum, Established Principles and Unresolved Problems in Carcinogenesis, 60 J. of Nat'l Cancer Inst. 723 (1978)). Cytotoxicity and the subsequent regeneration of tissue could also have a direct bearing on the spontaneous mutation rates of cells as a result of alteration of nucleotide pools or levels of critical ions (Fersht, Fidelity of replication of phage 0X174 DNA by DNA polymerase III holoenzyme, 76 Proc. of Nat'l Acad. of Sci. 4946 (1979); Kunkel & Loeb, Effect of Divalent Metal Ion Activators and Deoxyribonucleoside Triosphate Pools on In Vitro Mutagenesis, 254 J. of Biological Chemistry 5718 (1979); Sirover, Dube & Loeb, Metal Activation of Escherichia Coli, DNA Polymerase I, 254 J. of Biological Chemistry 107 (1979)). Moreover, the fact that a greater amount of DNA synthesis occurs in regenerating tissue leads one to believe that a greater number of total DNA replication errors might result.

In contrast to OSHA's rigid classification system, Weisburger and Williams have developed a more flexible method that classifies carcinogens into eight categories (Weisburger and Williams, Carcinogen Testing: Current Problems and New Approaches, 214 Sci. 401 (1981)). This system, which is described below, incorporates the genotoxic-nongenotoxic distinction.

Table 1. Classes of carcinogenic chemicals.

Type	Mode of action	Example
	Genotoxic	
1. Direct-acting	Electrophile, organic compound, genotoxic, interacts with DNA	Ethylene imine
2. Procarcinogen	Requires conversion through metabolic activation by host or in vitro to type 1	Vinyl chloride, benzo[*a*]pyrene, 2-naphthylamine, dimethylnitrosamine
3. Inorganic carcinogen	Not directly genotoxic, leads to changes in DNA by selective alteration in fidelity of DNA replication	Nickel, chromium
	Epigenetic	
4. Solid-state carcinogen	Exact mechanism unknown: usually affects only mesenchymal cells and tissues; physical form vital	Polymer or metal foils; asbestos
5. Hormone	Usually not genotoxic; mainly alters endocrine system balance and differentiation; often acts as promoter	Estradiol, diethylstilbestrol
6. Immunosuppressor	Usually not genotoxic; mainly stimulates "virally induced," transplanted, or metastatic neoplasms	Azathioprine, antilymphocytic serum
7. Cocarcinogen	Not genotoxic or carcinogenic, but enhances effect of type 1 or type 2 agent when given at the same time. May modify conversion of type 2 to type 1	Phorbol esters, pyrene, catechol, ethanol, *n*-dodecane, SO_2
8. Promoter	Not genotoxic or carcinogenic, but enhances effect of type 1 or type 2 agent when given subsequently	Phorbol esters, phenol, anthralin, bile acids, tryptophan metabolites, saccharin

OSHA would not be breaking new ground by incorporating the genotoxic-nongenotoxic distinction into its carcinogen classification system. To the contrary, it would be joining the Food and Drug Administration (FDA)[6] and the Environmental Protection Agency (EPA)[7], which have already adopted this concept.

6 The FDA recently declined to classify selenium (38 Fed. Reg. 10,458), beverage alcohol (39 Fed. Reg. 1,355) and other hepatotoxic agents as carcinogens, despite the fact high doses unquestionably cause liver cancer in experimental animals. The FDA recognized that the increased incidence of liver cancer was not due to the inherent characteristics of these substances, but was a result of the substantial toxic insult to the liver from the high dos administered.

7 In February and March of 1982, the EPA conducted workshops to address the problem of nongenotoxic (epigenetic) carcinogens. At those workshops, the EPA specifically noted:

The genotoxic-nongenotoxic distinction however, is not the only scientific concept that the cancer policy's classification system does not address. OSHA has also ignored the role of the body's defense mechanisms in carcinogenesis. The formation of a tumor is a multistage event involving a wide variety of biochemical mechanisms, including DNA repair and immune surveillance. It has been demonstrated that each stage of carcinogenesis is matched by a defense barrier, which can modulate the consequences of the impending alteration. Therefore, exposure to some carcinogens may not necessarily start an individual on an unalterable course towards cancer. Instead, the body may succumb only after its defenses have been breached by a "sufficient insult." The existence of such defense mechanisms clearly support the proposition that there are threshold levels for nongenotoxic carcinogens, as well as practical threshold levels for genotoxic carcinogens.

7 (Cont'd. from page 6)

> Somatic cell gene mutation is thought to show a one-to-one correspondence between dose and effect and is held to have no threshold. Regulatory agencies, espousing this belief, adopted a very protective stance toward human health and therefore decreed that all carcinogens should be treated as genotoxins, as though their dose/response relationships were linear and without threshold. . . . More recently, other mechanisms of cancer have been suggested. These mechanisms are thought not to involve direct action of the chemical with the DNA and have thus been termed epigenetic (nongenotoxic). Epigenetic mechanisms, such as inhibition of DNA synthesis or repair enzymes, are thought to have threshold dose/response relationships.

OSHA has also made some questionable assumptions about the value of animals as predictors of human responses to carcinogens. By giving animal studies the same weight as human studies, OSHA has overlooked some important scientific evidence. There are intrinsic physiologic and metabolic differences between animals and humans that have to be considered before any meaningful assessment of human risk can be made. Moreover, unlike humans, some animal strains are predisposed to develop tumors independent of any chemical exposure. The present cancer policy does not account for these distinctions between animals and humans.

The cancer policy's classification system also fails to address differences between various species of test animals. Under the present policy, all experimental studies with mammals are treated equally, but the scientific evidence does not support this assumption. Different species of test animals may vary in their relative rates of metabolizing xenobiotics. An exhaustive study in this area was conducted with chloroform where 60 mg/1 kg were administered to rats, squirrel monkeys and three strains of mice. Approximately 92% of the chloroform was metabolized in the mice, 80% in the rats and only 22% in the monkeys. Moreover, data from the National Cancer Institute indicate that mice are 4.2 times more susceptible to liver tumors than rats. Accordingly, on the basis of metabolism and other evidence, it appears that monkeys and humans are the least sensitive to chloroform of any species tested.[8]

8 Brown, Langley, Smith & Taylor, Metabolism of Chloroform, 4 Xenobiotica No. 3, at 151 (1974); Reitz, Gehring & Park, Carcinogenic Risk Estimation for Chloroform, 16 Food & Cosm. Toxicology 511 (1981).

There is also evidence, based on comparative metabolism, that casts doubt on the wisdom of using mice in carcinogenic studies.[9] De Serves, for example, used a defined carcinogen, 2-acetamidofluorene (AAF), to compare the mutagenic potential of microsomal preparations. AAF was allowed to incubate with microsomal preparations from mice, rats, guinea pigs, rabbits, dogs and monkeys. After incubation, preparations from five of the species tested (all except monkeys) were found to cause mutagenic responses in the Ames assay. Moreover, in long term bioassays, four of the six species tested (mice, rats, rabbits and dogs) demonstrated the tumorogenic effects of AAF. In another study, monkeys who were fed AAF for up to eight years failed to develop tumors or lesions even suggestive of neoplasea. (R. O'Gara & R. Adamson, Pathology of Simian Primates at 190 (1972). Mice, therefore, are clearly not good predictors of the effects of AAF on primates, but the cancer policy's present classification system precludes OSHA from considering this evidence.

The foregoing discussion describes some of the scientific problems with OSHA's method of classifying carcinogens. OSHA's policy does not consider the genetoxic-nongenotoxic distinction, the body's defense mechanisms or differences between animal and human experience with carcinogens. Moreover, it does not assign different weights to animal studies in relation to their value as human predictors and it ignores the problems of using mice as experimental animals. Instead, the cancer policy establishes a rather crude and inflexible classification system where all potential carcinogens

9 P. Grasso, The Mouse and Carcinogenicity Testing (1977)

are forced into the same mold. This type of uniform approach may make the administration of the cancer policy easier for the regulators, but the disciplines of chemistry and biology are not amenable to such a simplistic approach.

In addition to these scientific considerations, OSHA must also consider some legal problems that affect its classification system. Section 6(b)(5) of the Occupational Safety and Health Act specifically provides that when the Secretary promulgates a standard dealing with toxic materials or harmful physical agents, he must base the standard on the "best evidence available."

This provision in the Act was addressed in the Fifth Circuit's decision in the Benzene case.[10] The benzene standard barred all dermal contact with benzene. To support this provision, OSHA relied on old studies which concluded that benzene could penetrate the skin. These studies were quite crude by modern standards and were of questionable scientific validity. In its decision, the Fifth Circuit vacated the dermal contact provision of the benzene standard because OSHA did not comply with Section 6(b)(5)'s directive to use the "best evidence available." The Fifth Circuit's decision was appealed, but the Supreme Court never reached the "best evidence" issue. Instead, the entire benzene standard was vacated due to a more fundamental deficiency, i.e., OSHA had not shown there was a "significant risk of harm." Thus, the Fifth Circuit's strict interpretation of the Act's "best evidence" requirement is still good law.

10 American Petroleum Inst. v. OSHA, 581 F.2d 493 (5th Cir. 1975) aff'd on other grounds, Industrial Union Dept. v American Petroleum Inst., 100 S.Ct. 2844 (1980).

When OSHA promulgated the cancer policy's classification system, it cast a blind eye towards all the countervailing scientific evidence discussed above. Accordingly, the cancer policy's classification system does not comply with the "best evidence" provision in Section 6(b)(5) and is contrary to the Fifth Circuit's decision in the Benzene case.

The Supreme Court's decision in the Benzene case raises additional concerns about OSHA's classification system. In the plurality decision, Justice Stevens noted that:

> Section 3(8) (of the Act) requires the Secretary to find as a threshold matter that the toxic substance in question poses a significant health risk in the workplace and that a new, lower standard is therefore "reasonably necessary or appropriate to provide safe or healthful employment and places of employment."11

It is difficult to assess "significant health risks in the workplace" accurately with the present system for classifying carcinogens. By adopting a no-threshold policy and simply classifying carcinogen studies as either positive or negative, OSHA has not taken advantage of the total evidence available. These limitations on the scientific evidence considered make OSHA's determinations regarding "significant health risks" scientifically suspect.

Another area for legal examination is Executive Order 12291, which provides that: "Administrative decisions shall be based on adequate information concerning the need for and consequences of proposed government action." The scientific

11 Industrial Union Dept. v. American Petroleum Inst., 100 S.Ct. 2844, 2850 (1980).

deficiencies in the cancer policy's classification system clearly raise questions about the adequacy of the information considered to support it.

There are many ways to classify carcinogens that are scientifically more sound than the method described in the OSHA cancer policy. Of these, Robert Squire's method takes advantage of a great amount of scientific evidence.[12] The Squire method of classification ranks carcinogens by assigning numerical values to various elements of toxicological evidence. Squire's factors for consideration and their respective numerical weights are described below:

Table 1. Proposed system for ranking animal carcinogens.

Factor	Score
A. Number of different species affected	
Two or more	15
One	5
B. Number of histogenetically different types of neoplasms in one or more species	
Three or more	15
Two	10
One	5
C. Spontaneous incidence in appropriate control groups of neoplasms induced in treated groups	
Less than 1 percent	15
1 to 10 percent	10
10 to 20 percent	5
More than 20 percent	1
D. Dose-response relationships (cumulative oral dose equivalents per kilogram of body weight per day for 2 years)*	
Less than 1 microgram	15
1 microgram to 1 milligram	10
1 milligram to 1 gram	5
More than 1 gram	1
E. Malignancy of induced neoplasms	
More than 50 percent	15
25 to 50 percent	10
Less than 25 percent	5
No malignancy	1
F. Genotoxicity, measured in an appropriate battery of tests	
Positive	25
Incompletely positive	10
Negative	0

*Based on estimated consumption of 100 grams of diet per kilogram of body weight. Scoring could also be developed for inhalation or other appropriate routes.

12 Squire, Ranking Animal Carcinogens: A Proposed Regulatory Approach, 214 Sci. 877 (1981).

The total score for a particular substance can then be used to determine its proper classification:

Table 2. Ranking animal carcinogens into five classes according to total factor score.

Total factor score	Carcinogen class	Regulatory options
86 to 100	I	Restrict or ban
71 to 85	II	
56 to 70	III	
41 to 55	IV	
Less than 41	V	Several options (no action, limited use, labelling, public education)

The factors considered in Squire's system are quite broad. If OSHA adopted such a system, the list of factors could be amended and the numerical weights reassigned to accommodate the growth of scientific knowledge. This type of ranking system would meet both the scientific and the statutory mandate to use the "best evidence available." Moreover, it would assist OSHA in assessing "significant health risks" and would meet the requirements of the Executive Order.

II QUANTITATIVE RISK ASSESSMENT SHOULD BE USED TO ASSIST OSHA IN DEVELOPING PERMISSIBLE EXPOSURE LEVELS

The Squire classification system determines which substances should be regulated and establishes priorities for regulating those substances. It does not, however, provide any answers about permissible exposure levels, i.e., it does not determine the concentrations at which substances become hazardous.

Prior to the Supreme Court's decision in the Benzene case, OSHA adhered to a zero risk policy and set permissible exposure limits at the lowest feasible level. Technological feasibility was based upon the outer limits of technology and economic feasibility, i.e., the cost of attaining the permissible exposure level, was not considered until the viability of a major portion of an industry was threatened. Therefore, a few plants, and perhaps even a few companies, were expendable.

The zero risk policy was rejected by the Supreme Court in the Benzene case, where Justice Stevens noted that:

> [T]he statute was not designed to require employers to provide absolutely risk-free workplaces wherever it is technologically feasible to do so, so long as the cost is not great enough to destroy an entire industry. Rather, both the language and the structure of the Act, as well as the legislative history indicate that it was intended to require the elimination, as far as feasible, of significant risks of harm.
>
> . . . [B]efore promulgating any standard, the Secretary must make a finding that the workplaces in question are not safe. But "safe" is not the equivalent of "risk-free." [100 S.Ct. 2844, at 2864]

As a result of the Benzene decision, OSHA deleted the "lowest feasible" language from that portion of the standard that addressed permissible exposure levels. Nevertheless, the standard still retains some elements of the zero risk policy since the no-threshold provision (29 C.F.R. § 1990.143(b)) still treats all carcinogens as genotoxic substances that have no safe exposure levels.

The Cotton Dust case was decided about one year after the Benzene case. In the Cotton Dust decision, the Supreme Court held that the term "feasible," in Section 6(b)(5) of the Act, merely means "capable of being done." The Court further noted that "Congress itself defined the basic relationship between costs and benefits, by placing the benefit of worker health above all other considerations save those of making attainment of the benefit achievable."[13]

There are many ways to meet the requirements of the Cotton Dust case, i.e., many ways to establish feasible permissible exposure levels without compromising worker health. However, the decision in the Cotton Dust case must be read in light of the Supreme Court's rejection of the zero risk policy in the Benzene case. Moreover, the Act itself limits the holding in the Cotton Dust case because the "feasibility" and "worker health" provisions in the Act ride in tandem with the mandate to use the "best evidence available". Section 6(b)(5) provides in part:

> The Secretary . . . shall set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health . . . .

These restrictions in Section 6(b)(5) and the case law must also be read in light of Executive Order 12291, which specifically directs that:

> 1. Administrative decisions be based upon adequate information . . . .

13 101 S.Ct. 2478, at 2490.

2. Among alternative approaches to any given regulatory objective, the alternative involving the least net cost to society will be chosen; and

3. Agencies shall set regulatory priorities with the aim of maximizing the aggregate net benefits to society taking into account the condition of the particular industries affected by regulations, the condition of the national economy, and other regulatory actions contemplated for the future.

On the basis of the foregoing, it appears that the zero risk policy for setting permissible exposure levels is no longer viable. What must be developed in its place is a system that will establish permissible exposure levels that (1) are feasible, i.e., "capable of being done," (2) do not compromise employee health, (3) utilize the best evidence available, (4) are based upon adequate information, and (5) minimize the cost to industry and society as a whole.

To fulfill these requirements, Reynolds recommends that permissible exposure levels be determined by utilizing some type of quantitative risk assessment. Quantitative risk assessment might be simply defined as a method of risk extrapolation where known data is used to predict what might be expected in an area where there is no data. In dealing with potential carcinogens, the evaluation of risk is often complex. Complications arise primarily due to four factors:

1. Most cancer data is acquired as a result of experiments with rodents, instead of primates or humans.

2. The dosages used to induce cancer in experimental animals is usually high.

3. The background incidence of cancer among experimental animals is often high, which makes it difficult to determine whether a bioassay is positive or negative.

4. Present scientific knowledge does not provide a definitive answer about thresholds for carcinogens.

As a result of these considerations, it is difficult to extrapolate from known data into unknown areas because the extrapolation line is, to some extent, based upon belief rather than scientific fact. Munro and Krewski have warned that quantification of human risk on the basis of laboratory studies should be approached with great caution.[14] Other investigators, however, such as Van Ryzin, have recommended a number of quantitative risk models to obtain answers at or near the experimental range.[15]

The Megamouse (ED_{01}) study has demonstrated that most quantitative risk models are equally predictive of risk to a limit of 10^{-2}. Beyond that point, the models begin to diverge drastically to a point where biological relevance is lost.[16] Therefore, any prediction lower than 10^{-2} is open to serious question. As a result of this apparent confidence limitation,

14 Munro & Krewski, Risk Assessment and Regulatory Decision Making, 19 Food & Cosm. Toxicology 549 (1981).

15 Van Ryzin, Quantitative Risk Assessment, 22 J. of Med. 321 (1980).

16 Innovations in Cancer Risk Assessment (ED_{01}, 3 J. of Envtl. Pathology & Toxicology 1 (1980).

OSHA must do more than merely plug in one of the traditional mathematic models. Instead, OSHA should assess quantitative risk by using a mathematic model in conjunction with a safety factor. The mathematic model could be used to predict risk from biological data to the 10^{-2} limit. Then, a safety factor, or a combination of safety factors, could be used to consider the total data base, including negative data. This mathematic model-safety factor method would also distinguish the scientific elements of setting permissible exposure levels from the elements based upon policy decisions. An example of such a quantitative risk model is described below:

Non Genotoxic Carcinogens: These chemicals are threshold toxins and traditional approaches can be used.

$$\text{Acceptable Human Exposure (mg/day)} = \frac{\text{NOAEL (mg/kg/day)} \times 70\ \text{kg}}{100}$$

NOAEL = No-Observed-Adverse-Effect Level in experimental animals.

70 kg = assumed average human weight

100 = 100-fold uncertainty factor which represents 10 for extrapolating from the average animal to the average human and 10 for extrapolating from the average to the sensitive human.

Genotoxic Carcinogen : Model is devised to accommodate genotoxic carcinogens and compounds where genotoxicity has not been well defined by experimental evidence.

$$\text{Acceptable Human Exposure (mg/day)} = \frac{[\text{Model } (10^{-2})] \times [\text{Human Equivalent dose}]}{10^{1} \times 10^{2} \ldots}$$

Approximate Risk Level

10^{-2} **Model:** Mathematical model (probit, multihit, multistage, etc.) utilized to predict risk to 10^{-2} from experimental animal data. (Used to predict only what would be expected to occur in rats, mice, etc.) The use of the 95% confidence interval of these models is equivalent to an additional safety factor of 2 to 5 fold, i. e., for an experiment of 10 animals $\cong$ 5 for 100 animals $\cong$ 3, 1,000 $\cong$ 1.8.

10^{-1} **Human Equivalent Dose:** Model commonly used, involves:

$$\frac{\left[\frac{\text{length of exposure}}{\text{length of observation}}\right]\left[\frac{\text{length of observation}}{\text{life span of animal}}\right]^{\frac{3}{4}}}{\sqrt[3]{\frac{70 \text{ kg (average man)}}{\text{average animal weight}}}}$$

This is a conservative model and should be modified where pharmakinetic data is available. When no comparative metabolic data is available, this model will yield a safety factor of $\sim$5 to 6 fold in the conversion of rat data to a human equivalent dose and $\sim$ 13 fold for the conversion of mouse data.

10^{-1} 10_1 = uncertainty factor for extrapolating from average to sensitive man.

10^{-2} 10_2 = uncertainty factor associated with data base. With good negative data in other experimental animals, a factor of 1 might be used.

TOTAL RISK FACTOR

10^{-3} 10 . . . = policy and other parameter

This type of quantitative risk model is a useful tool for developing permissible exposure levels and meets the requirements of the case law, the Act and the Executive Order. It is flexible enough to accommodate the growth of scientific knowledge and clearly uses the best evidence available to develop permissible exposure levels. In addition, the safety factor in the model can be utilized to meet the Cotton Dust mandate to protect worker health. Quantitative risk assessment is also compatible with feasibility assessment and efforts to reduce the cost of regulation.

III THE CANCER POLICY'S STRONG PREFERENCE FOR ENGINEERING CONTROLS SHOULD BE DELETED SO THE ISSUE OF CONTROLS CAN BE ADDRESSED ON A CASE BY CASE BASIS

A method of quantitative risk assessment may be useful for developing permissible exposure levels, but it does not address the issue of how these levels should be achieved. As it is presently drafted, the cancer policy expresses a strong preference for engineering and administrative controls as a means of attaining permissible exposure levels. Personal protective equipment, such as respirators, are permitted only after all feasible engineering and administrative controls have been implemented.[17] This strong preference for controls is

17 There are many provisions in the standard that express the agency's preference for engineering and administrative controls. However, the model standard at 29 C.F.R.§ 1990.151(g)(1) (1978) probably best summarizes the agency's position:

> (i) The employer shall institute engineering or work practice controls to reduce and maintain employee exposure to _____ to or below the permissible exposure limits, except to the extent that the employer establishes that such controls are not feasible.
> (ii) Engineering and work practice controls shall be implemented to reduce exposures even if they will not be sufficient to reduce exposures to or below the permissible exposure limits.

part of OSHA's zero risk policy because the preference extends to the outer limits of engineering technology and does not consider cost until the viability of a substantial part of an industry is threatened.

The rejection of cost-benefit analysis in the Cotton Dust case has been cited in support of the preference for engineering controls. In that case, the Supreme Court noted that "Congress itself defined the basic relationship between costs and benefits, by placing the 'benefit' of worker health above all other considerations save those making attainment of this benefit unachievable."[18] The cost-benefit analysis discussed in the Cotton Dust case, however, only pertains to that phase of the rule making procedure where the permissible exposure level is established, i.e., where worker health considerations are examined to set the permissible exposure level.[19] Cost-benefit analysis does not pertain to the next phase of the rule making process where OSHA considers the means by which the established permissible exposure level should be attained. The assessment of the costs of controls vis-a-vis the costs of personal protective equipment involves cost-effectiveness analysis. This type of cost-effectiveness analysis, which pertains to the means of compliance, should not be confused with the cost-benefit analysis discussed in the Cotton Dust case,

18 101 S.Ct. 2478, at 2490.

19 It follows that the directive in Cotton Dust to protect worker health should be integrated into the safety factor factor used in the quantitative risk assessment.

which addresses the establishment of permissible exposure levels. The Cotton Dust case, therefore, does not bar the consideration of cost-effectiveness analysis when determining the means of compliance.

The cancer policy's preference for engineering controls is not compatible with cost-effectiveness analysis beause it is part of the zero risk policy that pushes controls to the limits of technology with little or no regard for cost. This zero risk policy was specifically rejected in the Benzene case, where the Supreme Court declared that "safe" was not equivalent to "risk-free." When the Cotton Dust case is examined in light of the Benzene holding, it becomes apparent that the standard's inflexible position on engineering controls is contrary to the case law.

The preference for controls is also in conflict with Section 6(b)(5) of the Act, which requires OSHA to use the best scientific evidence available. The preference for administrative and engineering controls is based upon the assumption that personal protective equipment is inferior to controls. However, since the standard was promulgated, there have been dramatic improvements in personal protective equipment, particularly in the area of respirator technology.

In support of its bias against respirators, OSHA recently raised seven points as grounds for its objections.[20] These seven points, and countervailing arguments, are outlined below:

20 General Industry Standards & Interpretations, 1 O.S.H. Subscription Service 889 (1982) (as codified at 29 C[illegible] § 1910.1029).

1. Poor facial fit--Proper fit was a problem in the past, but this is no longer a major area of concern. There has been a great deal of research on facial characteristics and manufacturers have developed respirators in sufficient sizes and shapes to accommodate almost everyone. In addition, several fit tests have been developed to determine which respirator is compatible with a particular employee's facial characteristics.

2. Breathing resistance--As the level of an employee's activity increases, the breathing resistance of the respirator increases. Reynolds Metals Company has had over 9,000 employees in respirator programs since 1978. Breathing resistance has not been a problem, though this might be due to the "healthy worker effect." In those isolated cases where breathing resistance is a problem, the 3M W-316 Airhat provides an adequate solution.

3. Heat stress--The problem of heat stress involves the whole body, not just the small portion of the face covered by a respirator. Therefore, it is highly unlikely that respirators contribute to heat stress. Moreover, where heat stress problems do exist, respirators can be used to alleviate the problem by using air supplied respirators with vortex cooling tubes.

4. Vision difficulties--The development of wide angle facepieces have drastically reduced the signifiance of this problem.

5. Voice communications--In low noise areas, the flexibility of inhalation valves permits voice communication. In high noise areas, experience has indicated that hand signals are an effective alternative to voice communications. Moreover, in high noise areas where voice communications are essential, respirators can be equipped with communication devices.

6. Jaw movement--Talking or laughing sometimes temporarily breaks the seal of a respirator. Jaw movement, however, has been incorporated into most fit testing procedures and is calculated in the fit factor.

7. Skin irritation--In rare instances, the rubber or plasticizers in respirators have caused irritation among hypersensitive individuals, but new developments with silicone and other nonreactive materials should solve this problem.

The employees' failure to wear respirators is another objection that should be addressed, though it was not mentioned in OSHA's list. The experience of industry as a whole has revealed that employees will wear respirators where: (1) the respirator program is supported by management, (2) the employees

receive thorough initial training, (3) training is reviewed regularly, and (4) there is a rigid enforcement policy. In those situations where participation is less than total, one of these four elements is usually deficient. Such deficiencies, however, can be overcome.

When reevaluating its objections to respirators, OSHA should also consider advances in the development of protection factors for respirators. Reynolds supports the concept of an overall protection factor (PF^1) that combines a fit test factor (FF) with a filter element protection factor (PFe). An overall protection factor for a particular respirator could be determined for each employee by using the following equation:

$$PF^1 = \frac{FF + PFe}{PFe + FF-1}$$

The first variable in this equation is the fit factor (FF), which can be determined through normal quantitative fit testing on each employee. The second variable is the filter element protection factor (PFe). The (PFe) for each respirator can be determined by operating two stationary sample pumps in the same work area for an eight hour period. Each pump should be equipped with a test patch. The first test patch should collect contaminants in the unfiltered air of the work environment. The second should collect contaminants from air passed through the respirator's filter material. The (PFe) is obtained by comparing the amount of contaminant on the two test patches.

Respirator protection, therefore, has come a long way from the days when employees merely tied handkerchiefs over their faces. But OSHA has not taken full advantage of advances in respirator protection because the cancer policy is still wed to the preference for engineering and administrative controls. OSHA's failure to seriously consider this evidence is contrary to the spirit of scientific inquiry and violates the Act's mandate to consider the best evidence available.

The standard's preference for engineering controls also violates Executive Order 12291, which clearly supports cost-effectiveness analyses. As noted in the prior discussion, the Executive Order specifically provides that agencies must choose the least costly method of achieving a particular goal and must consider the industries affected, the national economy and future regulations.[21]

On the basis of the foregoing, it is clear that the standard's strong preference for administrative and engineering controls is contrary to the case law, the statutory mandate to use the best evidence available, and the directive in Executive Order 12291. Accordingly, those provisions in the standard that create this ~~ri~~gid preference should be deleted.

To replace the preference, Reynolds recommends that the issue of engineering controls vis-a-vis personal protective equipment be examined on a case by case basis. OSHA must recognize that each carcinogenic chemical has its own unique

21 Executive Order 12291 § 2(d) and (e).

characteristics. A strong genotoxic carcinogen like vinyl chloride monomer should not have the same permissible exposure level as a weak nongenotoxic carcinogen like chloroform. There must be similar flexibility in determining the means by which the various permissible exposure levels should be achieved. The type of controls available in a vinyl chloride plant might be quite different from those available in a chloroform plant. Respirator protection factors might also differ to create a unique cost-effectiveness balance in each case.

This case by case approach offers OSHA innumerable options in its rule making proceedings. In some situations, engineering controls might be the only acceptable means of achieving the permissible exposure level. In other cases, a two tiered system might be implemented where engineering controls would be required to reach one level, e.g., ten parts per million, and then an option of respirators or engineering controls might be offered to further reduce exposure to another level, e.g., two parts per million. For some chemicals, the prescribed method for achieving the permissible exposure level might vary from industry to industry depending upon the types of controls available.

This flexible approach to controls and respirators is more complex than the rigid preference and, as a result, it would be more difficult to administer. But biology, chemistry and the means of mass production are complex subjects. Denying this complexity for reasons of ease of administration will not

resolve the hard issues that arise when industry must implement new technology.

This case by case approach also meets the requirements of the law. It complies with the holding in the Cotton Dust case because it provides OSHA with a wide range of options to develop feasible means of protecting worker health. At the same time, it encourages the consideration of the best evidence available, as required by the Act, and does not involve the zero risk policy that was rejected in the Benzene case. Moreover, the case by case approach complies with the Executive Order because it permits the adoption of the most cost-effective means to protect employee health.

III CONCLUSION

The foregoing discussion of the cancer policy might be summarized as follows:

1. The cancer policy's method for classifying carcinogens is not supported by science or the law. It should be replaced by a ranking system, similar to the Squire method, that will accommodate the growth of scientific knowledge.
2. The no-threshold provision in the standard, as applied to the establishment of permissible exposure levels, is not supported by science or the law and should be deleted. To assist OSHA in developing permissible exposure levels, the agency should adopt a method of quantitative risk assessment.

3. The cancer policy's preference for engineering and administrative controls is not supported by science or the law and should be deleted so the issue of controls can be addressed on a case by case basis.

Respectfully submitted,

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