

ETHYL CORPORATION

TOXICOLOGY AND INDUSTRIAL HYGIENE DEPARTMENT

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January 3, 1978

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LAW DEPARTMENT	
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FILE	

Mr. D. F. Peters
Hunton and Williams
P. O. Box 1535
Richmond, VA 23212

Re: Second Draft - OSHA Proposal to
Regulate Suspect Carcinogens

Dear Mr. Peters:

Gary has asked that I send the attached second draft proposal to OSHA regarding their plans to regulate suspect carcinogens in the workplace. Note that we have added the section you contributed as Section L and made the other changes you suggested. Thanks very much for your contributions. Also, we have added a new section, Section F, covering potency variations of carcinogens and recommendations on risk/benefit analysis. Please send us any additional suggestions you have. Suggestions are also requested from the other recipients of this memo.

We must now submit our final draft comments by
January 30.

Sincerely,

J. Roger Mangham
J. Roger Mangham

JRM:bto

Attachment

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Produced under Order 1/11/00 in Rosa v. Conoco #90-4837 c/w Landon #97-
14th Judicial District Court, State of Louisiana. All claims of private
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VC1188

Second Draft

COMMENTS ON:

OSHA'S PROPOSED RULES

Identification, Classification and
Regulation of Toxic Substances
Posing a Potential Occupational
Carcinogenic Risk

Ethyl Corporation
December 30, 1977

Produced under Order 1/11/00 in Ross v. Conoco #90-4837 c/w London #97-7949
14th Judicial District Court, State of Louisiana. All claims of privilege,
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A. Summary

OSHA proposes to establish by generic rule certain pre-somptions as to the health effects and risks involved with chemical substances or uses associated with a particular substance. Historically, the control of human exposures to chemicals, including carcinogens, has been based on the specific evaluation of the hazards of the individual chemicals on a case by case basis. This has succeeded well in that citizens' groups such as ACGIH, ANSI, ASTM, AIHA, etc., have been formed to preside over the development of standards, such as TWA's (TLV's), LD₅₀'s, skin and eye irritation ratings, etc. The result has been a steady decline over the years of worker injury and death in the chemical industry--and indeed, an increased longevity among the general population of the industrialized nations. The recent increased concern about chronic effects, such as carcinogenicity, mutagenicity, teratogenicity and reproductive effects should not cause us to lose sight of our previous successes in dealing with toxic manifestations of chemicals--and the continued development of mechanisms to bring about changes as new understandings occur.

In the Proposed Rules OSHA couches its approach to regulation in an "attitude of prudence". While this may strike a positive moralistic note, it sets the stage for promulgation of inappropriate regulations and caters to the "advocate" investigator who inadvertently prejudices his findings in the design of his experiments. As recently noted by Dr. Arthur Furst, a noted expert on cancer, cancer can be produced from 90% of the chemicals encountered if the experiment is deliberately designed to accomplish that result.

OSHA should be cautioned against hasty action based on inadequately established "scientific data" that has not been subject to thorough scientific peer review. Rather, the agency should start from a "neutral" position and rely on evidence only insofar as it has been carefully developed,

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well replicated, thoroughly checked and given a searching peer review.

Ideally, the sequence of events leading to an administrative rule affecting the use of a substance on health grounds would be as follows:

1. The experiment
2. Interpretation
3. Peer review and publication
4. Review by interested parties
5. Administrative response

In the present proposal, steps 2 through 4 would be skipped entirely with the basic experiment leading directly to the administrative response. Any such simplistic short-cutting would be a disservice to scientific analysis and to sound administrative planning.

As a general rule, good human epidemiological evidence should take priority over animal study results. There is now excellent evidence for acceptance of a threshold level for exposure to chemical carcinogens below which safe exposure limits can be set. Further, carcinogens vary in potency, with some being a million times or more greater in potency than others. Potency variations, along with variations in the route of exposure and pharmacokinetic variables, make it essential that each proven or potential carcinogen be subjected to a thorough, realistic risk/benefit analysis before regulatory action is taken.

Accordingly, Ethyl strongly recommends that there be no standardization of the regulatory response to toxicological experimental results. Rather, the so-called generic approach to rule making should deal with such facets as: notification of use and emergencies, regulated areas, methods of compliance, housekeeping, waste disposal, general medical surveillance, employee training and education, precautionary signs and labels, record keeping and the like.

B. Background

The historical approach to the control of human exposures to hazardous chemicals has been an individualized one. This has been imminently successful, as witnessed by an increased longevity among the people of industrialized nations. Worker injury and death in the chemical industry has shown a steady decline over the years. This approach should not now be changed to regulate compounds on a stereotyped basis using assumed toxicological relationships, where the connection among the individual chemicals is little more than theoretical in nature and where results from studies have not been adequately discussed in public hearings.

This is not to say that individual chemicals cannot be rated (after thorough experimental study) for their specific ability to produce toxic reactions. Thus, standardized toxicological ratings for individual chemicals have to date proven themselves successful in application in the workplace and in the environment of TWA's (TLV's), LD₅₀'s, LC₅₀'s, skin and eye irritation ratings, etc. Also, published information such as the DOT shipping regulations, MCA technical bulletins, AIHA's Hygienic Guide series and the like rely for the most part on rating the acute toxicity potential of individual chemicals.

C. Scientific Experimental Results Need Peer R view Before Promulgation as Regulations

On p. 54171, Col. 1, of the Proposed Rules, it is stated (emphasis added):

"Section 1990.111 sets forth the circumstances under which the Secretary determines that the evidence rebuts the presumption of a Category I classification. This section is one of the key sections of this proposed set of regulations. The Secretary may find that a Category I classification of a substance is not warranted if he scientifically determines on the basis of the evidence: (a) that the alleged carcinogenic effect based on animal data clearly resulted from nonspecific physical, rather than chemical induction; (b) that the route of exposure was grossly inappropriate relative to the potential occupational routes of human exposure; (c) that the animal or human studies submitted for review were only suggestive; (d) that the human or animal studies are totally inadequate to establish any conclusion with respect to the carcinogenicity or noncarcinogenicity of the toxic substances; or (e) that for some other scientific reason, the positive results in experimental mammals are not relevant to man. Any such determination by the Secretary shall be after consultation with the Director of NIOSH and published in the Federal Register. In the event that the Secretary finds that a Category I classification has been rebutted, he shall classify the substance as either a Category II or III toxic substance."

We agree that this is a key section in the Proposed Rules, but we disagree with the proposed mechanism. No matter how talented and unbiased the Secretary is, this

type of decision is for scientists to make. Historically, this has been by a peer review mechanism which allows for the interplay of a variety of scientific orientations and disciplines. We feel this should continue.

Section 1990.111 of the Proposed Rules carries with it a presumption that the chemical in question is carcinogenic. This sets a tone and attitude in OSHA, and in the public view, that there is a problem with the chemical under consideration. This should not be. The Secretary should make no presumption regarding the danger or safety of a compound. When data becomes available the Secretary should set in motion procedures to evaluate fully the study, but there should be no presumption of safety or danger until the evaluation is complete.

In many cases today, industry and government rely on preliminary results of studies. If the OSHA administrator acts before the full, final report is available and the data are evaluated, unnecessary restrictions could be placed on the workplace and, indeed, chemicals could be forced off the market without a fair hearing.

An excellent illustration of the need for peer group review is provided at 42 Fed. Reg. 54179, Col. 2, of the OSHA proposal. There it is said (emphasis added):

"The use of precautionary labels on containers of protective clothing contaminated with the toxic substance is required. We are mindful that no evidence may presently exist that laundry workers who handle contaminated clothing containing any specific carcinogen exhibit an excess of cancer. However, no evidence exists to the contrary, and in light of our experience with other carcinogens (e.g. asbestos) and the preventative nature of the Act, we have decided to include a requirement for precautionary labels for contaminated clothing. Moreover, OSHA believes it is as appropriate that

individuals who are engaged in handling and laundering the contaminated clothing be apprised of the hazard and practices to be avoided when handling the clothing as it is to inform the other primary employees."

Can this statement truly be characterized as "scientifically based"? What about articles of clothing contacted with vinyl chloride monomer, a fugitive gas? What about OSHA's requiring that a material or procedure be shown to be safe? This cannot be done! It can only be shown that a material or procedure is not dangerous.

It would be a serious error for the administrator to set policy which deprives interested parties of a fair hearing. Difficulties inevitably arise if an immediate regulatory response is given as each bit of scientific information feeds into the regulatory process. The mechanism must be established and time must be allowed for a mutual interaction of all parties involved, permitting the following sequence of events:

1. The experiment
2. Interpretation
3. Peer review and publication
4. Review by interested parties
5. Administrative response

D. Human Epidemiological Evidence Should Have Priority Over Animal Study Results

OSHA's proposal states the following as to the relative merits of animal test data as against human epidemiological evidence (42 Fed. Reg. 54161, Col. 3) (emphasis added):

"And, it should be noted that certain chemicals may be carcinogenic in certain species, including man, but not in others. For example, betanaphthylamine, a known carcinogen in man, monkeys and dogs, is not apparently carcinogenic in rats or rabbits. Hence, positive studies in any mammalian species will, as a general rule, always supersede negative findings in another species. (UICC 1969, p.18; NCI, 1970, p. 2; NCAB, report, p. 9).

Thus, OSHA believes that, as a practical rather than a theoretical matter, positive animal data should supersede negative human data, in general, because of the inherent defects in such human studies, as pointed out above."

This statement misses the basic idea of toxicological experimentation, which is to find out what effects individual chemicals have on man. When the effects on man are known, why use animal data? It is the moral problem involved in experimenting on man which led to experimentation on animals in the first place. Indeed, in the development of new foods, food additives, drugs, and cosmetics, after an initial animal experimentation phase of study, experimental work has to be cautiously extended to man himself.

Animal evidence can be important, and indeed, teaches us what to look for in epidemiologic studies. But the fact must be recognized that man and animals--and, indeed, individual animals--react differently to chemicals. This very difference permits the use of particular chemicals as both drugs and pesticides. In these cases we are able to rely on the established fact that certain drugs are more toxic to pathogens than to man, and certain pesticides are more toxic to pests than to man.

Furthermore, absolute toxicity in the use of drugs and pesticides is not the only consideration. Another important aspect is the mode of administration. Thus, insecticides and repellents which are toxic orally or by inhalation frequently may be applied without harm to the skin of animals or man--because the skin serves as an effective barrier to the poison. Thus, toxicologists consider it inappropriate to rely heavily on data relative to the oral toxicity of a chemical which is essentially subject only to inhalation or dermal contact, and vice versa, in the use situation.

Because of the foregoing considerations, good epidemiological evidence should supersede animal evidence of, say, weak carcinogenicity. Animal data does not assure a chemical will or will not cause cancer in man. In the case where a chemical tested on animals only is to be recommended by OSHA as a substitute for a more established one with a clean epidemiological record, there is a distinct possibility that the carcinogenicity hazard to man will actually be increased. Thus, OSHA's Proposed Rules, as formulated, offer the distinct possibility of increasing workplace hazards rather than decreasing them.

D. Threshold Theory vs One Hit Theory for Carcinogens

From a practical standpoint, it has been demonstrated for many carcinogens that safe exposure limits can be set. This is the best evidence for accepting that there is, indeed, a threshold level of exposure below which the carcinogen can be considered to be essentially harmless to man. For example, lead has been shown to be a carcinogen in animals yet many epidemiological studies show it does not cause cancer in man. Also, cadmium is known to produce cancer in animals, yet low levels in man do not cause cancer. These two metals are naturally present as trace elements in each of us, yet we do not all get cancer. According to the "one hit theory", exposure to these traces of metals would eventually result in cancer if we live long enough. The phrase, if we live long enough, represents the greatest weakness of the one hit theory. Isn't it also the case that we will all die of pneumonia if we only avoid other diseases long enough? Industry experience teaches that thousands of workers have been exposed to low levels of vinyl chloride vapors without ill effect. Only some of those who have been exposed to high levels have developed the characteristic angiosarcoma.

The one hit theory is not supported by good evidence. To the contrary, carcinogens, as do other toxicants, exhibit a dose-response curve. In fact, Dr. H. E. Stokinger (J. Am. Water Works Assn., July, 1977, pp 399-402) recently stated: "To extrapolate the significant cancer incidence obtained only at the high concentrations is sheer folly".

In another paper, Dr. P. G. Watanabe, et al ("Summary of the Studies Conducted on the Pharmacokinetics/Metabolism of Vinyl Chloride in Rats", Toxicology Research Laboratory, Dow Chemical Co., Midland, Mich., May 31, 1977) found that: "1) the metabolism of VC to a reactive metabolite which is ultimately responsible for carcinogenicity is a saturable process; and 2) the detoxification of VC at exposure levels

below 10 ppm is more efficient than at higher levels and this diminished ability to detoxify VC at higher levels correlates with the induction of hepatic angiosarcoma". The paper went on to say: "The dose-related increase of hepatic angiosarcoma in rats exposed to VC concentrations ranging from 50-500 ppm (Maltoni data) correlates well with the dose-related depression of GSH (hepatic glutathione sulfhydryl)". Overall, the indications are that at concentrations of 50 ppm and less the vinyl free radical from VC is completely annihilated by the liver sulfhydryl.

E. Nachtomi (Biochem. Pharmacol. 19, 1970, pp 2853-2860) has reported that glutathione is also involved in the metabolism of ethylene dibromide, primarily in the liver and to a lesser extent in the kidneys. He has shown that the capacity of rat liver and kidney to metabolize EDB exceeds the amount of EDB inhaled from an atmosphere containing 25 ppm (192.5 mg/m^3) by a factor of about 100.

The case for an acceptable level of exposure to carcinogens is made by Dr. J. A. Zapp (Am. Ind. Hyg. Assoc. Journal, Sept. 1977, pp 425-431) as follows:

"As the dose of a carcinogen is increased, the proportion of exposed animals developing tumors is not only increased, but the time to appearance of tumors is decreased. As the dose of carcinogen is decreased, the proportion of exposed animals developing tumors is not only decreased, but the time to appearance of tumors is increased. Druckery, in Germany, proposed a mathematical relationship which is very simply expressed:

$$Dt^n = k$$

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Here D=total dose of carcinogen, t=time to appearance of tumors, and n is an exponent greater than one which expresses relative potency of the carcinogen. In Druckery's own experiments with multiple dose levels of a potent carcinogen, he eventually reached a low dose level which did not produce any tumors. He reasoned, by extrapolation,

that this dose would have produced tumors if only the animals could live long enough.

A World Health Organization Scientific Group commented on the phenomenon as follows:

'The summation effect described by Druckerey and others is not questioned and his equation characterizing carcinogenic potency may be accepted. Nevertheless, every organism has a limited life span and in this sense there is, for each individual a real threshold'."

This hypothesis makes an assumption that an individual and the population from which he is drawn remains constantly susceptible to a carcinogen. The action of cancer "promoters" is sufficient to show us that something more is needed. That would seem to be a clear understanding of the threshold which can be moved in a predictable way. Prediction requires, for any effect, a data base which we all agree is incomplete today. But no new mechanism is needed, especially the currently "fashionable" one hit theory.

It is important to emphasize that detoxification mechanisms for many chemical carcinogens, such as VC and EDB above, are saturable processes. Thus, very high dosing levels in animal studies are generally inappropriate since the excessiv amount of the carcinogen in the test animal is not metabolized in the same fashion it would be at low level in that sp cies -- the normal condition which exists in the workplace when good industrial hygiene practices are employed. The Proposed Rules, on p. 54161, Col.3, make the contrary point:

"The testing of chemicals at constant high exposure levels, at or approaching the maximum tolerated dose level, is not inappropriate and is indeed required to overcome the statistical insensitivity of laboratory bioassays conducted with the limited numbers of animals that can b handled in practical laboratory conditions (WHO Tech. Rept 220, p. 9:

Mrak Commission, p 487: UIAC 1969, p. 17). As the NCI Ad Hoc Committee's report to the Surgeon General stated:

. . . bioassay methods have remained tools of low sensitivity, capable only of detecting the highest peaks of carcinogenic activity. The factor which limits bioassay sensitivity is usually the small number of test animals used. If the bioassay design has a low probability of detecting carcinogenic effects produced by hazards at levels comparable to those present in environmental samples, then tests at such levels are wastes of time, effort and money. The need to test levels higher than those found in the environment is thus founded.^(p.7)"

The point made would be true if we wanted to generalize (predict) the case for high exposure levels for 200 million rats. However, the testing objective is to determine the capacity of a chemical to induce cancer by any one of a number of mechanisms. Thus, as indicated above, the very high dosing can perform the undesired function of overwhelming the normal detoxification and/or excretion mechanisms. An example of this is the excessive chelation of body minerals by the use of large doses of a chelating chemical. The upset in the body's mineral balance in such a case may cause severe toxic effects where lower, more tolerable doses would not be unreasonably toxic. It certainly seems unreasonable to dose animals for lifetime studies for carcinogenesis evaluation at such excessive levels that the animals are sickly, i.e., are in a compensatory state, the entire time.

Dr. H. E. Stokinger put the relationship of suspected animal carcinogens and human cancer very clearly into perspective in a paper presented in Kansas City, Missouri, on October 25, 1976 ("The ACGIH Classification Scheme for Occupational Carcinogens"). In his discussion he stated:

"The finding of a substance to be tumorigenic, often in a half-dead mouse or rat from intolerable doses, as it was in the case of chloroform and trichlorethylene, is not Ipsso Facto evidence that it will be carcinogenic in man under controlled, working conditions."

He went on to say,

"Examples of the misleading nature of extrapolating original data on tumorigenesis to man are accumulating almost weekly; ethylene dibromide, an industrial chemical, has been shown to elicit squamous cell carcinomas of the stomach in mice and rats at very high incidence (87% and 76%), yet nearly 50 years of industrial experience has revealed no evidence of adverse health effects in the manufacture and handling of ethylene dibromide".

F. Variation in the Potency of and Mode of Exposure to Carcinogens Provides Latitude So That Control of Individual Chemicals Can Be Based on a Risk/Benefit Analysis

The Proposed Rules take the position that an experimental model will provide a simple yes or no answer as to whether a chemical is a carcinogen, and that all positive tests will require the same regulatory response. This approach neglects the well-established principle that chemical carcinogens vary greatly in potency.

Bruce N. Ames, a biochemist at the University of California at Berkeley, presented his views on this subject at the 174th national meeting of the American Chemical Society on August 31, 1977. Ames' report dealt with work he and his co-workers have done in relating mutagenicity and carcinogenicity of chemicals. Ames said, "We have to think quantitatively and look for the most potent carcinogens. We haven't had this knowledge until recently." In addition to potency, the amount of exposure to a chemical must be considered in evaluating risk, Ames said. For example, he observed that cigarette smoke has been shown to be a relatively weak carcinogen when compared to other substances; however, smoking is particularly damaging because of the amount of exposure smokers receive. From his studies, Ames has found that some substances are a million times more mutagenic than others; and he says that a similar range seems to exist for carcinogenicity. He cited the example of aflatoxin which has been shown to be one million times more potent as a carcinogen than trichloroethylene. Ames contended that information about such differences should be used by the decision makers to whom is delegated the authority to provide regulations for controlling human exposures to carcinogens.

The subject of potency was addressed effectively by Row and Raven in their book, "The Prevention of Cancer",

when they stated a positive result in a laboratory test will most likely be significant if the dose used was small (or realistic); if the route of administration was similar to that in man, and if the result was confirmed in the same species or in other species. They are saying, essentially, that it is easy to call bis-chloromethyl ether a human carcinogen but it is difficult to quantitate the carcinogenic risk of saccharin for man.

A "potent carcinogen" must be defined--and this has been done by the American Conference of Governmental Industrial Hygienists. They say ("TLVs^B for Chemical Substances in the Workroom Environment" - 1977) that a potent carcinogen is one which produces cancer in an experimental model when the atmospheric exposure is at a concentration of one milligram per cubic meter or less. Thus, chemicals which do not produce cancer at this atmospheric concentration are not potent carcinogens. Also, ACGIH goes on to say, on p. 40 of the booklet: "Substances occurring in the occupational environment found carcinogenic for animals may be grouped into three classes, those of high, intermediate and low potency." Clearly, all carcinogens do not present the same risk and thus do not require the same regulatory response.

It should be emphasized that the evaluation of carcinogenic hazard for man should be based on a judgment of all available information. That is, the evaluation is based not only on a carcinogenic bioassay, toxicity tests, epidemiological data, and on the extent and route of exposure of man, but also on metabolic, biochemical, and pharmacokinetic studies. This is to say that each chemical must be evaluated relative to the nature of its absorption, distribution, metabolism, retention, and excretion.

In a recent article (Science, Vol. 198, November 1977, pp. 693-699), Jerome Cornfield provides an excellent

treatment of carcinogenic risk assessment. Cornfield states that in many cases, important benefits are lost if a substance is banned after proving carcinogenic to experimental animals in high doses. He states that the magnitude of the risk must be balanced against the benefit conferred. He goes on further to describe a more fundamental problem--that of "conservative" risk assessments. Such risk assessments, he says, distort the cost-benefit analysis since an exaggerated estimate of risk cannot be balanced against a sober analysis of benefit. He goes on to conclude that "conservative" risk assessments are inappropriate in decision-making. Rather, the more rational approach is to base judgment on expected risks and expected benefits. Cornfield also says that the decision-maker who uses a "conservative" risk assessment should not proceed under the guise of having made the appropriate mathematical assumptions. He recommends that, if a value judgment is made, this should be clearly stated, accepted as such and not be introduced in such an intellectually muddled way that no one knows which are the facts and which the judgments.

OSHA thus should face the difficult problem of addressing itself to carcinogenicity risk/benefit and evaluate both the risk and the benefit in a realistic way. In some cases the need for a risk/benefit analysis is obvious, e.g. use of pesticides to prevent malaria epidemics, medical X-ray technology, chemotherapy, etc. But the same analysis must be made even where the risks and the benefits are less clear. For the long-term welfare of the country, it seems essential that OSHA make the effort.

G. Evidence Suggests No Cancer Epidemic Due to Workplace Chemical Exposures

The Proposed Rules, 42 Fed. Reg., 54156, Col. 2, state:

" . . . Thus, what is true of carcinogenesis for an individual or a working population is also true for society, namely that an epidemic of cancer may be in the making while exposure to the unknown carcinogenic agent continues for decades, multiplying its potential effects".

This "scare tactic" has no basis in fact as there is no evidence of a cancer epidemic in the workplace. In fact, modern chemical workers have enjoyed an increasingly healthy work environment as injury and death from occupational exposure have steadily declined. This is one manifestation of the overall increased longevity among the people of industrialized nations.

H. Animal Tests Should Be Well-designed, Unequivocal and Complete

OSHA suggests in the Proposed Rules that a substance be placed in Category I Toxic Substances if evidence concerning such substance was developed in a single mammalian species, and if those results have been replicated in the same species in another experiment or supported by short-term tests, as defined. This delineation is clearly inadequate. If the test was done improperly the first time, it will prove nothing to repeat the test on the same species of animal in the same improper manner.

Certainly, animal testing is subject to wide variations because of the nature of work with biological systems. Further, it is recognized that many of the commercial toxicology testing laboratories in this country are putting out work of uneven quality. Both FDA and EPA have officially acknowledged this fact. Besides the obvious difficulties arising from poor quality work, problems arise because of strain differences in susceptibilities in the test animals, variations in length of "life-time" tests, use of improper protocols (including, for example, improper route of toxicant administration), use of animals inappropriate to the study, disease in the test colonies, calamities such as utility failures, not doing histopathology evaluations on some of the test animals because of untimely deaths, tissue autolysis before evaluation, etc.

The histopathology evaluations are themselves subject to rather wide variation, as is well known. In this area, whether a tumor is benign or malignant has been the subject of considerable debate--and different interpretations have accordingly affected the test results reported. OSHA has suggested that benign tumors can cause death. However, in our view this should be considered a reversible disease in humans since an operation can solve the problem.

NCI, in particular, has relied heavily on gavage studies. Many investigators think this approach is often inappropriate,

especially where expected human contacts would be almost altogether by other routes. In the case of EDB, for example, industrial workplace exposures would be by skin contact or inhalation. Yet EDB was recently proposed for classification as a workplace carcinogen by NIOSH (Criteria Document for EDB) based on the results of one gavage study.

In 1973, Olsen, et al (J. Nat'l. Cancer Inst., 51, 1973, pp 1993-95) reported the development of squamous cell carcinoma in rats and mice following daily doses (40-200 mg/kg/day) of EDB in corn oil by intubation for 52 weeks. This was an extreme insult to the animals as EDB is a severe irritant in contact with skin or eyes. Exposure of humans to high concentration of the vapor has caused the development of respiratory tract inflammation (Marmetschke, Vierteljahresschr Gerichtl Med Oeff Sanitastawes, 40, 1910, pp 61-76). It is not surprising that continued irritation of the stomach produces a response to EDB.

Robbins and Angell (Basic Pathology, 2nd Ed., 1976, W. B. Saunders Co., p 117) state that "protracted chronic inflammation predisposes to squamous cell carcinomas; furthermore, neglected cases may become deeply invasive and metastasize to surrounding tissues". This type of inflammation was very probably elicited in the EDB animal feeding studies. This would explain the observations of Olsen et al who found diffuse squamous cell hyperplasia in the forestomachs (cardiac portion) at the site of administration with many papillomatous projections which eventually metastasized by direct invasion through the stomach wall into the peritoneal cavity--and in some animals by the hematogenous route to the lungs and other tissues.

We emphasize that the squamous cells occurred at the site of application, the forestomach of the rat, a portion of the anatomy which does not have a counterpart in humans. Such a study is clearly inadequate as a predictor of cancer in humans.

That studies such as Olsen et al are inadequate was recognized in the report prepared for the Surgeon General in 1970 by the Ad Hoc Committee of the NCI. That report dealt with problems of exposure to chemical agents. It stated in a discussion of extrapolation of cancer in animals to man that while a correlation can usually be made, exceptions should be considered where the carcinogenic effect is clearly shown to result from physical, rather than chemical, induction, or where the route of administration is shown to be grossly inappropriate in terms of conceivable human exposure.

The foregoing discussion and examples deal with problems encountered by the most well-meaning of researchers. What about the "advocate" type of investigator? Whether he realizes it or not, he prejudices the findings usually in the design of the experiment. For this type of investigation, peer review is the best hope for bringing about a more rational evaluation of the test program. Illustrative of how far "off base" a biased experimenter could go, Dr. Arthur Furst, a noted expert on cancer, stated before the Moss Subcommittee on Consumer Protection that he could produce cancer 90% of the time using any chemical, if he were given the freedom to design the experiment as he chose. Clearly it is not proper for the administrator of OSHA to decide which are proper studies. This requires intensive review and hearings.

I. OSHA Regulations Should Not Be Anti-Industry

In a number of respects the Proposed Rules show a marked anti-chemical industry bias. On p. 54180, Col. 2, it is said that employers must provide employees or their representatives with the opportunity to observe monitoring of employee exposures to toxic substances or harmful physical agents. This work could extend for periods of time ranging from hours to days or even weeks. If the employee or his Union want this, it should be provided for through the usual "bargaining" between an employer and its employees. Only in this way will the costs be evaluated and appropriate guidelines specified.

A similar area of concern appears on p. 54190, Col. 2-3. This specifies that employees who wear respirators shall be allowed to wash their face and the respirator facepiece to prevent potential skin irritation associated with respirator use. Should the employee be allowed 10 minutes an hour for this? Longer? What about proper washing of a respirator facepiece? Will the employee have to be supervised by the company's safety representative during this operation? Here again, this should be handled by "bargaining" so that costs can be controlled and appropriate guidelines specified.

On p. 54192, Col. 1, is a similar, yet perhaps more serious example of OSHA's intrusion into an area heretofore left to employee-employer bargaining interactions. The Proposed Rule would provide access to the employee's medical records to a physician designated by the affected employee, former employee, or designated representative. This proposal constitutes a violation of the worker's right to privacy and its enactment could result in the use of employee records for nefarious purposes. This rule is tantamount to publishing the OSHA log at each plant.

The Proposed Rules frequently give the distinct impression that OSHA intends to work toward the prohibition of the manufacture of chemicals. In this way, the document works against the national interests in a most insidious way. How many of us are really ready to modify our lifestyle as would be necessary if we gave up the products of the chemical industry--food additives, drugs, fertilizers, pesticides, plastics, gasoline and additives, automotive lubricants and finishes, etc?

J. Chemicals Should Not be Grouped for Regulation by
Generic Class

The Proposed Rules state on p. 54168, Col. 3, that OSHA does not propose to rely upon structural similarities between known carcinogens and other substances to regulate those other toxic substances as carcinogens. We agree with this approach. While structural similarities lend themselves to the development of theoretical relationships, such relationships should not be used to justify a presumption of a toxicological significance for regulatory purposes. Instead, theories should be used in their well-established role of guiding scientific thought and experimentation. The structural (or other) grouping of chemicals is a poor guideline in the regulatory process for specifying use of certain industrial hygiene techniques, analytical methods, safety equipment, reporting rules, and the like.

K. Identification of a Suitable Substitute Should Include the Opportunity for Input from the Public

The Proposed Rules state that "established carcinogens" for which there are substitutes will be banned, i.e., a zero tolerance set. These "substitutes" can themselves constitute a hazard. Are they themselves potential carcinogens? If they have been cleared only in animal studies, is it reasonable to substitute them for a chemical shown to be mildly carcinogenic to animals but "clear" in good, long-term human epidemiological studies?

The selection process for these substitute chemicals needs to be carefully monitored by the public. A notice of the selection of such substitutes should be published in the Federal Register and affected parties given an adequate opportunity for comment.

- L. OSHA's Attempt To Establish, By This Rulemaking Proceeding, Generic Policy Determinations That Would Preclude Debate On Such Determinations In Subsequent Rulemakings On Individual Substances, Is Illegal

Perhaps the most disturbing aspect of the proposed general regulation is its attempt to establish, once and for all, certain policy determinations that will govern all subsequent proceedings to prescribe standards for individual substances. Foremost among those policy determinations would be the question of whether animal test data may properly be extrapolated to indicate evidence of carcinogenesis in humans. The agency proposes to make a decision on that issue here and now; once made it would not be subject to challenge or debate in later rulemaking proceedings addressed to specific substances. As OSHA explains:

"It is OSHA's intention, once this proposal is duly promulgated, to foreclose, in subsequent 6(b) rulemakings on individual substances, the rehearing of the validity of this classification system and most other policy determinations made in this proposal, including the procedural structure intended to be followed.

****(D)uring the subsequent section 6(b) proceedings, interested parties would be foreclosed from the present endless debate concerning whether permissible exposure limits to humans can be related or extrapolated to those levels of exposure in test animals that indicated evidence of carcinogenesis." 42 Fed. Reg. 54154 (Oct. 4, 1977).

This attempt at a "quick fix" on such a highly controversial issue is remarkable and is vulnerable to serious legal

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challenge. To begin with, there is no basis for the proposition that in each and every case, regardless of the substance involved, the work environment in which it is present for human exposure, or the nature of the animal tests performed, animal test data can properly be extrapolated to indicate human risk. No responsible authority questions the fact that a given chemical substance can have varying effects upon man and animals, depending upon the nature of the substance itself and the mode of its administration. The use of certain substances both as a drug for human use and as a pesticide illustrates the varying effects that can be expected between man and animals. Further, the manner of administration, whether the substance was applied orally, by inhalation or by touch, frequently affects the level of toxicity produced and bears directly on the extent to which similar effects can be expected from human exposure. No single chemical substance can be prejudged on the basis of animal test data, as each case is different.

Moreover, any effort to preclude comment and debate on such policy determinations in subsequent rulemakings would subvert the intent of Congress and would deny the fundamental guarantee of due process. Congress specifically provided in Section 6 of the Act, 29 U.S.C. § 655(b), that each rulemaking proceeding to prescribe standards for individual substances shall include full opportunity for the submission of written data or comments on the proposed standard, and a public hearing if requested by an "interested person". To foreclose

comment on a prior determined policy question that is at the heart of the merits of the subject is to deny this fundamental right to comment and hearing. Further, the Act provides that upon judicial review, the Secretary's determinations must be supported by "substantial evidence in the record considered as a whole". 29 U.S.C. § 655(b). A policy determination supported not by evidence in the instant record under review, but at best by the record of a previous proceeding, cannot withstand the standard for review so clearly prescribed by Congress.

OSHA attempts to justify its proposal in this regard under the authority of cases such as United States v. Storer Broadcasting Co., 351 U.S. 192 (1956); FPC v. Texaco, Inc., 377 U.S. 33 (1964); and Air Lines Pilots Ass'n. v. Quesada, 276 F.2d 892 (D.C.Cir.1960). In each of those cases, however, the policy determination was truly generic (it was either right or wrong in its initial formulation), and it would not vary from one case to another. In Storer, the Court upheld an FCC rule that no applicant for a TV broadcast license could own five or more stations; in Texaco, the Court upheld an FPC rule providing for summary rejection of gas contracts containing pricing provisions other than those specified as permissible by regulation; and in Quesada, the D. C. Circuit upheld a CAB rule denying commercial flying licenses to pilots over 60 years of age. As characterized by the Supreme Court in Texaco, such rules "do not pass on the merits of a certificate of public convenience and necessity; they merely prescribe qualifications for applicants". 377 U.S. at 42.

By contrast, the appropriateness of a policy determination on the question of whether animal test data should be extrapolated as evidence of carcinogenesis in humans will vary from case to case depending upon the nature of the substance, the manner in which the animal tests were performed, the expected mode of exposure to human populations, and most importantly, the extent to which there exist sound epidemiological data on the subject. In some cases, such extrapolation may be proper; in others it will not be.

Case law under the Occupational Safety and Health Act confirms the inappropriateness of generic rulemaking by OSHA, even as to matters that may be characterized as legislative policy determinations. In Synthetic Organic Chemical Mfrs. Ass'n. v. Brennan, 503 F.2d 1155 (3rd.Cir.1974), the Third Circuit reviewed the appropriateness of an extrapolation from animal test data to human risk in the light of specific justifications offered by the Secretary for such extrapolations in a proceeding involving ethyleneimine. While the Court upheld the extrapolation in that case, it nevertheless emphasized its unwillingness to accord absolute deference to the Secretary in such matters, 503 F.2d at 1159, and the statutory requirement that each rulemaking proceeding include a statement of the reasons for the proposed action, covering "policy determinations as well as factual findings". 503 F.2d at 1160. A review of such determinations and the reasons therefore is necessary in each case in order to assure,

in the Court's words, "Consistency between the Secretary's rule and the statutory language and purpose." 503 F.2d at 1159.

M. Generic Standard Approach Is Suitable Only for Handling Certain Procedural Matters

A "standardized" approach can be properly utilized with respect to certain procedural aspects of rule-making, as for example, the following: notification of use and emergencies, regulated areas, methods of compliance (e.g., NIOSH has published lists of acceptable protective equipment), housekeeping, waste disposal, general medical surveillance, employee training and education, precautionary signs and labels, record keeping, etc. In fact, many of these areas have already been developed into a standardized approach by such groups as ANSI, ASTM, AIHA, etc. For the reasons discussed above under item L, however, generic policy determinations of a substantive nature are inappropriate and of questionable legal validity.