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January 27, 1978

RECEIVED
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LAW DEPT.

MEMORANDUM FOR THE ALTERNATIVES
COMMITTEE AND THE SCIENTIFIC COMMITTEE

Re: AIHC Alternative Proposal

Attached are corrections, additions, modifications, improvements and amplifications to the January 9 version of the alternative proposal. They reflect inputs from all sources.

Please review these and respond in writing to me with any comments. If a change is proposed, please submit the wording of the change in writing. To facilitate your review, we are enclosing herewith only the portions of the Alternative that contain suggested changes (other than changes of some page numbers) from the January 9 version, and have indicated the places where changes have been made.

Concern has been expressed that the discussion of risk/benefit analyses may be misinterpreted as implying that risks may be balanced against, among other things, profits. This is emphatically not so; benefits are benefits to society as a whole. We believe the latter represents a fair reading of the Alternative and the suggested revisions do not specifically mention or disclaim profits.

To get the revisions out to the interested parties in a timely fashion, we must have your comments by February 4, 1978.

AP00052115

As you will see, the "Preface" has been deleted. The revisions now suggested have been prepared with a view toward submission of the Alternative as testimony, to be presented at the hearing by an AIHC panel. Since the Preface had been prepared for other purposes, which have by now largely been served, it will not be included in the testimony.

Although I would have strongly preferred to respond individually to all of your comments that we have received and to thank all of those who have contributed to the Alternative effort, time has not permitted that courtesy. We would, however, like to take this opportunity to express our thanks to all of you. I found all of your comments thoughtful as well as constructive; unfortunately because they reflected differing emphasis and differing points of view, it was not possible to accommodate all of them. I do believe that there is a very substantial consensus in support of the essence of the Alternative.



Donald L. Morgan

DLM:jsd

Enclosure

- These pages indicate changes from the January 9, 1978 version. (1) The "Preface" (pp. iv - xi) has been deleted.
- (2) Attached pages 88 - 92 are new.
- (3) Key for other changes:

[] signifies deletion from Jan. 9 version
underscoring or vertical line in
left hand margin signifies new or
changed material.

AIHC RECOMMENDED ALTERNATIVES

TO OSHA'S GENERIC CARCINOGEN PROPOSAL

- (4) Attached pages show all textual changes. Because of additions, towards the end you will find that material, or some material, from a page of the Jan. 9 version appears one or two pages later in the attached papers.

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AP00052117

for men born during the 5 years around 1861, but increased to 2.9 per 1000 for men born around 1886 -- a 29 fold difference in only 25 years. Thus, in assessing whether an industrial chemical is increasing the incidence of death for any particular form of cancer, it is necessary to compare the observed incidence in the exposed population with the incidence to be expected in an unexposed population not only of the same sex and age-structure but also of the same cohort-structure. In England and Wales, where better data are available than for the United States, the death rates for cancers of various kinds in each sex have been compared for different cohorts with birthdates from 1851 onwards, and, with some exceptions (the foremost of which is cancer of the lung in both sexes), these data show no recent evidence of an increasing risk of death from cancer. On the contrary, the death rates have actually been falling for several forms of the disease. Case, R. A. M. "Cohort Analysis of Cancer Mortality in England and Wales, 1911-1954, by Site and Sex". Br. J. Preventive and Social Medicine 10, 172 (1956).

In the OSHA proposal (42 F.R. 54150, Column 2, first paragraph), it is stated that the death rate from cancer today is higher than expected even after allowing for greater longevity as a consequence of lower death rates from infectious diseases and other advances in medicine, and for improved diagnosis. This is not accurate in view of the American Cancer Society, United States Government, and England and Wales statistics, when increased cigarette smoking is taken into account.

B. Industrial chemicals represent a minor fraction of environmental causes of cancer.

It is often stated that perhaps as much as 90 percent of

and contaminants, may contribute to as much as 50 percent of cancer.^{1/}
The American Cancer Society estimates that smoking cigarettes may account for as much as 80 percent of all lung cancers -- the leading cause of cancer deaths in males in the United States.^{2/} Non-ionizing radiation, mostly in sunlight, has been estimated by NCI officials to account for 5 to 8 percent of all cancers. (Dr. Newell's testimony of June 15, 1977 (page 20), noted above, estimated 5 percent; Dr. Gio B. Gori, also of NCI, estimated 8 percent for male and 8 percent for female in a letter to Mr. E. V. Anderson dated May 10, 1977.) Dr. Newell's testimony also estimated (page 20) that alcohol, when combined with use of tobacco products, accounted for about 2 percent of cancers annually.

The best estimate is that occupational exposure to industrial chemicals has accounted for about 1 to 5 percent of all cancers.^{3/} This

1/ Statement by Gio B. Gori, Ph.D., Deputy Director, Division of Cancer Cause and Prevention, National Cancer Institute, presented before the Select Committee on Nutrition and Human Needs, United States Senate, Wednesday, July 28, 1976. Figure 19: "Percent of total cancer incidence related to diet 40.9% male; 60.1% female."

2/ "Lung cancer - Cigarette smoking causes at least 80% of lung cancer." American Cancer Society, 1977 Cancer Facts and Figures, page 5; "Lung cancer constitutes 22% of cancers in males." American Cancer Society, "Cancer Incidence by Site and Sex", Ca-a Cancer Journal for Clinicians, January/February 1977, Volume 27, No. 1, Page 26.

3/ Dr. Newell's June 15, 1977, testimony (page 20) estimated "5 percent related to occupational exposures such as asbestos, vinyl chloride, benzene, beta-naphthylamine and others." Dr. Gori's letter of May 10, 1977, to Mr. E. V. Anderson estimates occupational causation at 3 percent for males and less than 1 percent for females. A guest editorial by Ernest L. Wynder, M.D., and Dr. Gori in the April, 1977, issue of the Journal of the National Cancer Institute, (p. 825) states at page 830:

"Bailar (personal communication) estimated that the occupational contribution to total cancer incidence in males lies between 1 and 5%, and a similar estimate was made by Nelson (personal communication). General estimates of the percentage of all human cancers related to occupational exposure range between 1 and 10%."

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of the possibility occupational hazards, and greatly improved measures have come into common use to reduce employee exposure to potentially harmful industrial chemicals. See, e.g., Ferber, Hill & Cobb, American Industrial Hygiene Association Journal, January, 1976, pp. 61-68 (control of potential exposure to benzidine).

C. The alleged failure of prior OSHA regulatory efforts and need for a generic standard.

To justify the oversimplifications and arbitrary rigidity of its proposed categorical approach, OSHA makes much of its supposed inadequacies over the past seven years in the regulation of industrial carcinogens. One can question the accuracy of this self-effacing criticism. []

In 1972 OSHA wrote to its expert advisor, NIOSH, requesting information on all known industrial carcinogens. NIOSH responded by carrying out a literature survey and by publicly requesting information -- on 15 substances -- in a notice published in the Federal Register on July 6, 1972. NIOSH subsequently advised OSHA that there appeared to be 15 occupational carcinogens of which some were known human carcinogens and some were implicated solely on the basis of bioassay experiments. This advice was subsequently modified by the deletion of one of the materials, dimethyl sulfate, leaving 14 carcinogens that NIOSH believed to be in use then, or to have previously been in use, in American workplaces. In 1973 OSHA promulgated an Emergency Temporary Standard limiting employee exposure with respect to all 14 chemicals and commenced a permanent rulemaking which was completed in January of 1974.^{1/} What more OSHA could have been

^{1/} See 39 F.R. 3756 (Jan. 29, 1974). The 14 included a number regarded as known human carcinogens, and several regarded only as known or highly suspect animal carcinogens. (continued on next page)

expected to have accomplished by then is left unsaid by the current self-criticism, which also ignores the fact that in 1977 OSHA demonstrated that it could act very promptly to regulate industrial substances implicated as potential carcinogens (DBCP).^{1/}

Much of the apparent subsequent gap between the regulatory need and OSHA's response is attributable not so much to lack of zeal on OSHA's part as to a number of other considerations. Two, but only two, considerations are the striking increase in recent years in the amount of experimental testing of chemical substances for evidence of carcinogenicity, and the acceleration of the reporting of the results of these tests. Another consideration, however, has been a very controversial modification in OSHA's operative criteria for assessing carcinogenicity. It was the informed view of NIOSH in 1973 that clear evidence of carcinogenicity should be required in two mammalian species before a substance could appropriately be regarded as posing a carcinogenic risk to man insofar as regulatory activities are concerned,^{2/} but OSHA now proposes to use much less reliable evidence as a basis for regulations.

To justify this shift in position, and to demonstrate a need for its new proposal, OSHA points to the "large number of potential carcinogens already identified by NIOSH", an apparent

(continued from previous page) The 14 are: 2-Acetylamino fluorene; 4-Amino diphenyl; Benzidine; 3,3'-Dichlorobenzidine; 4-Dimethylaminoazobenzene; alpha-Naphthylamine; beta-Naphthylamine; 4-Nitrobiphenyl; N-Nitrosodimethylamine; beta-Propiolactone; bis (chloromethyl) ether; Chloromethyl Methyl ether; 4,4'-Methylene-bis (2-chloroaniline); and Ethyleneimine.

^{1/} 1977 also demonstrated the imprudence of undue resort to the ETS procedure -- with respect to benzene.

^{2/} See, e.g., 39 F.R. 3757, third column (Jan. 29, 1974).

available at the time that the decision must be made, and other factors pertinent to the case under consideration. Each case must be considered on its own and the criteria appropriate for one agent may not necessarily apply to another." (58 J. Nat'l Cancer Inst. 461, Feb. 1977.) (emphasis added)

Although OSHA's preamble does cite the work of the NCAB Subcommittee (while ignoring its advice), many of the references cited elsewhere in the preamble reflect views expressed seven or more years ago; many of these are already outdated, imprecise or otherwise inaccurate in light of current references, or are superseded by the more recent NCI statement. Indeed, the references cited by OSHA in support of its proposal reflect a single biased perspective of the problems of occupational carcinogenesis.^{1/} For example, the references fail to report the very considerable body of learning supporting the no-effect level hypothesis concerning cancer causation.

It is manifestly unwise to disregard the discoveries made in the past few years by cancer researchers and to ignore for the foreseeable future developments currently underway or soon to be realized. In fact, such an approach is, as noted above, beyond OSHA's authority since the Occupational Safety and Health Act requires that health standards shall reflect "the latest available scientific data in the field" among other considerations. Indeed, federal regulatory authorities should plan on making a general reassessment of the state of the relevant science at least every five years, if not continuously, and should also reassess prior decisions in light of whatever additional data have become

^{1/} Attached hereto as Appendix A is a list of references supporting the AIHC Alternative.

Note: The Appendix is not yet ready

consequences of the rule,
of the effect on the national economy, small
business, technological innovation, the environ-
ment, and public health."

It is inconceivable that Congress intended that benefits
be considered in regulating all of these public hazards, and others
as well, but be ignored in regulating occupational hazards.

I. Government agencies have approved carcinogenic
risks from chemicals under other regulatory laws.

The federal government has assumed a broad mandate to
assure the safety of all food. Yet ⁶the following food substances
remain available for daily consumption in spite of ⁷scientific
studies showing that under certain conditions each is carcinogenic
in at least one species of mammalian test animals:

Egg yolk and egg white 1/
Vitamin D2 2/
Calcium 3/
Lactose and maltose 4/
Selenium 5/
Beverage alcohol 6/
⁷

Similarly, the government has failed to remove bacon and ham from the

1/ J. Szepsenwol, Proc. Soc. Exp. Bio. and Med. 116:1136 (1964).

2/ G. H. Gass and W. T. Allaben, 1 RCS J. Med. Sci. 5:477 (1977).

3/ L. Krook, L. Lutwak, K. McEntee, Guest Editorial, "Dietary
Calcium, Ultimobranchial Tumors and Osteopetrosis in the Bull",
22 Am. J. Clinical Nutrition, No. 2, pp. 115-118 (Feb. 1969).

4/ K. Yamagiwa, Japanese J. Cancer Res. 46:No. 1 (1955) 48:555 (1957).

5/ 38 F.R. 10458 (April 27, 1973); 39 F.R. 1355 (Jan. 8, 1974).

6/ 38 F.R. 10460 (April 27, 1973); 39 F.R. 42748, 3d Col. (Dec. 6,
1974).

market although they are known to contain nitrosamines or to produce nitrosamines in the body when consumed. The government has also chosen not to prevent restaurants from charcoal broiling meat, which produces carcinogenic benz-a-pyrene. Indeed, FDA has set tolerances for aflatoxin in peanuts and corn, which by FDA's own estimates raise a risk of 66 lifetime cancers per 100,000^{1/} persons.

Congress has, in the Saccharin Study and Labeling Act, expressed unwillingness to remove known carcinogens from the market without a benefit/risk analysis. The congressional moratorium was enacted with the understanding that saccharin presents a risk of approximately 1500-2000 cases of bladder cancer per year within the United States.^{2/}

J. Non-chemical risks are a part of daily life.

In everyday life, man is exposed to numerous risks of fatalities which society accepts. Some of these risks pose quantifiable risks of cancer, based on mathematical projections. For example, jet flying at normal cruising altitudes increases exposure to cosmic rays capable of inducing cancer. Some such cancers prove fatal. For airline pilots flying 50 hours each month at 35,000 feet, the risk of induction of a fatal cancer each year is 5 out of 100,000. In other words, if there were 100,000 such pilots, 5 would be expected

1/ Food Chemical News, November 14, 1977, pp. 3-4; see also page 43 Below.

2/ Sen. Rep. No. 95-253, 95th Cong., 1st Sess., p. 6 (1977). This report states that these figures were derived from Canadian studies and conclusions, and were confirmed by FDA Commissioner Kennedy. These conclusions may be debatable; the point is that Congress was willing to accept their possible validity, but nonetheless decided that saccharin should continue to be available.

to develop each year a cancer that would prove fatal; these 5 cases of cancer would be caused by the increased exposure to cosmic rays. For a group of 100,000 frequent airline passengers, who travel a good deal less than the pilots, only 1.5 fatal cases of cosmic-ray induced cancer would be expected each year.

For a group of 100,000 passengers who took only one transcontinental flight a year, less than one cancer fatality due to increased exposure to cosmic rays would be expected. If this group were increased to one million, 0.5 cases would be expected. If the group were 2 million, one case of cancer fatality per year would be expected. These risks may be expressed in tabular form as follows.

<u>Activity</u>	<u>Annual Projected Deaths Per 100,000 Participants</u>
<u>Cosmic Ray Exposure</u>	
- Commercial airline pilot	5.00
- Frequent airline passenger	1.50
- One transcontinental flight/year	0.05
<u>Other Radiation Exposure</u>	
- Average U.S. diagnostic medical X-Ray	1.00
- Natural background radiation at sea level	1.50

One can also quantify the yearly risk of death from other causes for a group of 100,000 people. Of such a group, the number expected to die of accidental electrocution is 0.5; the number expected to die from accidental poisoning by solids or liquids is 0.6; the number expected to die by accidental poisoning by gases or vapors is 0.7; and the number expected to suffer a fatal fall is 7.7 people.

Some risks are knowingly assumed on a voluntry risk; some risks are encountered on an involuntary basis, and other risks could well be regarded as partially assumed voluntarily. Different social

conclusions may follow from the degree of voluntariness, but it should be recognized that voluntariness is often a question of degree.

In its pursuit of recreation, generally regarded as voluntary, the human race engages in and tolerates many activities of relatively high risk. The following activities and their degree of risk are illustrative:

<u>Activity</u>		<u>Annual Projected Deaths Per 100,000 Participants</u>
Football	)	4
Automobile racing	)	120
Horse racing	) Averaged	130
Motorcycle racing	) order	180
Power boating	) participants	.17
Amateur boxing	)	2
Skiing	) 40 hours/year	3
Canoeing	) engaged in	40
Rock climbing	) sport	100
Sunbathing (curable skin cancer)	)	500
Fishing (drowning)	)	1
Drowning (all recreational causes)	)	1.9

Society has chosen not to prohibit any of these activities, or even activities with much higher risks (e.g., the Indianapolis 500). There are relatively few activities which pose such a high risk that society has banned them completely (e.g., going over Niagara Falls in a barrel or attempting suicide).

Nor are these risks limited to recreational activity. The following annual risks of death from causes other than cancer in

selected occupations show that benefits are considered in public regulation of occupational hazards as well:

<u>Occupational Activity</u>	<u>Annual Projected Deaths Per 100,000 Workers</u>
Coal mining ^{1/} - Black lung disease (1969)	800
Coal mining - Accident (1970-74 average)	130
Airline pilot - Accident	30
Typical jet flying - Air accident	10
Manufacturing - total	8
Fire fighters - total (1971-72 average)	80
Steel worker - Accident (1969-71 average)	60
Railroad worker - All accidents except grade crossings)	400

(References for the foregoing risk figures include B. G. Ferris, New Eng. J. Med., 268 430 (1963); F. D. Sowby, Health Phys., 11, 879 (1965); C. Starr, Science, 165, 1232 (1969); K. S. Clarke, J. Am. Med. Assoc., 197, 894 (1966); Statistical Bulletin, Metropolitan Life Insurance Co. (May 1977.); Accident Facts, 1976 ed.; Statistical Abstract of the U.S.)

II. Principal Desirable Modifications in the OSHA Proposal.

A. Recognition of the complexity and evolution of the science.

It seems only realistic to modify the OSHA proposal, as AIHC recommends, so as not to regard the present (or the past) state of the relevant science as frozen. The OSHA proposal "freezes" science in two ways: in the manner and extent to which regulatory

^{1/} In view of the very high risks of coal mining, which surely should be reduced, the Administration's energy policy, which encourages coal mining, highlights the need to consider the benefits.

propositions are to be foreclosed from future consideration in individual chemical rulemakings; and in the proposed obstacles that OSHA would create to allowing itself to take advantage of, or to utilize, improvements or developments in relevant learning, e.g., on DNA repair. The latter problem arises from the fact that OSHA would not entertain any modifications of the rigidities of its proposed approach except by way of a formal rulemaking that would modify the pending categorical rulemaking proposal. The problems of obtaining even a very clearly warranted modification of such a rulemaking appear to be truly formidable. Enormous bureaucratic inertia would have to be overcome, and even if that were possible, very substantial time would be required.

The AIHC proposal proceeds on the basis that if a categorical approach is desirable and necessary to enable OSHA to deal effectively with potential carcinogens, there is still no statutory authority -- or need -- to preclude interested parties from presenting evidence, with respect to any particular chemical, to counter any conclusion of carcinogenic risk that might otherwise be drawn on the basis of the general principles on which the OSHA proposal intends to rely. In the absence of such countervailing evidence, it may be appropriate for OSHA to use general principles, without having to support them with personal testimony time and again. For example, the AIHC proposal would permit use, prima facie, of mammalian test data to categorize a chemical as posing some occupational carcinogenic risk. AIHC would not, however, preclude interested parties who believed they had compelling evidence, from attempting to persuade OSHA that its general principles should not be regarded as

warranting such regulatory action (e.g., in the particular circumstances of some improperly designed mammalian test or some future unforeseeable case).

B. Recognition that not all carcinogens pose the same risk to humans.

The amounts of different chemicals known to have non-carcinogenic toxic effects can vary by several orders of magnitude;^{1/} a different permissible exposure limit for each is therefore appropriate and justified. Since it has been demonstrated that the amounts of different substances that produce carcinogenic effects can likewise differ by a million fold or more,^{2/} it seems irrational for the OSHA proposal to proceed on the basis that all known and potential carcinogens pose equivalent risks (by requiring the "lowest feasible" permissible exposure level in all cases). Carcinogens, like noncarcinogen toxins, should be classified or ranked in terms of potency, and regulated according to the degree of hazard that their use or uses present to employees. For example, bischloromethylether is a very potent known human carcinogen; vinyl chloride is much less potent. More severe controls clearly are warranted for the former. Greater priority should be accorded to regulating a substance that is a potent carcinogen than a substance

^{1/} Modern toxicology is based on experimental evidence demonstrating that a dose-response relationship exists for toxic substances and that there is some dose level below which no response occurs. Although there may be scientific dispute at present whether there are threshold or no-effect levels for carcinogens, there is a strong body of scientific opinion embracing this concept, supported by the current NCIR study on 2-Acetylaminofluorene and the Oak Ridge radiation study.

^{2/} Compare, for example, aflatoxin with saccharin.

demonstrate the dose-response phenomenon. This singular study, which utilized large numbers of animals and multiple dose levels, also demonstrated that latency, expressed as time-to-tumor from first dose, is clearly a function of dose, confirming Druckrey's classical observations on latency and dose-response. Set out below in Figure 5 is a graph contained in the NCTR draft study which clearly illustrates the dose-response relationship in liver tumorigenesis for 2-AAF.^{1/}

The principal ways by which the AIHC proposal would take into account dose-response and time-to-tumor data include determining the actual hazards presented by a chemical (which must include consideration of how it is in fact used), and otherwise ascertaining socially acceptable or permissible exposure levels. It is proper and logical for OSHA to set a lower exposure level for a highly potent carcinogen than for one shown to be only weakly potent.

- C. Recognition of benefits, including economic benefits, as well as risks; establishment of acceptable exposure levels or acceptable risks.

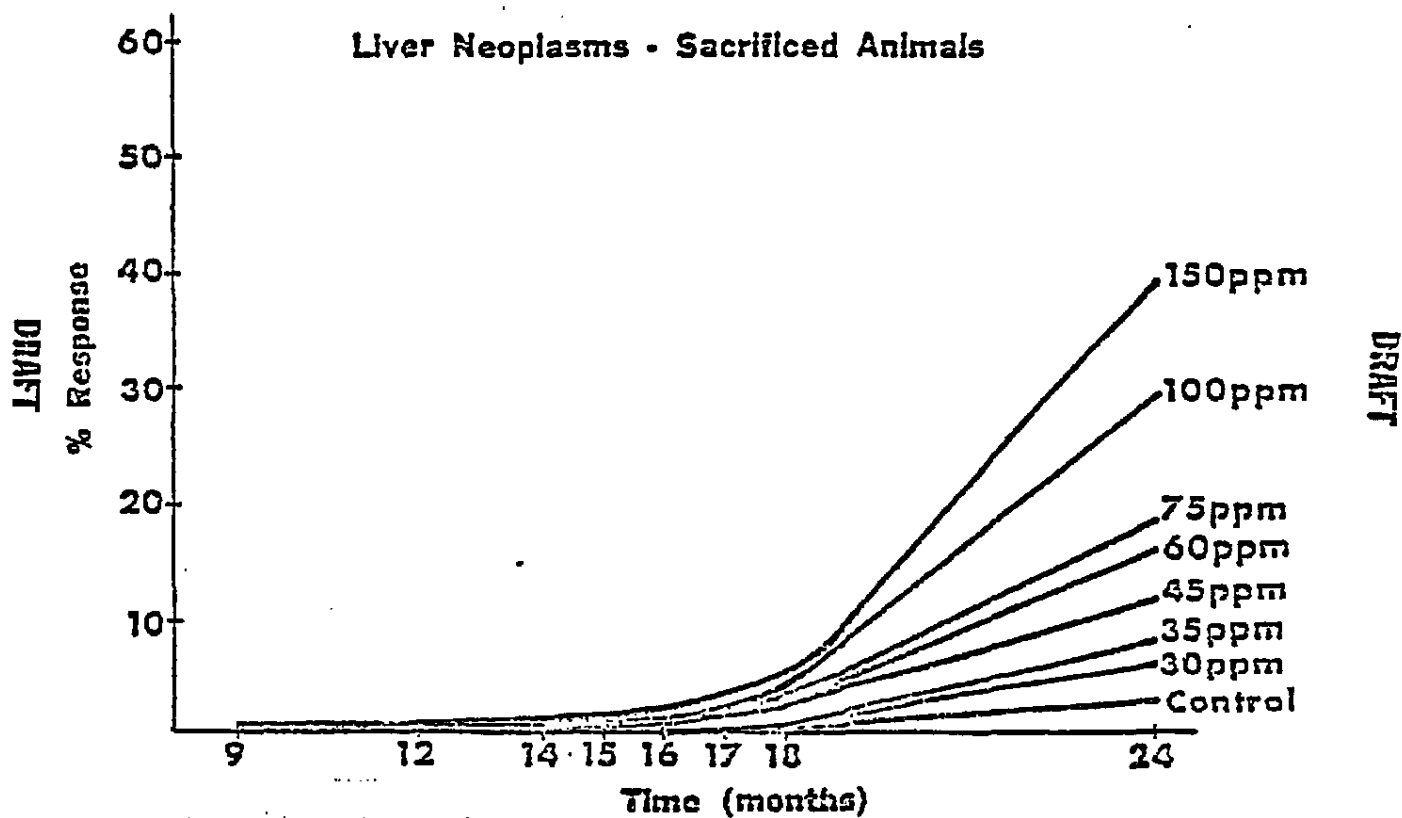
The AIHC alternative does not proceed on the illusory basis that a risk-free industrial environment is attainable.^{2/} Rather, it deals candidly with assessment of risk and benefits.

The first step in this process is the assessment of car-

1/ The NCTR data on 2-AAF show a no-effect or "apparent minimal effect" level for the bladder around 60 ppm. See Figure 10, Nov. 28, 1977, draft NCTR study on 2-AAF.

2/ William W. Lowrance, Of Acceptable Risk, William Kaufman, Inc., Los Altos, Calif., 1976, p. 11: "Since the taking of both personal and societal risks is inherent in human activity, there can be no hope of reducing all risk to zero. Rather, as when steering any course, we must continually adjust our headings so as to enjoy the greatest benefit at the lowest risk and cost."

FIGURE 5



(Figure 12, Nov. 28, 1977, draft NCTR Study on 2-AAF)

tion even of any replicated finding to man, especially where the replication is in but one species.

By sanctioning a replicated test in a single mammalian species to corroborate a positive result and to categorize a chemical as a carcinogen (extrapolating from such animal data to humans), the OSHA proposal ignores the lack of validity in many such "replicated" animal studies which may be the result of variations in test procedures and conditions. Among these variations might be interspecies differences in metabolism, methodological differences in statistical treatment of data, differences in the basic diets fed to the animals, differences as to the applicability of certain tumor systems (e.g., hepatomas in mice), the presence of other volatile toxic substances where an experiment was conducted, and differences in animal husbandry.^{1/}

Two biological circumstances also dramatize the need for careful appraisal of animal data. Estrogens and androgens are carcinogenic to experimental species, and for estrogens, carcinogenicity in humans has been documented. Yet estrogens are ever-present at sub-threshold or no-effect levels in the entire earth's population and are essential to life. Similarly, metals such as chromium and cobalt and perhaps ² selenium and even arsenic, are essential to man in small amounts but carcinogenic in excessive amounts.^{2/}

1/ Merely changing the type of wood shavings beneath mouse cages from pine to redwood will set off epidemic cancer in certain strains.

2/ Dr. Kraybill of NCI, in another paper presented to the Chemical Selection Subgroup of the Clearinghouse on Environmental Carcinogens on February 2, 1977, entitled "Some Concepts and Remarks on Presumptive Negative Chemicals, Biological Intermediates, Endogenous Chemicals, Nutrients," discusses additional substances which are required by the body physiologically, biochemically (continued on next page)

or other disease.^{1/}

Further, there is evidence that micro nutrients, such as selenium, which in low doses produce no harmful effects on man, indeed may be necessary to life, produce well defined toxic effects, including carcinogenicity, in animals. See page 39 above. And the human nutrient calcium fed to bulls at only 3.5 to 5.9 times the amounts the National Research Council has concluded they require, has produced ultimobranchial tumors in the thyroid glands in 30 percent of the animals.^{2/} Clearly, humans are not at risk the same way from calcium.

Negative human data on the toxicity of carcinogenic materials are seldom seen in scientific journals, and certainly never in the popular press. These data are for the most part in "company files" and there is little incentive for making them known -- much less for developing more data -- since, as the OSHA proposal demonstrates, little importance is attached to this information relative to positive animal studies. The AIHC proposal would encourage the compilation and disclosure of such data, and would in many cases provide a better factual and scientific basis for rule-making than can be provided by extrapolation from animal data.

G. Regulatory priorities.

The OSHA proposal contemplates what appears to be a hap-

1/ See Gerarde & Gerarde, J. Occup. Med. 16(5), 322-344 (1974); MacIntyre, J. Occup. Med. 17(1), 23-26 (1975).

2/ L. Krook, et al., "Dietary Calcium, Ultimobranchial Tumors and Osteopetrosis in the Bull", 22 Amer. Journal of Clinical Nutrition, No. 2, pp. 115-118, February, 1969.

hazard approach to regulatory priorities: It is suggested that the large number of materials on the NIOSH subfile of "suspect carcinogens" may be considered in alphabetical order (42 FR. 54169, Column 3), and priorities for additional materials would depend upon the happenstance of the timing of OSHA's receipt of information from any source. The latter would deprive OSHA of the ability to exercise judgment in establishing priorities for rulemaking. For example, under the OSHA proposal, the filing of a "citizen petition" could force OSHA to give equal priority to such seemingly unequal problems as selenium, ⁵² an essential human nutrient, ⁵⁷ peanuts, asphalt, and carbon tetrachloride.

The AIHC proposal reflects the view that OSHA should retain the flexibility to exercise informed judgment and should consider regulating first those materials that are known or seriously alleged to be human carcinogens or highly potent animal carcinogens. (Priority should also depend upon the degree and extent of employee exposure.) Materials in this category are surely a much more manageable number for regulatory and compliance purposes than the "universe" described by the NIOSH subfile, and are very likely to account for the great majority of the potential occupational hazards being encountered in domestic workplaces. This approach would enable greater benefits to be achieved, and ensure greater acceptance by those being regulated, in view of its manifest reasonableness. Such acceptance is highly desirable in a democratic society.

H. Categorization of substances not found in domestic workplaces.

Unlike the OSHA proposal, the AIHC alternative would not call for formal categorization, by publication in the Federal Register,

protection. Indeed, by freeing industrial hygiene resources of unnecessary regulatory burdens, the exemption should promote employee protection in other areas.

M. Special regulatory approaches to laboratories and construction.

In general, regulations appropriate for the industrial workplace are not appropriate for laboratories, whether quality-control, pure research, or some admixture of both. OSHA's failure to distinguish between laboratory and non-laboratory workplaces is unreasonable. OSHA's proposed requirements for laboratory workplaces could lead to the unintended consequence of impeding important research on cancer and other serious health problems.

AIHC believes that special regulations for laboratories are appropriate. Probably a single work-practices oriented regulation for laboratories would be sufficient.

Similarly, construction presents very special problems, as OSHA has recognized in regulation of asbestos, and special regulation for construction activity would be necessary.

Thus, while the categorization aspects of the AIHC proposal could apply to laboratories and construction, the regulatory response would generally be different than it would be for production operations. Similarly, a different response might be appropriate for transportation and agriculture.

N. Appropriate timing and scope of assessment of economic environmental impacts; due process.

The AIHC proposal does not itself deal with issues as to the timing or scope of assessment of economic and environmental impacts of implementation. Because of the comparative flexibility of that proposal, it should be appropriate to assess those impacts

variety of political and other pressures to which regulatory agencies are subjected, including perceived needs to respond to the expressed wishes of their historical constituencies.^{1/} A further reason would be to improve the expertise of those making the categorizations, by improving utilization of expert resources. There is no abundance or surplus of good scientific talent in this area; it seems reasonable to expect that the federal government would on the average enlist the services of better qualified individuals if it needed to provide only a single classification panel, rather than a panel or similar authority for each of a variety of regulatory agencies. The AIHC proposal contemplates that the activities and decisions of the Panel would be governed by the Administrative Procedure Act. The Panel would be established pursuant to the Reorganization Act.

III. Tentative Nature of AIHC Endorsement of Categorical Approach.

The AIHC alternate does not proceed on the basis of agreement with OSHA's assertions of a compelling need to simplify science and facts by categorization. (See pages 10-19 above.) Accordingly, the following proposal is only a conditional endorsement of a categorical approach, an endorsement that depends in material

^{1/} Cf. "Informing Workers and Employers about Occupational Cancer," June, 1977, National Research Council Report (PB-269 599) for OSHA, p. 20:

"The decision to inform those in affected workplaces of the hazard of a chemical is not to be taken lightly, as it involves the commitment of substantial resources. For that reason we believe it essential that a single national source, such as DHEW, be charged with making the decision that workers are at risk. This source should be, to the extent possible, credible to both management and labor; therefore, it should not be involved in the regulatory process. But, it must not be so remote from the realities of the workplace that it cannot make an appropriate assessment of risk, or at least announce its decision in a form that can be translated to a specific occupational situation."

3. The specificity of the type and site of cancer.
4. Confirmation, or lack of confirmation, by other independent studies.
5. The suitability of the control group used for the confirmation of excessive risk, particularly the extent to which exposed and control groups are similar in respects other than exposure to the suspect agent, e.g., ethnic, socio-economic, dietary, exposure to other chemicals, use of tobacco.
6. Whether there is evidence of a dose-response relationship.
7. Whether the observed carcinogenic effect is likely to be direct or indirect, e.g., explicable in terms of a biological mechanism which is irrelevant to the occupational exposure.
8. Whether well-documented individual case reports or studies show that the substance in question has in fact, or with a high degree of probability, caused cancer in humans, even though the number of cases is too small to apply epidemiologic or statistical tests.

Potency or seriousness of risk shall be determined on the basis of epidemiologic or other human experience data where exposure data are available or where exposure intensities can reasonably be estimated. In the absence of such information, any available mammalian bioassay dose-response data shall be used.

In evaluating mammalian test data for relative potency, the guides set forth in Category II, (Subpart E below, page 67) for assessing the potency of confirmed animal oncogens shall be used.

Note: Where neither human dose-response data (including estimated exposure levels) nor experimental mammalian dose-response data are available and potency cannot be determined, regulatory priorities

should consider, and should be influenced by, the quality and amount of available human data. For example, where epidemiologic evidence shows that occupational exposure to a substance has increased the age-standardized risk of development of any form of cancer by a factor of 10-fold or more, the substance should generally be assumed to be a potent carcinogen. (Examples here include occupational exposure a few decades ago to beta-naphthylamine or some nickel refining operations.) Such an assumption may be questioned in particular circumstances, such as where the form of cancer is very rare, and a weak carcinogen could produce a large increase in the age-standardized risk for that form of cancer.

CATEGORY II. CONFIRMED ANIMAL ONCOGENS.

- A. Oncogens of High Potency.
- B. Oncogens of Intermediate Potency.
- C. Oncogens of Low Potency.

Criteria: Well documented results of adequate mammalian bioassays in at least two different species showing a statistically significant increased age-standardized risk of tumor development in test animals over that occurring in matched and exposed controls, where an appropriate route of administration was used and where the doses were not excessive, shall be sufficient, in the absence of countervailing information, to warrant classification as a confirmed animal oncogen.

A. Definition of Oncogen. A number of the terms used in this general criterion are more fully stated below. This general criterion contemplates attribution of some regulatory significance

- metabolic and pharmacokinetic data, if available
- number, type and site of tumors
- number of animals developing tumors
- temporal pattern of tumor appearance, taking into account the distinctions between (i) fatal and non-fatal tumors, (ii) tumors which are evident during life (e.g., skin and sub-cutaneous tumors) and tumors which can only be discovered at necropsy
- the quality of the pathology studies, both microscopic and macroscopic
- method of statistical analysis and statistical significance of positive results
- dose response relationships
- adequacy of reporting of the bioassay

E. Relative potency of response. The general concept of the relationship between the magnitude of the dose resulting in tumors in experimental animals and the potential risk to man from industrial substances, as advanced by the ACGIH,^{1/} is reasonable and sensible; modifications from the ACGIH numbers are used to accord with current accepted test protocols. The additional concept of induction period (time from first contact to the appearance of tumors) is also applied in the definitions of potency of response to exposure to industrial substances in experimental mammalian studies. Accordingly, responses for which adequate bioassay results of statistically significant tumor occurrence are available shall be categorized by potency in light of the following guidelines^{2/} for bioassays of

1/ ACGIH, "Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1977", pages 41-43.

2/ These guidelines are not without exception. For example, they do not address exposure to fibers or (continued on next page)

the hamster, mouse, or rat:

1. Response to respiratory route exposure.

A. Response of high potency.

(1) Inhalation exposure 6 to 7 hours per day, five days³ per week, for a major portion of a lifetime, to dosages below 1 mg/m³ with an excess of tumors appearing at any time during the study;

(2) Inhalation exposure 6 to 7 hours per day, five days per week, for a major portion of a lifetime, to any non-excessive dosage with tumors appearing in 12 months or less; or

(3) Exposure to a single intratracheally administered dose not exceeding 1 mg of particulate, or liquid, per 100 ml or less of animal minute respiratory volume, with an excess of tumors appearing at any time during the study.

B. Response of intermediate potency.

(1) Inhalation exposure 6 to 7 hours per day, five days per week, for a major portion of a lifetime, with dosages between 1 and 10 mg/m³ with an excess of tumors appearing at any time during the study; or

(2) Inhalation exposure 6 to 7 hours per day, five days per week, for a major portion of a lifetime, to any non-excessive dosage with tumors first appearing in 12 to 18 months, or

(3) Exposure to a single intratracheally administered dose from 1 mg to 10 mg of particulate, or liquid, per 100 ml or less of animal minute respiratory volume, with an excess of tumors appearing at any time during the study.

2/ (continued from previous page) particulates. The Panel should exercise informed judgment in evaluating the results of experimental exposures to such materials.

B. Response of intermediate potency.

(1) Exposure by repeated peroral dosing at dosage between 1 and 50 mg/kg/day, with an excess of tumors appearing at any time during the study; or

(2) Exposure by repeated peroral dosing at any non-excessive dosage with tumors appearing in 12 to 18 months.

C. Response of low potency.

(1) Exposure by repeated peroral dosing at a dosage greater than 50 mg/kg/day, but non-excessive, with an excess of tumors appearing at any time during the study; or

(2) Exposure by repeated peroral dosing at any non-excessive dosage with tumors appearing after 18 months.

CATEGORY III. Substances for Further Testing.

Criteria:

Mammalian bioassays that do not satisfy Category II requirements but that do show statistically significant increases in tumors, for examples: positive results in a single species; positive results but only in studies using excessive doses; positive results but only in studies where the route of administration, or exposure conditions, are of questionable relevance to human exposure.^{1/}

Note: A Category III classification does not necessarily lead to a low regulatory priority. A good study in one species may warrant high priority, as may studies using high doses if human exposure levels are in the same order of magnitude.

^{1/} Results of "short-term" tests would serve as guides to further testing, and would not themselves warrant categorization. See pages 40-42 above.

other appropriate information sufficient to quantify risks to employees, OSHA shall, in light of such information, specify permissible exposure levels that reflect analyses of risks and benefits. In deciding upon such a level, OSHA shall perform analyses of risks and benefits in accordance with Subpart C below, to the extent such analyses can be very promptly performed. Where the available epidemiologic data are sufficient to help evaluate dose-response and potency issues, such data shall be considered in establishing permissible exposure levels. These exposure levels shall generally be achieved by means of engineering controls, to the extent technically and economically feasible, augmented by administrative controls and personal protective equipment as necessary. OSHA shall require that this exposure level be achieved as soon as feasible, and may require as an interim measure that exposure levels be reduced immediately through a readily available practical combination of engineering and administrative controls and personal protective equipment.

The permissible exposure levels (in ETS and permanent standards) may vary from chemical to chemical, depending upon the analyses of risks and benefits. Means of controlling exposure may vary from one use of a chemical to another. Limitations of surface accumulations of a chemical should be expressed in quantitative terms.

(b) Where an ETS is to be issued and sufficient data are not available to quantify risks to employees, OSHA shall advise the Interagency Testing Committee established pursuant to the Toxic Substances Control Act of the desirability of requiring testing under that Act. The ETS shall specify a permissible exposure level that

ministrative controls and personal protective equipment as appropriate.

(c) Where an ETS not based on data sufficient to quantify risks has been issued and such data do not become available within six months, an "interim" permanent standard similar to the ETS shall be issued, to be in effect no longer than five years. If during that three years' period such data become available, a revised permanent standard may be issued that establishes an acceptable exposure level derived in part from such data, and also from analyses of risks, hazards, costs, and benefits. If such data do not become available, the regular permanent standard shall establish an exposure level that is the lowest level technically and economically achievable. Compliance with permissible exposure levels shall generally require all feasible use of engineering controls, augmented as appropriate by administrative controls and personal protective equipment.

(d) A permanent standard shall exclude mixtures containing less than specified percentages of the substance being regulated, (or shall specify with particularity the mixtures that are being regulated), and shall not apply to workplaces where the substance is present only in excluded mixtures. Such percentages may differ for different uses or mixtures and shall be determined in light of analyses of risks and benefits² performed in accordance with Subpart C below.

(e) A permanent standard shall provide partial exemptions for workplaces below an action level.

(f) Where OSHA decides not to issue an ETS, it shall consider institution of a permanent rulemaking under Section 6(b) of the Act based on regulatory priorities, unless it shall determine that

such a rulemaking is not necessary to protect employees. As part of such a rulemaking, OSHA should advise the ITC of the need for dose-response data if they do not exist. Permissible exposure levels and other regulatory provisions should be established in the same manner as called for in the preceding subparagraphs (a) through (e).

7.
B. Category II Classification.

1. Emergency temporary standard. Upon classification of a substance as a Confirmed Animal Oncogen, OSHA shall as soon as possible decide, in each case, whether actual employee exposures constitute a "grave danger" within the purview of Section 6(c) of the Act and whether an Emergency Temporary Standard is necessary to protect employees from such danger. Such determination shall consider (a) the evidence of potential carcinogenic risks (e.g., carcinogenic potency as indicated by experimental data, dose-response relationships, metabolism, duration and amount of exposure, route of exposure); (b) evaluation of actual hazards (e.g., physical and chemical properties, degree of occupational exposure, likelihood of a carcinogenic event); and (c) epidemiologic or other human experience evidence.

Upon completion of such a determination, OSHA shall immediately commence the development of an ETS if the criteria specified in Section 6(c) for such issuance have been satisfied. In developing an ETS (as well as in developing a permanent standard), OSHA shall perform analyses of risks and benefits in accordance with Subpart C below.

(a) Where an ETS is to be issued and where there are available dose-response data in one or more appropriate mammalian species or other appropriate information sufficient to quantify risks to employees, OSHA shall, in light of such information, specify permissible exposure levels that reflect analyses of risks and benefits. In deciding upon such a level, OSHA shall perform analyses of risks and benefits in accordance with Subpart C below, to the extent such analyses can be very promptly performed. Any available epidemiologic or other human experience data shall be considered in establishing permissible exposure levels. These exposure levels shall generally be achieved by means of engineering controls, to the extent technically and economically feasible, augmented by administrative controls and personal protective equipment as appropriate. OSHA shall require that this exposure level be achieved as soon as feasible, and may require as an interim measure that exposure levels be reduced immediately through a readily available practical combination of engineering and administrative controls and personal protective equipment.

The permissible exposure levels (in ETS and permanent standards) may vary from chemical to chemical, depending upon the analyses of risks and benefits. Means of control may vary from one use of a chemical to another. Limitations of surface accumulations of a chemical should be expressed in quantitative terms.

(b) Where an ETS is to be issued and sufficient data are not available to quantify risks to employees, OSHA shall advise the Interagency Testing Committee established pursuant to the Toxic Substances Control Act of the desirability of requiring testing

consider institution of a permanent rulemaking under Section 6(b) of the Act based on regulatory priorities, unless it shall determine that such a rulemaking is not necessary to protect employees. As part of such a rulemaking, OSHA should advise the ITC of the need for dose-response data if they do not exist. Permissible exposure levels and other regulatory provisions should be established in the same manner as called for in the preceding subparagraphs (a) through (e).

C. Analyses of risks and benefits for Category I and Category II Substances.

In establishing permissible exposure levels and other requirements of a specific standard, OSHA shall analyze risks (including hazards) and benefits to society (including costs to society) and shall state in writing the manner in which each of the factors listed below, among others, has been considered.

1. Risks. As used herein, risks refers to the observed carcinogenic or tumorigenic properties or propensities of a chemical substance. It is anticipated that the decision of the Data Evaluation and Classification Panel would generally include adequate discussion of risk factors. Risk factors include:

- (a) evidence of carcinogenic potency, whether epidemiologic or experimental animal evidence;
- (b) dose-response relationships and associated metabolic and pharmacokinetic data, if available;
- (c) evidence of negative human or epidemiologic experience with the substance, where only experimental animal evidence tends to implicate a chemical substance. (It is recognized

that while epidemiologic evidence cannot conclusively show that a substance is not carcinogenic to humans, such evidence would be relevant to the assessment of risks and should ^{be} ~~used~~ be used in that process);

- (d) whether the evidence of carcinogenicity consists only of experimental results, as opposed to epidemiology;
- (e) the number of mammalian species for which evidence of carcinogenicity exists; and for each such species:

- 1. Characteristics of tumor(s) products

- a. Benign
- b. Malignant
- c. Life shortening

- 2. Dose Response

- a. (Sub)threshold level(s)
- b. Time to appearance of tumor
- c. Slope of dose-response curve

- 3. Biological Variation

- a. Tissue (organ)
- b. Sex
- c. Strain
- d. Species

- 4. Route of Exposure

- a. Respiratory (inhalation)
- b. Percutaneous (dermal)

c. Gastrointestinal (oral)

5. Dose

a. Concentration

b. Volume

6. Exposure Characteristics

a. Frequency

b. Continuous

c. Intermittent

d. Duration

(f) the number and quality of any negative mammalian experiments;

(g) the kind of mechanism, or combination of mechanisms, producing observed carcinogenic effects.

2. Hazards. As used herein, hazards refers to conditions relevant to the likelihood, given certain risks within the foregoing definition, of a carcinogenic event due to use of a chemical substance in the workplace. Hazard factors shall be evaluated as and when necessary and shall include:

(a) the number of workplaces in which the substance is present;

(b) the number, age, sex, health and occupation of employees in such workplaces;

(c) the conditions of manufacture or use of such substance in various workplaces;

(d) the frequency, duration, and intensity of exposure of employees (1) at present,

HEALTH PROGRAM MANAGEMENT

To ensure prompt and reasonable action to limit employee exposure to known or suspect carcinogens, and to ensure compliance with any permissible exposure levels, each employer shall prepare and implement written plans, as follows:

1. Means to Reduce Employee Exposure to Known or Suspect Carcinogens.

Because workplaces vary substantially -- in terms of how a substance is used, the number of employees present, the age of the plant, the duration and intensity, and frequency of exposures, and many other variables -- it will often be appropriate for different employers to take different actions to reduce employee exposures to known or suspect carcinogens. AIHC recommends that for each workplace the employer use the best practicable combination of engineering controls, administrative controls, and work practice controls to reduce such exposures. The following table lists actions that employers should consider.

AIHC recommends employer considerations of such factors upon learning of the presence of a substance in the workplace that is a known or suspect carcinogen, regardless of the status of regulatory action. AIHC similarly recommends that any OSHA guidelines in anticipation of regulatory action, reflect such factors.

Where regulatory action has been taken and OSHA has specified permissible exposure levels, OSHA should require employers to prepare, for each workplace where a regulated substance is present (other than in mixtures excluded from regulation), a written determination whether exposure levels higher than an

action level are likely to be experienced. If the determination indicates the action level is likely to be exceeded, the employer must prepare a written program, to assure compliance with permissible exposure levels, that is regarded as the "best practicable combination" for the particular workplace. This program must reflect consideration of the priority actions indicated by the following table. This table does not reflect economic considerations, since these can be, and should be, considered on a case-by-case basis. As employer's plan which does not choose the more restrictive action must explain why that action was not practicable or applicable and thus show that the action has been considered.

The program must be made available to any interested employee, employee representative, or OSHA, upon request. From time to time the program may be revised, in writing.

Compliance with such a program will not excuse failure to comply with a permissible exposure level. The requirement to prepare a written program is in addition to the requirement to comply with a permissible exposure level.

Where exposure levels in an area are above action levels for substances classified in Category I or II, administrative controls should generally include restriction of access to authorized employees and the placing of signs at entrances to the area. For Category I substances the signs should state "Restricted Area, Authorized Personnel Only, Cancer Suspect Agent," and the name of the substance. For Category II substances the signs should state "Restricted Area, Authorized Personnel Only," and give the name of the substance. Because use of the word "Cancer" can be

counterproductive with respect to health and safety, producing stress and other undesirable effects, the word should not be required for signs for Category II substances. Authorized employees should be informed of the nature of the potential hazard and should be well trained to perform whatever work they will be doing in the area, whether routine production, emergency, maintenance, or other work.

Control Factors Table

WORK FACTORS TO BE EMPLOYED

(In Best Practicable Combinations) Degree of Control

Near Term Action

Administrative Control

Administrative controls would include limiting work hours, rotating personnel, designation of work areas, provision of mandatory showers where applicable, etc.

Limited Access to Workplace

- (a) Completely restricted (badges, pass codes, etc.)
- (b) Controlled (sign in/out).

Personnel Selection

- (a) Highly qualified (by education, training or experience.
- (b) Semi-skilled.

Worker Info and Training

- (a) High degree (emergency response, containment procedures, shut down procedures plus the following):
- (b) Medium degree (protective equipment and its functions/malfunctions, biological implications, procedures for routine maintenance.

Housekeeping

- (a) Intensive (equipment check in/out procedures special procedures for clean up and disposal plus all below).
- (b) Less intensive (written standard operating procedures for normal operations,

WORK FACTORS TO BE EMPLOYED

(In Best Practicable Combinations) Degree of Control

Near Term Action (continued)

	segregated secure storage areas for product).
Industrial Hygiene	Monitoring as required to assure compliance with permissible exposure levels.
Protective Clothing and Equipment	(a) Change rooms and daily clothing change. Provision to secure clothing before cleaning. (b) Work clothing to be left at work and provision to segregate work clothes from street clothes. Work clothes to be cleaned by employer.
Respiratory Protection	As required to insure compliance with permissible exposure levels.
Engineering Controls	(a) Redundant systems, alarms, etc. (b) Control workplace emissions by tightening up process. (c) Complying with good manufacturing practice; no open vessels, etc.

Long Term Action

Set up Exposure Records	(a) Exposure record for individual employee (above action level). (b) Exposure record for job classification (above action level).
Engineering (structure or process) Modifications	In general, increased emphasis on engineering, structural or process controls.

2. Medical Program.

For employees who may be exposed above action levels to substances classified in Category I or II, the employer shall establish a medical program with the guidance of a trained

physician. The employer shall inform the physician of the nature and category of any such classified substance, and of the evidence underlying the classification. The physician shall exercise independent professional judgment regarding the medical program, including the scope and frequency of medical examinations, the selection of biological determinations for a specific substance. The medical program must be appropriate for the particular substance. The program shall be expressed in writing and be made available to such employees, a representative of such employees, or to OSHA upon request. A program for a specific substance may be integrated with one or more programs for other classified substances and may be integrated with any general medical program provided by the employer. It is anticipated that OSHA may provide guidelines for such programs and may require particular examinations or procedures to be included in a program unless equivalent or better alternatives are used.

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For your information.

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