DOW CHEMICAL U.S.A.

MIDLAND, MICHIGAN 48640

November 11, 1977

TO: MEMBER COMPANIES IN CHEMICAL
AND CHEMICALLY-RELATED INDUSTRIES

All of you have probably heard by now about OSHA's proposed new "comprehensive carcinogen policy." Attached to this note is a letter from your trade association describing the current situation, and seeking your participation and financial support.

I agreed to lead our effort to bring reason to the OSHA proposal because I am convinced the issue is of critical importance to all of us. I want to assure you that this task has my highest priority, and to emphasize that it will take a major effort from all of us to get the job done.

I hope you will generously support this effort financially, and that you will plan to testify at the upcoming hearings. We need you.

Sincerely,

Paul F. Oreffice
President
Dow Chemical U.S.A.

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Attachment

AP00049425

Air Products and Chemicals INC.

ALLENTOWN, PENNSYLVANIA 18105

20 December 1977

Dr. E. D. Blanchard
E. I. duPont de Nemours & Co., Inc.
Organic Chem. Department
Dyes and Chemicals Division
Wilmington, Delaware 19898

DEC 22 1977

Dear Dr. Blanchard:

It was a pleasure meeting you at the AIHC meeting at Chicago last week, and to see the considerable amount of work that has been accomplished by your committee. As you requested, several of us at Air Products have reviewed the draft "Summary Analysis" which you distributed, and our comments are attached.

This is a good piece of work, and is very constructive in its approach. We understand the problems of putting together a committee product, and feel sure that the few rough spots will be smoothed out in the review process. Peter Hutt is an excellent man for this.

We hope that our comments are helpful, and if we can be of any assistance to you or your committee, please feel free to call on us.

Very truly yours,

ORIGINAL SIGNED BY

John T. Barr
Assistant Director
Plastics Research and Development

JTB/sjl
Enc.
cc: F. Hoerger - Dow Chemical
bcc: R. Fleming
R. H. Schenck
L. B. Tepper, M.D.

AP00049426

Air Products and Chemicals INC.

21 December 1977

Comments on the Draft of 14 December

"Summary Analysis of Reasons to Modify OSHA Proposal"

1. Page 1, line 5.

"Entirely" is a bit too strong - use primarily, or substantially. There are some due to industrial exposure.

2. Page 2.

We should emphasize our intent to control to the greatest practical extent those cases due to occupational exposure.

3. Page 3, last paragraph.

I hope we can challenge the OSHA claim more strongly, and use U.S. data to the extent that it is available.

4. Page 4, section B.

Would "influenced" be a better word than "related," in the second line?

5. Page 5, first paragraph.

For comparison, calculate lung cancer as a percent of the total cancer cases. A quick reading of the third paragraph would suggest a conflict with the tobacco cases at 2%. Perhaps a little rewording could fix that.

Also, we hope that we avoid the sin we accuse others of, that is, quoting out of context. We don't have the full Newell paper, but may we suggest caution in erring on the conservative side in quotes.

6. Page 6, quote.

See comment 2, relative to the 600 cases.

7. Page 7, second paragraph.

Here you use stringent in a good sense. In the next paragraph, we suggest substitution of "inflexible" for "stringent," and also on page 29, second paragraph.

Perhaps it would help to emphasize that the NIOSH list of 15 were known human carcinogens, while the present list is far less rigorous in its derivation, and includes tumorgens from implantation tests, etc.

AP00049427

8. Page 10, section D.

We suggest that you add, after "freeze," - "the regulator process at the present level of knowledge of" . . . science, etc.

Here, and page 72, could be proper places to discuss the need for knowledge of the mechanism of carcinogenesis, e.g., selenium is not a human carcinogen because of its different metabolic pathway than, say, vinyl chloride.

9. Page 12, first paragraph.

Here it could be useful to discuss the FDA approach of no detectable residue at a concentration that gives an acceptable risk. Mr. Hutt can be helpful here.

10. Page 13.

In the final draft it will help the reader to identify the AIHC proposal location by section, appendix number, etc.

11. Page 14.

It will be useful to separate the attack rate and the dose response contributions to potency. That is, just what does cause effects to differ? Is it exposure levels, or effectiveness at equal concentrations? This type of discussion can help our cause.

12. Page 15, section I.

Why limit personal protection to one hour/day? This should depend on the protective device used. We prefer the primary suggestion to this alternative.

13. Page 17, first full paragraph.

Perhaps you could point out that society has judged in many cases that it is at the limit of acceptable intervention by government. Costle of EPA made just such a comment to Dick Fleming in a meeting on 22 November.

Dick Wilson of Harvard has several papers out on relative risks. He is on the list of expert witnesses for April 4. I am sure you can get many more examples from his work. I can send you some, if you wish.

14. Page 18, second paragraph, third line.

Insert "risk" before "free."

AP00049428

15. Page 21, first partial paragraph, line 11.

Change "should" to "can" or "may," to make the statement stronger?

16. Page 22, section D, line 9.

We are not able to prove no bad effect of human hormones, so perhaps we should omit "at subthreshold or no-effect levels."

See also the last part of comment 8 on mechanism.

17. Page 23.

It could be useful to cite here the recent paper by Purchase, et. al., Nature 264, December 16, 1976, page 624, on the reliability of the "quick tests."

18. Page 24.

We must anticipate the charge that we wait until men die before we act, so emphasize that regulation will occur on other grounds than human epidemiology.

We should be sure that we understand why FDA permits 1 ppb aflatoxin in peanut butter. Do they say it is safe, or no-effect, or is it a technical limit?

19. Page 26, last paragraph.

Don't emphasize Paision vs. Jules, let the courts say it, as on page 21, but don't overemphasize it. Maybe we should drop or reword "Congress . . . rolls."

20. Page 27, first paragraph.

We doubt that a ban of a substance by OSHA would be legal, but it would not be unconstitutional, would it? Do you refer to lack of due process?

21. Page 27, second full paragraph.

The wording of the fifth line is scrambled. This argument can be expanded to cover the very complex administrative problems that will arise. For example, each use of a substance may have quite different substitutes. The hearings could be very prolonged on just this point.

22. Page 30, section L, line 13.

A further reason would be to obtain a higher level expertise on the part of those making the categorizations. The present wording is not entirely clear.

AP00049429

23. Page 32, point 4.

It would also be desirable to improve the working relationship between NIOSH and OSHA, and improve the capability of NIOSH. OSHA could guide NIOSH as to high exposures and large groups of exposed workers to help establish priorities.

24. Page 35, section V.

Laboratories have persons more highly trained than plants, and who are capable of proper handling of chemicals, if they have been informed of their hazards.

In addition, there could be no further research on banned chemicals, thus hampering studies of great potential value.

25. Page 36, Classification Panel.

This is a very good idea, but its establishing needs gash legal research to avoid the problem that regulatory action can be taken only by governmental employees. What if OSHA refused to abide by the decision of the Panel? Who would enforce?

26. Page 38, Categorization

Here again, as on page 14 (comment 11) there is danger of confusion of attack rate and dose response.

A complete rationalization of the numerical limits is needed in the full document. For example, you say earlier that vinyl chloride is a weak carcinogen, and we agree. But, angiosarcoma is a very rare disease, and the incidence is greater than ten times background in persons heavily exposed for long periods. Does this then make it potent?

Also, some development of the need for understanding of mechanism is needed. On page 40, in the paragraph numbered A, it can be pointed out that the zymbal gland of rodents is a fat-rich, rapidly multiplying specialized cell that concentrates some materials such as vinyl chloride, and differentiation of results in such cases is justified.

All this is to emphasize the point that a rigid categorization before the facts are developed is unworkable.

27. Page 41, section B.

Some materials are so toxic that the doses suggested here will be above the maximum tolerable. Thus, the upper limit would be, say, 1,000 mg/m^3 or some fraction of the maximum tolerated in screening tests.

Again, these suggested limits need some supporting rationale by qualified experts.

AP00049430

28. Page 43, section 1 A (1).

Insert "statistically significant" before "excess."

29. Page 46, OSHA Regulatory Response

Nowhere in the OSHA proposal or in here is there a clear statement as to what happens to the 16-18 present carcinogens. Do we keep the present standards or start all over again with an ETS and hearings? We suggest a statement that these be left alone as having had adequate regulatory history.

30. Page 48, paragraph (C).

One point that should be considered is the probable concentration of the toxic impurity as it most likely occurs. Thus, the exemption should be as high as needed to exempt the usual mixtures, but otherwise as low as possible.

31. Page 49, paragraph 2 (A).

Why should the permanent standard continue the limits of the ETS? Better data should be available during the six months period to permit setting a more precise limit.

Do you contemplate continuance of the action level concept? It is not mentioned.

32. Page 51.

We suggest a more appropriate title for this section to be Toxicity, or Oncogenic Potency, and use Risks, or Hazards, for the section on page 52.

33. Page 54, paragraph 4 (B).

For clarity, add "direct" before the words "economic feasibility."

34. Page 55, first partial paragraph, line 5.

Insert "significant" before the words "health benefit."

AP00049431

OUTLINE FOR REBUTTAL TESTIMONY RE

OSHA'S PROPOSED CARCINOGEN POLICY

DEC 22 1977

To prepare ourselves to fully address the issues in the proposed policy "in a spirit of cooperation and candor" (page 8), we must realize the full magnitude of all the questions and issues which are presented in the proposal. Many of the "big issues" are obvious and will no doubt receive much attention in preparation of testimony and rebuttal arguments. However, to be successful in the OSHA Informal Hearing, we must be well prepared advocates who: 1) can responsibly address the issues in the proposal, large or small, and (2) address all OSHA proclamations of "policy".[1]

At the Informal Hearing beginning in March, (a hearing which will no doubt become adversarial at many points), we must be technically prepared for every point and at every turn. The naive "stateman" who expects to waltz through the Informal Hearing and address only the big issues of science or fact, will be doing himself a terrible disfavor. Preparation, not statesmanship alone, will carry the day.

[1]Page numbers referred to in this memorandum are taken from the preprint copy of the proposed regulation. The preprint copy is 278 pages long and bears the U.S. Government Printing Office Number 1977 0-247-285/6600. The preprint is identical to the proposed regulation published October 4, 1977 at 42 FR 54148-54195.

RECEIVED

DEC 9 1977

RICHARD FLEMING

AP00049432

Anchor Points for Rebuttal Preparation

Before listing individual questions and issues which are raised by the proposal, we should first look at some very basic underpinnings or anchor points which both we and OSHA will have to work with. These anchor points should serve as a good foundation for preparing our responses to the OSHA issues.

1. OSHA has proposed on page 5 several basic propositions which are fundamental to their proposal.

   A. "The term "carcinogen" although difficult to define as a matter of science, must be defined for purposes of overall regulatory activity."

   B. "That a toxic substance, determined as a carcinogen in a mammalian test animal system, as defined, is to be treated as a policy matter as posing our carcinogenic risk to humans."

   C. "That when OSHA is dealing with a toxic substance, identified as a carcinogen, as defined herein, the permissible exposure limits will be set as low as feasible."

AP00049433

D. "In cases where there are suitable substitutes that are found to be less hazardous to the worker, no occupational exposure to the toxic substance will be permitted."

E. "Unless there is evidence submitted in this rule-making sufficient to convince the Secretary of Labor that this general policy is incorrect mainly, that there is presently no means to generate a safe exposure level to a carcinogen, the permissible exposure limits will be set as low as feasible or occupational exposure will not be permitted in certain cases, both determinations to be made in the individual rulemakings conducted pursuant to this subpart."

2. OSHA has proposed some definitions of terms which in some cases are very broad and could be very troublesome in later rulemaking procedures. These definitions include:

A. "Potential occupational carcinogen" (page 202),

B. "Short term tests" (page 203),

C. "Suggestive" (page 203),

D. "Toxic substance" (page 203),

E. "Information" (page 205).

AP00049434

3. OSHA indicates that it does not believe that this "generic" form of standard setting will shortcut the employer's due process rulemaking rights because this rulemaking proceeding will allow full public debate on OSHA policy decisions and proposed regulatory framework (page 38). OSHA further indicates, however, that the case by case approached regulation must be replaced by the generic approach for these reasons:

A. To eliminate the relitigation of certain issues in each and every rulemaking.

B. To reduce the taxing of witnesses who have in the past been willing to testify.

C. To guarantee a continuity of approach in each and every case within the agencies and within the courts. Such continuity apparently has not heretofore been had.

D. To allow OSHA to function since its manpower resources are exceeded using the case by case approach.

E. To prevent the collapse of the rulemaking procedures because of the futility of effort in a case by case approach.

AP00049435

These latter five points appear to be the real and practical reason why OSHA desires an expedited generic procedure. Further evidence of this is found on pages 36 and 37 where OSHA states:

> "To dedicate substantial (and unavailable) resources to the rehearing, and record resubstantiation in each and every rulemaking, of these kinds of policy issues is truly nonproductive if we are honestly concerned about the health of workers and, possibly, the future of mankind."

4. OSHA has relied on at least four major issues of science upon which they feel there is no major scientific debate. These four concepts are listed on page 67 and are as follows:

   A. That there are practical and ethical difficulties in relying on epidemiological studies in man as a basis for establishing the lack of a carcinogenic potential of substances.

   B. That there are studies in experimental animals which are valid ways to establish a carcinogenic potential of a substance.

   C. That there are established minimal and optimal experimental conditions for testing for carcinogenicity.

D. That there are accepted kinds and methods of statistically significant changes in tumor incidents that may be observed in experimental animals and used to characterize carcinogenic potential.

These four major areas upon which OSHA feels there is scientific agreement are then supplemented by OSHA with other issues upon which OSHA relies and of which OSHA feels there is general agreement. These latter principles begin on page 67 of the proposal and continue through page 110 of the proposal. These latter points will be addressed seriatim later in this memorandum. For the time being we will call these later issues major sub-issues for rebuttal testimony and expertise.

5. Throughout the proposal, OSHA has expressly solicited "public comment". To be well prepared for the March Informal Hearing, we must address those areas on which OSHA solicites such comment. Failing to completely do so could put us in the position of having OSHA tell us later that we have waived our future rights to submit comment on these issues because we sat on our hands when OSHA expressly invited such comment.

AP00049437

Questions and Issues for Rebuttal Expertise and Testimony

In preparing ourselves for the Informal Hearing, we will find that many people are not aware of some "issues" in the proposal. To highlight these "silent issues", we have taken the proposal on a page by page basis and phrased questions based upon sentences within the proposal which seem to call for a response or a counter-question. In doing this, we have again relied upon the 278 page preprint version of the proposal. What follows is a listing of questions which should spark one to generate rebuttal testimony or to respond with a counter question. The numerically listed questions are generally phrased in the form of a question which could be answered. Each entry is referenced to a page number of the proposal preprint and is referenced to that part of the page wherein the question is found. For example, if the issue is found in the first 1/3 of the page it will be noted as page X(1/3). If the question is found in the lower of the page, it will be noted as page Y(3/3). Following then are the questions which could generate rebuttal testimony:

1. Page 2(1/3). Can the protective provisions of the proposed ETS be instituted immediately?

2. Page 2(2/3) (3/3). Will an employer ever be able to show "unique circumstances" which would warrant departure from the proposed provisions of the model standard?

AP00049438

3. Page 4(3/3). Is the term "suspect carcinogens" utilized in the NIOSH list of suspected carcinogens, a definition which should be allowed in the OSHA rulemaking procedures?

4. Page 5(1/3). Is the extra time required to scientifically resolve the "issues" really inconsistent with OSHA's statutory obligations, and is it really unacceptable to all?

5. Page 5(2/3)(3/3). Are the basic "propositions" really propositions of OSHA or are they in fact the "principles" formally exposed by the EPA?

6. Page 6(1/3). OSHA proposes to rely on human epidemiological studies, but does OSHA really factor in epidemiology into the proposed categorization of chemical substances?

7. Page 7(1/3). Has there really been full scientific debate prior to this time on the concepts which OSHA feels underly the proposed rulemaking?

8. Page 7(1/3). With such a drastic change in direction of rulemaking, are the policy decisions previously made by OSHA on the selected substances listed on page 7 necessarily the same policy decisions which must be made in the broad regulatory rulemaking proposed?

AP00049439

9. Page 7(3/3). Are the regulatory decisions of the other government agencies listed (EPA, FDA, CPSC) really applicable to OSHA decision making? Or, in the alternative, can it be said that the regulatory decisions made by these other agencies were made pursuant to different laws at different times when the basic understanding of cancer causes and prevention were less informed than they are today?

10. Page 8(3/3). Is OSHA really approaching this rulemaking in a spirit of cooperation and candor?

11. Page 9(2/3). OSHA's cite to §6(b)(5) of the law is incomplete. §6(b)(5) reads in part "development of standards under this section shall be based upon research, demonstrations, experiments, and such other information as may be appropriate. In addition to the attainment of the highest degree of health and safety protection for the employee, other considerations shall be the latest available scientific data in the field, the feasibility of standards, and experience gained <u>under this and other health and safety laws</u>".

Can it not be argued, therefore, that OSHA must, pursuant to §6(b)(5), be required on a continuing basis to permit research, demonstrations and experiments to be utilized in each and every rulemaking process?

12. Page 10(1/3). With reference to footnote 2, is it not true that the proposed rulemaking will practically preclude contemporaneous advances in science and technology as they apply to OSHA rulemaking in the future?

13. Page 10(1/3). Are the causes of cancer really eluding us?

14. Page 10(2/3). With the Toxic Substances Law on the books, is it true that with increasing number of environmental chemicals, the number of carcinogens also increases?

15. Page 10(3/3). OSHA notes that in its 6 year history it has only concluded 4 rulemaking proceedings in the health area. Can it not be said that part of the reason for such a small number of proceedings is that OSHA in its 6 year history has spent much of its time and used much of its manpower in promulgating consensus standards and basic safety standards such as fire extinguisher heights and ladder safety provisions?

16. Page 11(2/3). Is it not ture that much definitive evidence indicates that most cancers do not originate from a single transformed cell?

AP00049441

17. Page 11(3/3). Page 12(1/3). Is there a consistent scientific agreement as to the definitions of "sarcomas", "carcinomas" and "lymphomas"? Is it true that not all the features listed on page 12 accompany every malignant tumor.

18. Page 12(3/3). Does the fact that OSHA recognizes the "cumulative or synergistic" effects of agents but fails to include or acknowledge such effects in the proposed regulation give us reason to argue against the proposed model standards?

19. Page 14(2/3). Do we agree with the fact that more than half of the U.S. mortality today is attributable to heart disease and cancer?

20. Page 14(2/3). Do we agree with the 162.8 and 171.5 cancer death figures cited by OSHA?

21. Page 15(1/3). Is it true that the death rate for cancer sharply exceeds predictions?

22. Page 16(1/3). Do we agree that the annual cost of cancer is $15 billion?

23. Page 16(3/3). Is it true that states with high rates of cancer are the more industrialized states?

AP00049442

24. Page 17(1/3). Do not the other types of cancer risks listed by OSHA mitigate against the need to have such a rigid OSHA standard?

25. Page 17(2/3). Is there a consistent agreement that 60-90% of all cancer today may be related to environmental factors? If so, is it possible to break the 60-90% down into finer increments?

26. Page 18(1/3). Is it possible to show that the other kinds of environmental carcinogens as listed by OSHA should require more regulatory attention because of their relative potencies or relative exposures?

27. Page 18(2/3). Do we agree with the statement that occupational cancers may be preventable if the causative agents can be identified and human exposure to them eliminated or minimized?

28. Page 18(3/3). Has the production of synthetic organic chemicals really expanded by 255% in the past 10 years?

29. Page 18(3/3). Page 19(1/3). Do we agree with the OSHA assumption that any increase in cancer which may have been initiated in recent industrial development is <u>not</u> yet observable?

AP00049443

30. Page 19(2/3). OSHA states that the suspicion that all chemicals are capable of causing cancer if administered to experimental animals at sufficiently high doses is not true. Do we agree or disagree with this statement? Do we have the facts to approve or disprove this assertion?

31. Page 21(1/3). Is it true today in the era of concern for toxic substances that negative findings of carcinogenic bioassays are often not published and are even rejected for publication?

32. Page 22(all). OSHA appears to be trying to calm industry by noting that not all chemical agents are capable of causing cancer. It does this by citing the EPA decisions in DDT, Aldrin, Dieldrin and Chlordane Heptachlor. Isn't it true, however, that once an allegation has been made against a chemical substance that it is a "carcinogen", that trial by the press often makes it difficult and perhaps impossible to obtain a reasonable decision and a rule-making process?

33. Page 24(1/3). Do we agree with experimental evidence that apparently indicates that a single cell can be transformed by chemicals to produce a malignant tumor? (footnote 5).

AP00049444

34. Page 24(1/3). Do we agree with the one hit theory as expressed in terms of a "single biological event"?

35. Page 25(3/3). Do we agree that "it is impractical and imprudent to wait for results of epidemiology studies in man"?

36. Page 26(2/3). Do we have all of our facts and figures on the 28 chemical substances or mixtures which OSHA indicates are known to cause cancer in man?

37. Page 26(2/3). Do we agree with the statement that all human carcinogens with the exception of one (arsenic) are known to cause cancer in experimental animals.

38. Page 27(1/3). Do we agree with the 1975 NRC Pest Study which indicates that 12 of 13 human carcinogens are also known carcinogens in mice, rats and hampsters.

39. Page 28(1/3). Is it true that the courts have approved EPA's previous reliance on animal test data and other similar principles.

40. Page 29(3/3) and Page 30(1/3). Is it true that the OSHA law is a technology forcing law, i.e., that technological feasibility is not limited to devices already in use?

AP00049445

41. Page 30(1/3). Do we agree that medical examinations or other tests must be made available to employees at no cost?

42. Page 30(3/3). Do the sections of the law cited in the proposed standard indicate Congress's recognition that conclusive medical or scientific evidence does not exist for many toxic materials or agents?

43. Page 30(3/3). Do we agree that Congress mandated that standards should not be postponed because definitive scientific evidence is not currently available?

44. Page 30(3/3). Does the congressional history of the law indicate that Congress intended to preclude for every debate surrounding diverse medical opinion?

45. Page 32(1/3). Are there any facts or information which in hindsight will give us evidence to indicate that in 1977 we have gone beyond the "frontiers of scientific knowledge" which is often referred to by OSHA and which is the language of the AFL/CIO vs. Hodgson case?

46. Page 36(2/3). Is it true that the OSHA decisions on key issues in arsenic, coke oven emissions, benzene, and beryllium, were made by the agency as a matter of "policy" rather than a complete factual certainty at the time of that determination?

AP00049446

47. Page 36(3/3). Is OSHA's interpretation of SOCMA vs. Brennan (EI Standard) proper? i.e., was the court really saying that the extrapolation of animal carcinogenicity to human carcinogenicity is a matter for OSHA policy versus a matter for legislative action versus a matter of scientific fact versus a matter of legal fact?

48. Page 38(1/3). Is it reasonable or practicable to believe as OSHA has stated that in one rulemaking procedure all scientific bases can be debated and all their consequences delineated?

49. Page 38(3/3). Does the OSHA cited precedent really indicate that interested parties can be nominally deprived on a hearing on individual claims which may be contrary to previously announced and generally accepted policy?

50. Page 39(1/3). Is it not true that this generic rulemaking will deprive future interested parties in an arbitrary manner their statutory procedural rights?

51. Page 40(3/3). Is is not true that identifying carcinogenic potential is not the same as identifying carcinogens in humans?

AP00049447

52. Page 41(1/3). Do we agree that in this proposal, OSHA has not placed sole reliance upon short term tests and has not placed any reliance on a molecular structure or similarity?

53. Page 41(2/3). When good human studies can be or have been conducted on agents, why can't they then be the main basis for regulatory decision making?

54. Page 42(3/3). Why can't negative human studies, even when other chemicals are present in the study, be used to show that there is not risk from a specific chemical being studied?

55. Page 43(3/3). Can we put together a case that shows that negative epidemiology studies can be interpreted to indicate that there is no carcinogenic risk?

56. Page 44(3/3). OSHA has conceded that it has been found that individual variability in response to carcinogens is great. Therefore, should we ask that prior to regulation OSHA be required to prove that animal studies used to determine potential carcinogenicity have been so well conducted that all variable factors that affect human response have been held constant and the results that are achieved are truly due to the chemical itself and not to those other factors beyond OSHA's regulatory control?

57. Page 45(3/3). Is it possible to show that workers exposed to agents really have not developed a "false sense of security"?

58. Page 46(3/3). OSHA has conceded that some chemicals are virtually everywhere in the environment and has also conceded that there are possible synergistic effects of substances in the workplace. Is it not possible to use these admissions by OSHA as evidence of why a rigid generic regulation is not necessary and not desirable?

59. Page 46(3/3). Is it possible to prove the statement that OSHA has made that 99% of the U.S. population have residues of Dieldrin in their bodies?

60. Page 46(3/3). Is there evidence to indicate to OSHA that many humans have residues of many natural and necessary carcinogenic type agents in their bodies? i.e. selenium, nitrosamines, etc.

61. Page 47(1/3). OSHA has indicated (cited the 1970 NCI study) that as a theory it has been confirmed that a single chemical carcinogen cannot be evaluated out of the context of the total environmental exposure. OSHA has further acknowledged that the regulatory problem of synergism is still not resolved.

Can it be argued therefore, that the proposed generic standard and policy unfairly condemns a chemical substance in the work place because a regulation is not flexible enough to take into consideration synergistic effects or multiple exposures?

62. Page 47(3/3). Can OSHA prove its conjectural statement that "an epidemic of cancer may be in the making".

63. Page 48(3/3). Page 49(1/3). OSHA states that "not to at least qualitatively assume that such a chemical does pose a carcinogenic threat to man seems imprudent and could lead to disaster". Having said this, can it not be argued that OSHA therefore must protect the employees in a work place from all carcinogenic risks including those of alcohol, cigarettes, eggs, lima beans, apples, meats, etc.

64. Page 49(1/3). OSHA has noted that it has long accepted several principles which it states were adopted in the preamble to the standards to the 14 carcinogens. Can we not argue and request therefore, that all issues of science and all issues for debate in the rule making on the 14 carcinogens be admitted by judicial notice and made a part of this rule making record?

65. Page 51(1/3). OSHA cites the EPA Administrator's decision in the Aldrin Dealdrin matter. Can it be argued that the decisions were an EPA matter and the principles or issues thereunder are in fact different from the principles and issues in OSHA regulation? If this can be done, does it not make sense therefore to require that OSHA withdraw as its support for this proposal all reference to EPA regulations and decision making?

66. Page 51(3/3). OSHA likewise cites decisions by the FDA particularly that on the ban of chloroform. Can it not therefore be argued that FDA principles and decision making parameters are different than that from OSHA and that therefore references to FDA decisions must be withdrawn by OSHA in this rulemaking procedure?

67. Page 52(2/3). OSHA cites the banning of TRIS by the Consumer Product Safety Commission as precedent for proposed OSHA rulemaking. The citation however is incomplete in that it does not include reference to the North Carolina Court's decision in the banning of TRIS. Should we not therefore enter into the rulemaking record on this matter the decisions of the Judge in the North Carolina court on TRIS?

AP00049451

68. Page 53(1/3). Are we in agreement with the statement that "an investigator can study many generations of rodents in a single year"?

69. Page 54(1/3). Are we in agreement with the statement that "evidence indicates that a chemical that causes cancer in one animal species is likely to do so in most other species tested"?

70. Page 55(2/3). Here OSHA begins to trace the history of animal testing including criteria and principles applied to the design and interpretation of studies to illustrate the varying conditions accepted for testing for carcinogenicity in animals and the necessary reliance therefore on such data despite considerable uncertainties. The tracing of history is done through the writings of scientific advisory bodies and other government agencies and begins on page 55 with a 1959 report by the National Research Council of the National Academy of Science. The basic tracing of history ends on page 67 with a citation to the 1976 study by the National Cancer Advisory Board of NCI. The majority of the supporting reference material relates to food additives and FDA type problems.

AP00049452

The next few questions which follow herein will deal specifically with the sub-issues within these twelve pages or so of supporting scientific history as seen by OSHA. However, as a general question relating to these twelve pages of information, we should ask at least three general questions:

A. How much of this information has become outdated or narrowed in scope?

B. Do references to studies on government agencies other than OSHA properly belong in a rulemaking procedure within the Department of Labor?

C. Is there within each cited report disclaimers, modifiers, or additional text which when added to the abstracted portions of the text cited would give the reference citation a different meaning?

71. Page 55(3/3). Is it possible for OSHA to prove that a qualitative indication of potential human effects, using only portions of the expert or scientific discussions which are cited (and which admittedly review data with considerable uncertainties) are necessary or desirable to protect the worker and to furnish the worker with a safe and healthful workplace?

AP00049453

72. Page 56(2/3). Does the World Health Organization Tech Report No. 220 list recommendations which are interpreted to be "minimum safeguards"?

73. Page 56(3/3). Can OSHA show that the World Health Organization proposed using the most sensitive animals as opposed to not using insensitive animals?

74. Page 57(1/3). On what basis were the various animals utilized in the WHO report shown to be too insensitive?

75. Page 57(2/3). Is it not now true that the NCI maintains that, from a scientific viewpoint, levels of exposure that generate toxic effects other than cancer are too high for evaluating carcinogenicity?

76. Page 58(1/3). Does it appear that OSHA intends to regulate on the basis of past tests which may be considered entirely inadequate by today's standards and further, considering the differences of opinions between experts, does it appear that OSHA contends that it is capable of judging the accuracy and relevancy of animal tests to humans?

77. Page 59(3/3). Do we agree today with the MRAK Commission report which OSHA contends states that "remarkably

unanimous view on the general principles and criteria to be followed for carcinogenesis safety evaluations, widely accepted in principle by the scientific community"?

78. Page 60(3/3). Is it possible that OSHA can prove that the FDA panel in the 1969 study cited was not concerned with the problem of condeming chemicals based on cancer occurrence in rodent test animals overly sensitive as compared to man?

79. Page 62(1/3). In citing a National Research Council's 1970 study on the safety of food chemicals, OSHA indicates that the Committee stated "controlled experimental studies in man, though desirable, have limited predictive value". Can OSHA now show that good epidemiology studies are not suitable to predict future impact from exposure to chemicals?

80. Page 63(1/3) through 64(3/3). Does the 1970 report prepared for the Surgeon General by the Adhoc Committee of NCI contain information which when added to the abstracted portions of that report as cited by OSHA would tell a somewhat different story than what OSHA has portrayed?

81. Page 66(3/3) and 67(1/3). OSHA has taken broad liberties in citing the 1976 National Cancer Advisory Board reference. Another part of the report which appears in the first column

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of page 461 of the February, 1977 Journal of National Cancer reads as follows "the criteria which are described are general guidelines and no rigid, universal criteria. The complexity the problem dictates that the evaluation of potential human hazards of a given agent must be individualized in terms of the chemical and metabolic aspects of that agent, its intended use(s), the data available at the time 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."

Is it not possible to use this National Cancer Advisory Board reference to indicate the many fallacies in the partial citations to the several references used by OSHA in tracing the history of animal testing through the literature?

82. Page 68(2/3). OSHA notes that the mammalian species other than rat, mouse and perhaps hamster are generally impractical for use in full-scale bioassays. Do we agree completely with this statement?

83. Page 68(2/3). Do we agree completely with the statement that rats and mice are used in animal studies because of their known susceptibility to agents known to be carcinogenic

in humans as well as the animals' similarity in the mechanisms of tumor induction?

84. Page 68(3/3) through 71(3/3). On these pages OSHA attempts to utilize parts of opinions in matters before the EPA and the FDA. Is it possible to rebutt any of these statements by noting that interpretations by the EPA and/or the FDA are not necessarily binding on OSHA?

85. Page 72(1/3). Do we agree with the statement that valid negative results may be used to evaluate the evidence only if they are derived from tests which used both sexes of each species tested, exposed for their lifetime to a suitable dose range of the test material and the appropriate controls?

86. Page 72(2/3). As to negative test results, is it proper that OSHA should only be concerned with additional negative test results in species which have been reported as positive in other tests?

87. Page 72(3/3). Is it proper that OSHA should consider positive test results as superceding negative test results?

88. Page 73(1/3). Has OSHA properly addressed the problem of false negatives which OSHA contends are due to the insensitivity of laboratory bioassays because of limited numbers of animals and because of inter-species differences in susceptibility?

89. Page 73(2/3). In citing the FDA decision on chloroform, OSHA cites a portion of the FDA opinion which talks about saccharine. Is it possible to use the recent Congressional action on saccharine as a means to rebutt the inclusion in the proposal of the FDA chloroform ban?

90. Page 74(1/3). Do we agree with the statement that positive studies in any mammalian species will, as a general rule, always supercede negative findings in another species?

91. Page 74(2/3). Do we agree with the OSHA belief that "as a practical rather than a theoretical matter, positive animal data should supercede negative human data, in general, because of the inherent defects in such human studies, as pointed out above"?

92. Page 74(3/3). OSHA again uses an FDA citation, in this case DES (diethylstilbestrol). Is there information available which can be used to put the DES matter in perspective

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and to rebutt any issues that OSHA has raised in its short discussion on DES?

93. Page 74(3/3). Can OSHA show or prove why it should not be required to regulate food stuffs consumed by the worker in his working day which have not been proven to be clearly free of carcinogens of any type?

94. Page 75(1/3). Are we in agreement that animal testing must be done at constant high exposure levels to overcome the statistical insensitivity of laboratory bioassays conducted with a limited number of animals?

95. Page 75(2/3) through 78(1/3). OSHA again utilizes EPA and FDA decisions to support its proposed generic standards. Is it possible to develop information that would indicate that analogy to the EPA or FDA principles are inappropriate for OSHA rulemaking?

96. Page 78(3/3). Do we agree with OSHA's logic on the issue of species or organ-specificity? Further do we agree that there can be no presumption that the organ affected in the animal would necessarily be that at risk in man?

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97. Page 79(1/3). Do we agree or disagree with OSHA's very short analysis of statistical significance in animal testing?

98. Page 79(2/3)**. At this point, OSHA notes as discussion on pages 68-79 the five major sub-issues upon which there is general scientific agreement. It notes then, that other major sub-issues numbers 6-11, appearing on pages 79-103 of the proposal are recognized by OSHA to be "areas of scientific debate" upon which there is "opinions of specific experts appearing to be less fully in agreement". OSHA then notes that it "believes that responsible public rulemaking and prudence concerned with protecting the health of American workers mandates the decisions reached therein (i.e., decisions on pages 79 through 103.) Do we agree that prudence dictates that OSHA's beliefs are well-founded?

99. Page 79(3/3) and 80(1/3). Do we agree with OSHA's distinctions between malignant tumors and benign tumors?

100. Page 81(1/3). OSHA first cites the 1969 FDA panel report that seems to indicate that it is suggesting that it would be wise to take serious note of the occurrence of benign neoplasms in experimental studies. OSHA then indicates,

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however, that in more recent times expert agencies and committees seem to be more cautious when benign tumors have been noted. Do we agree that OSHA should take regulatory action when benign tumors have been observed?

101. Page 82(2/3). Doesn't the citation to the FDA panel report indicate that potency of a potential carcinogen should be including in reasonable rulemaking?

102. Page 84(1/3)(2/3). OSHA again taking great liberty, cites the National Cancer Assessment Board report cited in the Journal of National Cancer Institute, February, 1977. This reference also includes however, the following language which might be used to rebutt an inference from the language included in the OSHA proposal: "depending upon the particular case, benign neoplasms may represent a stage in the evolution of a malignant neoplasm and in other cases they may be 'end points' which do not readily undergo a transition to malignant neoplasms."

Is there more information in the NCBA report which could be used to rebutt an improper inference from the NCBA report?

103. Page 85(1/3). OSHA proposes to place as much weight on an experiment in which only benign tumors are observed, as upon experiments in which both malignant and benign tumors are induced. Do we agree with this statement?

104. Page 85(2/3). OSHA notes that science and expert committees do not support the belief that an agent which merely increases the frequency of the type of tumor which spontaneously occurs in untreated animals should not be classified as an augmenting or enhancing agent rather than a carcinogenic agent. Do we agree that there is no science that would say otherwise?

105. Page 85(3/3). OSHA again cites the National Cancer Advisory Board's reference in the February, 1977 Journal of National Cancer Institute. OSHA again has taken liberties with the citation. The citation should read ". . .in most of the current human epidemiologic approaches and certain animal bioassays it is not possible to differentiate clearly between initiating agents. . ." Is it not possible to use the complete opinion of the NCAB to rebutt the incomplete reference of OSHA in the proposal?

106. Page 86(1/3). OSHA notes that arguments have been made about the inapplicability of liver tumors in certain strains of mice, lymphosarcomas in mice and certain other tumors. Do we agree or disagree with the general OSHA policy on liver tumors in mice?

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107. Page 86(2/3). National Cancer Advisory Board references again cited. Is it not true that part of this report has been improperly characterized as a "caution against unequivocal reliance on certain types of bioassays"?

108. Page 87(1/3). Do we agree that animals with relatively high spontaneous tumor incidents are in fact more appropriate for assaying potential carcinogens than animals with low or zero spontaneous incidents?

109. Page 87(3/3). Do we agree with OSHA's proposed interpretation of the results of experiments wherein spontaneous tumor incidents have been observed?

110. Page 87(3/3) and Page 88(1/3). Do we agree with OSHA's examples of statistical significance?

111. Page 88(3/3). Do we agree that in animal tests tumors at sites other than the point of application should be reasonably regarded by OSHA as a potential risk to man irregardless of the relative administration of the agent?

112. Page 89(3/3). OSHA requests that specific public comment be made to its proposed principles regarding routes of exposure in animals as they relate to routes of exposure likely to occur in occupational situations. Are we in agreement or disagreement with the two principles listed at the bottom of page 89?

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113. Page 90(1/3). Do we agree that in particular, positive findings of carcinogenicity in one animal species should generally outweigh negative reports on another, in relation to human application?

114. Page 90(3/3). Are we in agreement with the agency's belief that a single positive result should act as a warning flag to OSHA which would result in OSHA categorizing the chemical substance?

115. Page 91(1/3). OSHA discusses the replication of a single animal species which is found to be positive. However, OSHA does not at this point in the proposal discuss the role of in vitro tests. The National Cancer Advisory Board opinion, however, which has been cited that page 90, does discuss the status of in vitro tests. Do we have additional information which would indicate that replication by single in vitro tests alone should not be sufficient to categorize a chemical substance as a category 1?

116. Page 91(3/3) and 92(1/3). OSHA recognizes that there are "other factors involved in carcinogencity tests which affect the degree of confidence in the results (e.g., choice of strain, spontaneous tumor incidence, duration of experiment, survival, intensiveness, and competence of pathological examination, etc). On page 92 OSHA expressly requests

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comments on this aspect of the proposed generic rule-making scheme. Does this not therefore seem the appropriate spot to submit rebuttal evidence on many major areas of concern relative to the extrapolation of animal data to humans. In this regard perhaps the NCAB report (February, 1977 Journal of National Cancer Institute, page 463) might be instructive. Herein the National Cancer Assessment Board notes "quantitative extrapolation from animal studies for the purposes of evaluating human risks entails large uncertainties at the present time. Each case must be individually evaluated, taking into consideration such factors as adequacy of experimental design, statistical significance of the data, dose response relationships, duration of exposure, route of administration, metabolism (including species variations), host susceptibility, co-factors and other modifying factors, and the amount of the material to which humans would be exposed."

117. Page 94(1/3). On the issue of dose-response, OSHA makes a statement that "in comparable tests systems, chemical carcinogens can vary in the responses they illicit by as much as a factor of 10^7". Do we agree with this statement?

118. Page 94(2/3). OSHA's logic to get to its conclusion that there is no means of predicting individual's thresholds appears to be pretty straightforward. Assuming that we

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disagree with this conclusion, is it possible to rebutt the logic which appears on page 94?

119. Page 94(3/3). OSHA nowhere in this area discusses the concept of threshold's for metabolites. Can we or should be develop rebuttal which would include information on the prediction of thresholds from metabolites?

120. Page 94(1/3). The World Health Organization citation includes a statement that cancer can occur in response to chemicals even after a single dose. Do we agree with this citation? If we do not agree, can we develop rebuttal information based upon our disagreement which would rebutt OSHA's posture on no-effect levels.

121. Page 96(1/3) through 98(1/3). On these 2-1/2 pages, OSHA utilizes predominantly certain information generated by or for the FDA. Can it be demonstrated that such FDA analogies are not appropriate to OSHA's rulemaking?

122. Page 98(3/3) and 99(1/3). OSHA notes that "once a qualitative presumption of carcinogenicity has been established for a substance, any exposure to the substance must be considered to be attended by risk when considering any given population. No exception to this point has yet been demonstrated". Do we agree with this conclusion? If we

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do not agree, can we find an exception which OSHA says has not yet been demonstrated?

123. Page 99(1/3). OSHA notes that it proposes to adopt the principle (i.e., any exposure is attended by risk) to establish qualitatively existence of risk posed by exposure to carcinogens, and hence to justify the classification of substances as category 1 or 2. OSHA then admits that not all individuals contract cancer because of exposure to a carcinogen. However, it then notes that it does not know who in any exposed population might be susceptible and at what levels. Can an argument be made in this area to rebutt OSHA's proposed principle?

124. Page 99(2/3)**. OSHA states that the regulatory decision to treat a carcinogen as having no safe or no-effect levels is supported by logic and decisions made by OSHA and other regulatory agencies. Is it possible to rebutt this decision with <u>facts</u> that would show that the logic of other agencies and the decisions of other bodies is erroneous?

125. Page 99(3/3). OSHA notes that it is unable at present to determine whether humans are more or less sensitive than test animals. Do we agree? If not how is it possible to show that there are relative sensitivities of test animals?

126. Page 100(1/3) through 101(3/3). On these two pages, OSHA comes to the conclusion that: "in regulating a toxic substance that meets the criteria of a category 1 toxic substance, the level exposure set by the standard is not a 'healthful', 'safe' or 'no-effect' level but a feasibility level". In coming to this conclusion, OSHA cites as support five different references including: (1) the 1958 Congressional action on the Delaney clause; (2) a 1961 World Health Organization report; (3) 1960 testimony of HEW before the House of Representatives; (4) a 1974 letter of then Secretary Weinberg of HEW to Congress which objected to amending the Delaney clause; and (5) a 1975 NIOSH statement in the arsenic criteria document.

Do we agree with OSHA's conclusion? Do we feel that the references are outdated or incomplete? Do we have facts or other references which could be utilized to rebutt OSHA's conclusion?

127. Page 102(1/3) through 103(2/3). On these two pages, OSHA discusses its view on quantification of risk (i.e., one form of risk assessment). OSHA starts with the premise that thresholds or no-effect levels can not be set for chemical carcinogens. OSHA concludes on page 102 therefore that quantification of risk if done at all, should be done only to determine the feasibility of regulatory provisions

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of any given standard (i.e., how feasible are the controls as compared to the risk) and should not be done as a part of the chemical agent categorization (i.e., is it a category 1, 2 or 3 carcinogen).

On page 103 OSHA expressly solicits comments on whether estimation i.e., quantification of risk should be attempted and if so which method should be employed. It should be noted however that quantification applies only to the required control techniques and commercial exposure levels and does not apply in OSHA's mind to the categorization of chemical agents. Do we have strong arguments and rebuttal in this area?

128. Page 103(3/3) through 106(2/3). On these pages, OSHA discusses its opinions on the role of short term or In vitro tests. OSHA cites at length the 1977 National Cancer Assessment Board report which has been previously cited and appears in February, 1977 Journal of National Cancer Institute. Do we agree that the NCAB report has been properly and completely cited and referenced?

At 105(3/3) OSHA notes that it does not regard short term tests as sufficiently well developed for use as a sole basis identification of carcinogenic potential.

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129. Page 106(1/3). OSHA indicates its approach to using short term tests in combination with a single bioassay tests for purposes of classifying an agent into category 1. In doing so, OSHA cites the FDA action on the banning of chloroform. Do we agree with the supporting rationale of OSHA?

130. Page 106(2/3) through 110(2/3). On these pages OSHA discusses the role of molecular structure or similarity (structure/function theory) and its role in regulation of chemical agents. OSHA comes to the conclusion (page 110(2/3)) that "at this time OSHA does not propose to rely upon structural similarities between known carcinogens and other substances to regulate those other toxic substances as carcinogens." OSHA then solicits specific public comment on this matter. Do we have comment or rebuttal?

131. Page 107(1/3). OSHA references as its support for its conclusion the 1970 NCI report to the Surgeon General. Do we agree that this citation is complete and factual?

132. Page 107(2/3). OSHA notes that it is not aware of any single molecular configuration, structural characteristic, or physical property of a chemical carcinogen that can be

pinpointed as a crucial cancer-inducing element or site. Do we agree with this statement?

133. Page 109(1/3). OSHA notes that "the limitations of our current knowledge of carcinogen metabolism fail to provide a basis for prediction..." Is this a statement which is factually supportable by OSHA?

134. Page 109(2/3). Even though OSHA apparently discards the structure/function theory as a basis for regulation, on this page OSHA includes three "masked" conclusions. (A) "it appears that single substituents can markedly affect carcinogenic potential; (b) it appears that isomers of carcinogenic materials may frequently exhibit noncarcinogenic effects; (c) steric properties of chemical compounds appear to be of major importance to the ultimate carcinogenic potentcy of the compound.

These three mini-conclusions by OSHA may have a substantial impact if at a later time OSHA changes its mind on the structure/function theory. Therefore, are we in agreement with these three mini conclusions and if not do we have rebuttal evidence?

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135. Page 110(3/3). OSHA notes that the Toxic Substances Control Act might "moot" (eliminate) the problem of regulation because this law might require testing based upon molecular or structural similarities. Are we in agreement? Do we have comments or rebuttal on the OSHA view of the interface between OSHA and TSCA?

Page 127(3/3). In this memorandum, major sub-issues for rebuttal testimony and expertise have not been listed for pages 111 through 197 of the proposal. One critical point in these pages however stands out and should perhaps be addressed.

On page 127 OSHA notes "no occupational exposure" does not mean a ban on the use of a substance: for example, a substance might be used or it can be used in a truly enclosed system. Do we agree with this definition of "no occupational exposure"?

J. S. H.
11/16/77

AP00049472

December 14, 1977

Summary Analysis of Reasons
To Modify OSHA Proposal*

I. The Problem in Proper Perspective.

A. Alleged increase in incidence of cancer.

The rationale advanced by OSHA in support of its proposal implies that this nation is in the midst of an epidemic of cancer and that the epidemic is largely if not entirely attributable to increased usage of industrial chemicals. As for the starting point for this argument, the increase in cancer, it is noteworthy that, using the turn of the century as a time against which to measure the present circumstances, while there has been an increase in the incidence of cancer it is ~~entirely~~ attributable to increases in longevity (the incidence of cancer increasing with age), and increased smoking of tobacco. When appropriate adjustments are made for these two forces, no overall increase in cancer is apparent for the United States. According to the American Cancer Society (1977 Cancer Facts and Figures, p. 6):

> "The overall incidence of cancer has decreased slightly in the past 25 years. . . . For men, the cancer death rate per 100,000 population has increased by over 50% since 1950 for blacks and by 20% for whites. The increased death rate is mainly the result of lung cancer which rose from 18 deaths per 100,000 in 1950 to 52 deaths per 100,000 in 1974. For women, since 1950 the death rate has declined by 5% for blacks and 10% for whites. This is due mainly to a sharp reduction in deaths caused by cancer of the uterine cervix which is attributed to increased use of Pap tests and regular checkups. There was also a decline in stomach cancer. However, the lung cancer rate has tripled from 4.0/100,000 in 1950 to 12.3 in 1974."

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* The OSHA proposal, entitled "Identification, Classification and Regulation of Toxic Substances Posing a Potential Occupational Carcinogenic Risk", appears as Part VI of the October 4, 1977, Federal Register.

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Moreover, leaving aside the kinds of cancers commonly associated with tobacco smoking, in general the same kinds of cancers prevalent today prevailed at the turn of the century, indicating that whatever causes other than longevity and tobacco that account for current cancer rates were, in general, present prior to the turn of the century and thus are not new industrial developments. This is not to imply that no exceptions exist, or that wholly different agents cannot cause the same kinds of cancer. Neither does this imply that more than one agent cannot be a significant contributor to the causation of a kind of cancer; indeed, a prominent example here is the combination of asbestos and smoking tobacco in the causation of lung cancer.

It should be noted also that males and females differ in risk of development of specified forms of cancer and for most but not all forms of the disease the risk of development increases logarithmically with age. In comparison the incidence of any form of cancer in two populations (e.g., an exposed population and an unexposed control population), therefore, it is essential to consider males and females separately and to take into account the age structures of the two populations. It is also necessary to take into account the fact that there may be changes in the background incidence of any particular form of cancer with the passage of time. Thus, the risk that a man aged 70 in 1970 will develop a particular form of cancer before he is 71 may be different from that of a man who celebrated his 70th birthday in 1930. The possible reasons for this are numerous.

The former for instance might have been of a generation

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exposed to mustard gas during the First World War while the latter was too old to enlist. In order to allow for differences of this kind, it is necessary to use cohort analysis procedures whereby men or women born during the span of say 5 years are considered to constitute a cohort for which the risk of development of particular forms of cancer during each year or group of 5 years of life can be calculated separately.

When this is done, for instance, for men born in England and Wales during the period 1861-1901 one finds that for each successive 5 years cohort and at each age from 40 to 80+ the risk of death from lung cancer increased. For instance, a man born during the 5 years around 1861 experienced a 0.1 per 1000 living risk of dying from lung cancer between the ages of 65 and 70 whereas men born around 1886 had a 2.9 per 1000 living risk of dying from the disease between the ages of 65 and 70 -- a 29 fold difference. In assessing whether an industrial chemical is increasing the incidence of death for any particular, if any, form of cancer, therefore, 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-structure and age-structure but also of the same cohort-structure.

In the OSHA proposal (Fed. Reg. p. 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. In England and Wales, for which better data are available than for the United States,

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the death rates for cancers of various kinds in each sex have been compared for different cohorts with birthdates from 1851 onwards with few exceptions, and except for cancer of the lung in both sexes, there has been no evidence during recent years of an increasing risk of death from cancer and for several forms of the disease the death rates have actually been falling. (Reference Case RAM - ?_

B. The relative significance of industrial chemicals.

While it may be true that perhaps as much as 90 percent of cancers are environmentally ~~related~~, it is important to note, as the OSHA preamble does not, that the great majority of environmental factors are not industrial chemicals, but rather are matters such as smoking habits, dietary habits, and exposure to solar radiation. As stated by Dr. Guy R. Newell, Acting Director, National Cancer Institute in his testimony to a subcommittee of the House Committee on Government Operations on June 15, 1977,

> "The term 'environment' must be defined. 'Environment', in its broadest sense, is the sum of everything around us--the water we drink and bath in, the food we eat, and the air we breathe and are almost constantly immersed in. Yes, even tobacco products we smoke or are smoked by others in our 'environment'.
>
> 'By "environment" we mean not only our air and water, but also food, drink, smoking, the workplace and the home, sunlight, and all other aspects of our personal lifestyle.'" (Report on Progress and Activities of the National Cancer Institute, p. 8.)

With "environmental" factors so defined, it may be instructive to consider the importance of the principal such factors. A team of researchers from the American Health Foundation and the National Cancer Institute have estimated that diet, exclusive of

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food additives and contaminants, may contribute to as much as 50 percent of the causes 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/]

Radiation, mostly through sunlight, has been estimated by NCI officials to account for 5 percent 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, gave radiation figures of 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 estimates are that industrial chemicals have accounted for about 1 to 5 percent of the total cancers.[3/] While

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1/ Statement by Gio B. Gori, PhD, 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. 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-napthylamine 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 (continued on following page)

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this is not an insignificant consideration, it is questionable whether the public is being well served if it is led to believe that industrial chemicals are the overwhelming cause of cancer in this country, since that would indicate that the concentration of preventive effects upon industrial activities would take care of the great majority of the problem. That notion is thoroughly misleading and could have very grave consequences for our society as a whole. For example, Dr. Harry B. Demopoulos, until recently the Director of the Cancer Institute of New Jersey, testified on November 5, 1976, before the New Jersey Senate Commission on the Incidence of Cancer, that:

> "Industry-related cancers form a very small and rather insignificant percentage of our cancer statistics. . . I have figured out about 600 excess deaths in New Jersey every year that you might blame on industry, or industry-related factors. This is 600 deaths out of 14,000. And, I submit that given a choice of where to focus, I would rather focus on the 13,400 deaths where we have no known relationship to industry and where we know some of the other factors that we can control through education and early detection. . . ."

Similarly, it is difficult to justify OSHA's preambular comparison, by implication in many places, of the total cost to our society of all cancers, with those (unspecified number of) cancers

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3/ (Continued from previous page) 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:

"Bailor (personal communication) estimated tht 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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attributable to exposure to industrial chemicals. While it is reasonable to compare costs and benefits even in such an emotion-laden area as cancer, it is only reasonable to compare the problems caused by the use of industrial chemicals with the benefits that are derived from them.

In any event, it seems clear that there is substantial reason to take stringent action regardless of regulatory responsibility where confirmed or highly probable causes of cancer have been identified as present in the workplace. In all probability, however, the extent of such causation is being reduced rather than increased, since there is increased awareness of the possibility of occupational hazard and greatly increased measures in common use to reduce employee exposure to industrial chemical substances.

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

To justify the oversimplifications and ~~stringency~~ inflexibility of its proposed categorical approach, OSHA makes much of its alleged inadequacies over the past seven years to regulate industrial carcinogens. One can question the accuracy, and thus suspect the motivation, for this self-debasing criticism. In 1972 OSHA wrote to its expert advisor NIOSH requesting information on all known industrial carcinogens. NIOSH responded by making a literature survey and by requesting information -- on fifteen substances -- by publication in the Federal Register on July 6, 1972. NIOSH subsequently advised OSHA that there appeared to be fifteen occupational carcinogens, some known human carcinogens and some implicated solely on the basis of bioassay experiments. This advice was subsequently modified by the deletion of one of the materials, dimethyl sulfate,

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leaving fourteen carcinogens that NIOSH then believed to be in use, or previously to have been used, in American workplaces. In 1973 OSHA promulgated an emergency temporary standard limiting employee exposure to all fourteen chemicals and commenced a permanent rule-making which itself was completed in January of 1974. See 39 Fed. Reg. 3756 (Jan. 29, 1974.) What more OSHA could have been expected to hae accomplished by then is left unsaid by the current self-debasement, which also ignores the more vigorous efforts OSHA has made during 1977 to regulate industrial substances that have been implicated as carcinogens.

Much of the apparent subsequent gap between the regulatory need and OSHA's response is attributable not so much to short-comings on OSHA's part as to a number of other considerations. One, but only one factor here is the substantial increase in recent years in experimental testing of chemical substances for evidence of carcinogenicity, and acceleration of the reporting of the results of the tests. Another factor, however, has been a very questionable modification in OSHA's operative criteria for assessing carcinogenicity. Thus, 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 were concerned. Now, however, OSHA proposes to use much less reliable evidence as a basis for regulations.

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

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"Suspected Carcinogens" subfile of the Registry of Toxic Effects of Chemical Substances. The Second Edition of this subfile, published in 1976, lists 2,415 substances. This does not at all indicate that there are that many carcinogens, or even that NIOSH believes that may be the case. Rather, the subfile is an uncritical compilation of published data about the chemicals; many perhaps as many as 510, are listed simply because some government agency has indicated an interest in testing them. As the Editor of the subfile has noted in the Preface:

> "This publication does not indict a substance as a human carcinogen. Rather it reports published data which suggest that the substance has caused neoplastic or carcinogenic effects. The experimental designs used in the cited studies may be unsuitable for prediction of human effects. Their inclusion in the Registry does not reflect an evaluation with respect to the adequacy of the data, or consideration of negative or contradictory studies.
>
> "The National Institute for Occupational Safety and Health (NIOSH) identifies a substance as a potential human carcinogen by means of the criteria document process. This involves exhaustive literature review and careful consideration by experts leading to a definitive conclusion. This subfile is published to serve as a guide to the literature, and as an indication of those substances which may require further research and evaluation."

As the Preface indicates, NIOSH itself does not regard the subfile as more than a "guide to the literature". It is, of course, necessary to establish priorities in this area; NIOSH has done so in selecting materials to be covered by Criteria Documents. An example of the difference between the subfile and Criteria Document is formaldehyde. This substance is reported in the subfile as having produced neoplastic effects, but the NIOSH

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Criteria Document on Formaldehyde, dated December, 1976, does not conclude that the material presents a carcinogenic hazard.

D. Complexity and rapid evolution of scientific learning with respect to carcinogenicity.

Sound and well informed decision making with respect to occupational exposure to potential carcinogens ought to take into account the fact that the scientific aspects of the causation of cancer are extraordinarily complex, and the fact that, as the result of various substantial commitments of research and testing commitments to ascertaining individual causes of cancer and to understanding the mechanisms of such causation, the state of the art is currently evolving very rapidly. This being so, it would be inappropriate to "freeze" science as of the present time, which the OSHA proposal would in large measure do. The inappropriateness of OSHA's approach appears clearly from the advice of the Subcommittee on Environmental Carcinogenesis of the National Cancer Advisory Board, a group charged by the Director of the National Cancer Institute (NCI) with developing criteria for assessing evidence of carcinogenicity which cautioned that:

> "in assembling these criteria, the subcommittee recognizes that at present there is no simple and universal definition of either carcinogenesis or neoplasia. The criteria which are described are general guidelines and not rigid, universal criteria. The complexity of the problem dictates that the evaluation of the potential human hazards of a given agent must be individualized in terms of the chemical and metabolic aspects of that agent, its intended use(s), the data 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 cri-

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teria appropriate for one agent may not necessarily apply to another." (58 J. Nat'l Cancer Inst. 461, Feb. 1977.)

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 reflects conclusions expressed seven or more years ago; many of these are already outdated and imprecise or otherwise inaccurate in light of current references. Indeed, even at best the cited references reflect only a single bias or perspective on the problems of occupational carcinogenesis. For example, they fail to reflect the very considerable body of learning supporting the no-effect level hypothesis.

It is manifestly unwise to disregard not only the developments of the past few years in better understanding the causes of cancer, but also to ignore for the foreseeable future developments currently underway or soon to be realized. Such a response is also quite questionable on a statutory basis 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, we think that federal regulatory authorities should plan on making a general reassessment of the state of the relevant science at least every five years, and should also reassess prior decisions in light of whatever additional data have become available. Particularly in an area of rapidly developing science and data, it would be unwise to proceed on the assumption that one could now make a decision that would be good for all time.

E. <u>The illusion of a no-risk society</u>.

The OSHA preamble makes much of the uncertainties or

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difficulties with respect to confidence in any safe level of exposure to a known or suspect carcinogen. Implicit in this notion, if not explicit, is the concept that "safe" within the meaning of the Act means entirely risk free, and the correlative notion that industrial or other useful activity can occur on a completely safe, risk-free basis. Neither proposition is warranted attainable, or sustainable. There are risks associated with all societal activities, and indeed there are risks associated with efforts to avoid activity. Moreover, in enacting the Occupational Safety and Health Act of 1970, Congress explicitly recognized the impossibility of assuring American workers a risk-free workplace. It follows, therefore, that there is a legitimate role for the evaluation of relative risk and the acceptance of some degree of risk, a concept commonly regarded as "acceptable risk". Even in an emotional, fright-laden context such as cancer, sound public policy must take into account the inevitability of some risk, and the necessity of evaluating such risk not only against alternative risk but also in light of the benefits of the substance being regulated.

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 the following recommendation would do, 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 propositions are to be foreclosed (at least for the time being) from future consideration in individual chemical

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rulemakings; and the proposed obstacles that OSHA would create to allowing itself to take advantage of, or to utilize, improvements or developments in relevant learning. 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 following proposal proceeds on the basis that although a categorical approach may be warranted, in the absence of countervailing data and expertise to enable OSHA to deal responsibly with currently accumulating evidence of carcinogenic or tumorigenic effects, there is now no warrant for precluding interested parties from presenting, on a case-by-case basis, evidence to counter any inference of actual occupational hazard that might otherwise be drawn from evidence tending to show carcinogenic potential of a chemical substance. For example, by use of a general principle that all mammalian test data were appropriate to warrant regulatory precautions against carcinogenic potential, OSHA could avoid the burden of establishing that proposition through direct testimony in individual rulemakings, and yet allow interested parties who believed they had compelling evidence to attempt to persuade OSHA that such evidence should not, in the particular circumstances of some improperly designed mammalian test or future unforseeable case, be regarded as warranting such regulatory action.

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

It is widely recognized that non-carcinogenic toxic effects of chemicals can differ by several orders of magnitude, and that different regulatory limitations are accordingly appropriate. Since it is demonstrable that carcinogenic effects also can differ by a million fold, it seems inappropriate for the OSHA proposal to proceed on the basis that all known and potential carcinogens pose equivalent risks. Rather, carcinogens should be classified or ranked in terms of carcinogenic potency, and regulated accordingly. For example, bischloromethylether is a very potent known human carcinogen; vinyl chloride is much less potent. Greater precautions clearly are warranted for the former. Moreover, greater priority should be accorded to regulating a substance that is a potent carcinogen than a substance that is a weak carcinogen. The following proposal calls for categorizing both human and animal carcinogens as "potent", "intermediate", or "weak"; these classifications are provided primarily to set regulatory priorities. They also would be a rough indicator of the regulatory controls to be imposed, with more stringent controls for the more potent carcinogens. However, the categories would not inflexibly determine the regulatory controls; such controls, including primarily the permissible exposure level, would be determined on a case-by-case basis in light of assessments of risks, hazards, benefits, and costs. Such controls, and such exposure levels, could, for example, differ for two substances in the same category, depending on the particular circumstances of each case.

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[Comment: In contrast to the foregoing approach, it has been argued that the regulatory controls should be determined by the categorization, along the following lines, which reflect a two-part rather than a tripartite subdivision of the human category:

I. Human Potent - best available technology without economic consideration, if necessary personal protection allowed up to one hour/day/man.

Human Weak - best practicable technology defined as use of engineering controls to the extent technically and economically feasible. When engineering controls do not attain the permissible level, install engineering controls and supplement with personal protection. Review every two years and install adequate practicable engineering controls.

II. Highly Potent, Animal - same as "human potent".

Intermediate Potency, Animal - same as "human weak".

Low Potency, Animal - same as human weak except no "two-year" review.]

In particular, the following proposed alternative would attribute regulatory significance to dose-response data, to data about the time between exposure to a chemical and induction of tumors, and other indications of relative potency of various known or suspect carcinogens. The principal mechanism through which the alternative would take into account these variables is in analyzing risks and otherwise ascertaining acceptable or permissible exposure levels. The proposal thus contemplates that it would be entirely appropriate for OSHA to set a lower exposure level for a potent carcinogen than for one that was shown to be only a very weak carcinogen.

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Indeed, it is not inconceivable that in some circumstances it would be appropriate to establish a lower level for a carcinogen that appeared to be very highly potent only on the basis of animal tests, than for a known human carcinogen of relatively low potency.

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

The following proposal does not proceed on the illusory basis that a risk-free industrial environment is attainable. Rather, it deals candidly with assessment of risk and benefits. A key aspect of the assessment of risk is the quantification of carcinogenic risk, that is, assessment of the likelihood of a carcinogenic event at a particular level of exposure. It is not presumed that there is presently any broad agreement on a particular method for quantification of such risk, or that any of the more frequently used or advocated methods to quantify risk is precise. Indeed, the ones commonly used are generally regarded as erring considerably on the side of safety and conservatism with respect to the calculation of the occurrence of carcinogenic risk. The proposal proceeds on the basis, however, that efforts to quantify risks can serve a useful purpose in comparing risks of exposure to a particular chemical with other occupational risks and with other risks commonly encountered and accepted, in our society.

Coal mining could serve as a useful example of a high risk occupation. There are about 100,000 coal miners in the United States. Although the incidence of black lung disease in 1977 is not yet available, in 1974 it was 800/yr, and each case led to a reduction in life expectancy of about 15 years. The accident rate in

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coal mines is 150-200/yr, leading to an overall risk of one percent (10^{-2}) per year. This risk is accepted -- but barely so. Society now correctly insists that it be reduced.

Many examples can be suggested for intermediate-risk activities where risks are judged acceptable, where the risk is one in ten thousand per year or greater, and neither workers nor society take any particular note of them. For example, a commercial airline pilot in the United States, flying close to the FAA maximum of 50 hr/month, flys 300,000 miles per year -- for a risk, if equal to that of his passengers -- of 3×10^{-4}/year. Many businessmen, consultants and even professors, fly 100,000 miles per year for a risk of 10^{-4}/year. These risks are well known from experience and there is no conservatism in their estimation.

Similar calculations show the general acceptance of risks that will usually be quantitatively bigger than the risks expected for well controlled occupational exposure to suspect carcinogens. Examples [to be amplified] here include swimming, truck driving, the use of automobiles. These all involve choice, for example the choice of living over a shop one owns, or in which one works, and living in the suburbs 15 miles away, which necessitates 30 miles of motoring per workday.

The biggest cancer risk to which Americans expose themselves is from cigarette smoking. This risk is so great than even those in a room 30 m^3 occupied by one smoker[1/] can be exposed to

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1/ Particular Polycyclic Organic Matter Study, by National Academy of Sciences - National Research Council, 1972, p. 29.

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1 mg/m^3 of benzo(a) pyrene -- equivalent to 1 cigarette every 10 days, or a risk of 2.5×10^{-5}. This is accepted without question by most people; this suggests that lesser occupational risks would be reasonable.

Indeed, by refusing to declining to regulate smoking in the workplace -- to avoid criticism from its labor constituency, among others -- OSHA has decided that the risks of such smoking are acceptable.

The concept of acceptable exposure level and acceptable risk also reflects the congressional realization that a perfectly risk free workplace is not attainable and that safety and health standards must be economically as well as technologically feasible. We believe that in many cases these levels would be higher than what OSHA intends as "lowest feasible" levels, with correspondingly different economic impact and employment dislocation.

The Act requires that OSHA in promulgating standards for toxic materials or harmful physical agents, "shall set the standard which most adequately assures, to the extent feasible, . . . that no employee will suffer material impairment of health or functional capacity (underscoring added)." § 6(b)(5), 29 U.S.C. § 655(b)(5). The Act further requires that such standards "shall be based upon research, demonstrations, experiments and such other information as may be appropriate" and that among "other considerations shall be . . . the feasibility of the standards (emphasis supplied)." Id.

In addition to the text of the Act, its legislative history and decisions construing the Act support the conclusion that economic issues must be considered in evaluating feasibility of pro-

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posed standards. The legislative history demonstrates a serious concern on the part of Congress to insure that economic and practical considerations as well as technical considerations are factored into the standard-setting process. Senator Javits, author of the key amendment which added the "feasibility" requirement to the Act, explained its meaning as follows:

> "As a result of this amendment the Secretary, in setting standards, is expressly required to consider feasibility of proposed standards. This is an improvement over the Daniels bill, which might be interpreted to require absolute health and safety in all cases, regardless of feasibility, and the Administration bill, which contains no criteria for standards at all." (Legislative History of the Occupational Safety and Health Act of 1970, Senate Committee on Labor and Public Welfare, 92nd Cong., 1st Sess. 197 (Comm. Print June 1971) ("Legislative History").)

Similarly, Senator Saxbe expressed concern about the impact of standards which might not consider economic factors:

> "We have seen great industrial nations which have lost their ability to compete. By that I do not mean to indicate, in connection with this bill, that we have to have a dangerous operation or an unsafe operation to compete. But I do know that in the competitive world of business today, we should not attach to safety unnecessary or harassing measures that would, in effect, limit production in areas that are not necessarily going to increase safety.
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> * * *
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> . . . About 12 years ago [the English Government] adopted a number of safety bills that were very idealistic in their concept, but so restraining to the place of work and so restraining on the assignment of employees that they served not to make the plant safer and to increase production, but rather to make the business less competitive, and, as a result, [England] lost business to German manufacturers producing the same item.

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> This is something that we must be objective about. We want ideal and safe working conditions. At the same time, we must have one eye on this and the other eye on permitting the manufacturer to be competitive, not at the expense of the workmen, but rather in a cooperative effort." (Legislative History at 321-327; see also Legislative History at 147-148, 464, 471-472.)

The courts of appeals have accordingly concluded that economic factors are an appropriate consideration in setting standards for toxic substances which are "feasible." In Industrial Union Department, AFL-CIO v. Hodgson, 499 F.2d 467 (D.C. Cir. 1974, Judge McGowan, in reviewing the OSHA standard for exposure to asbestos dust, concluded that the factors entering into the Secretary's conclusion could properly include problems of economic feasibility." 499 F.2d at 477. He amplified this conclusion as follows:

> "There can be no question that OSHA represents a decision to require safeguards for the health of employees even if such measures substantially increase production costs. This is not, however, the same thing as saying that Congress intended to require immediate implementation of all protective measures technologically achievable without regard for their economic impact. To the contrary, it would comport with common usage to say that a standard that is prohibitively expensive is not 'feasible.'" 499 F.2d at 477. (Footnote omitted; underscoring added.)

In AFL-CIO v. Brennan, 530 F.2d 109 (3d Cir. 1975), Judge Gibbons, in reviewing an OSHA safety standard for mechanical power presses, also ruled that the Secretary "may in the weighing process consider the economic consequences of his quasi-legislative standard-setting." 530 F.2d at 123.

While the courts in the above-cited cases were not faced

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with the precise question whether the Secretary was required to consider economic feasibility, the Secretary having in fact done so, the unmistakable language of the Act makes clear that the duty is mandatory, not permissive, and this is clearly reflected in the court decisions. As the Court of Appeals wrote in the IUD (asbestos) case, "Congress does not appear to have intended to protect employees by putting their employers out of business -- either by requiring protective devices unavailable under existing technology or by making financial viability generally impossible." 499 F.2d at 478. Among other things, these authorities indicate that OSHA ~~should~~ could not ban the use of any substance, which would generally be the result of a "no exposure" requirement.

In addition, while OSHA itself has reflected "feasibility" requirements in a number of prior rulemakings, the Review Commission in interpreting OSHA's noise standard to "effectuate the Congressional purposes underlying the Act," concluded that economics is indeed an integral part of feasibility, stating:

> "[W]e conclude that the standard should be interpreted to require those engineering and administrative controls which are economically, as well as technically feasible. Controls may be economically feasible even though they are expensive and increase production costs. But they will not be required without regard to the costs which must be incurred and the benefits they will achieve. In determining whether controls are economically feasible, all the relevant cost and benefit factors must be weighed." Secretary v. Continental Can Co., OSHRC Docket No. 3973 et al. (Decided August 24, 1976) (citations omitted).

The courts have proved to be of the same view. In Turner Co. v. Secretary of Labor, 561 F.2d 82, 83 (1977), the Court of Appeals for the Seventh Circuit held that "feasible" included both

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economic and technological aspects and thus meant "practicable", a construction "in accord with the clear intent of Congress and the purpose of the Occupational Safety and Health Act".

D. Different approach to animal data.

The OSHA proposal is relatively indiscriminate in attributing significance to mammalian test data irrespective of the size of dosage used, the overwhelming of normal detoxification mechanisms, and other experimental test conditions that are unrealistic for occupational purposes. Two biological circumstances dramatize the need for careful appraisal of animal data. Estrogens and androgens are carcinogenic to experimental species, and for estrogens, the occurrence of disease in humans has been documented. Yet estrogenic hormones are ever present ~~at subthreshold or no-effect levels~~ in the entire earth's population and are essential to life. Similarly, metals such as chromium, nickel, cobalt, selenium, and perhaps even arsenic are essential to man in small amounts but carcinogenic in excessive amounts. The following proposal would substantially differentiate among test results depending upon such criteria.

While the following proposal would require positive results in two different mammalian species in well designed and conducted experiments to warrant regulation as a carcinogen, it would not preclude OSHA from instituting a normal Section 6(b) rulemaking on a specific substance on the basis of a single such experiment where, in light of the best information available at the time, regulation for carcinogenic hazards might be appropriate.

E. The role of short-term tests.

OSHA's proposal would attribute some potentially signi-

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ficant regulatory consequence to the results of so-called short-term tests. The proposal is remarkably unspecific as to what is intended here; unanswered questions include how many tests are required, what results in various tests would be sufficient for regulatory purposes, what kinds of tests would be sufficient, and so forth. In contrast, the following proposal reflects the general state of the art, which is to the effect that short-term tests are currently so much more unreliable as predictors of human responses as not to be sufficient to warrant regulatory action other than to serve as guides for requiring conventional bioassay, biochemical, or metabolic testing. The proposal finds support in the "General Criteria for Assessing the Evidence of Carcinogenicity of Chemical Substances" prepared by the Subcommittee on Environmental Carcinogenesis of the National Cancer Advisory Board and published in 58 Journal of the National Cancer Institute 463 (February 1977):

> "At present, none of the short-term tests can be used to establish whether a compound will or will not be carcinogenic in humans or experimental animals. Positive results obtained in these systems suggest extensive testing of the agent in long-term animal bioassays, particularly if there are other reasons for testing. Negative results in a short-term test, however, do not establish the safety of the agent.
>
> "This Subcommittee is enthusiastic about the possible future use of *in vitro* tests as part of a screening system for potential carcinogens and believes that their further development and validation deserve high priority."

While the following proposal would not preclude subsequent attribution of regulatory significance to short-term tests, depending upon advances in scientific learning, the proposal would presently limit their use to serving as guides for further testing.

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Recognition of the value of epidemiological data.

The following proposal would attribute more significance to available epidemiological data than would the OSHA proposal which would even subordinate such data to positive results in an experimental bioassay. Since human data ~~is~~ are free from the difficulties of extrapolating from animals, it seems quite arbitrary and otherwise unscientific not to use it whenever it is available.

Human data could play a significant role in several aspects of the following proposal. First, such data could suffice to classify a substance as a known human carcinogen. Second, where appropriate, such data, with exposure level data, could indicate potency. On the other hand, such data could in some cases preclude carcinogenic classifications that might otherwise seem indicated on the basis of positive animal data. More generally, such data would be relevant in any risk assessment.

There is ample evidence to attribute significance to epidemiological data, whenever such data is available. For example, aflatoxin is a potent carcinogen in various mammalian species, but there is ample epidemiological evidence that, where nutrition is good, the material does not produce harmful effects in man, despite widespread exposure to it in peanuts, corn, maize and sorghum. Indeed, the FDA has recently specified acceptable food levels for aflatoxin of 1 part per billion, a level that has produced cancer in some animals. Similarly, there are micro nutrients such as selenium that in low doses produce no harmful effects on man, indeed are necessary to life, and yet that produce well defined toxic effects in animals including carcinogenicity. And calcium fed to bulls at

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only 3.5 to 5.8 times the National Research Council's recommended daily allowance for humans has produced tumor incidence of 30 percent.[1/]

G. Regulatory priorities.

The OSHA proposal contemplates what appears to be a haphazard approach to regulatory priorities, depending upon the happenstance of the timing of receipt of information not presently available, and suggesting for processing of the large number of materials on the NIOSH subfile of "suspect carcinogens" approaches such as alphabetical order. The following proposal reflects the view that OSHA should regulate first those materials that are known to be human carcinogens or highly potent animal carcinogens. 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 actual occupational hazards being encountered in domestic workplaces. This approach would enable greater benefits to be achieved, and 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 following one would not call for formal categorization, by publication in the Federal

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1/ Dr. H. F. Kraybill, Scientific Coordinator for Environmental Cancer, NCI, "Some Concepts and Remarks on Presumptive Negative Chemicals, Biological Intermediates, Endogenous Chemicals, Nutrients", paper delivered February 2, 1977, at the NCI Clearinghouse.

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Register, of a material that might be, within OSHA's scheme, a Category I, II, or III material but which is not present in United States workplaces. This aspect of the OSHA proposal appears to have virtually no ascertainable benefits. The basket category contemplated here, that is, chemicals that possibly could be regarded as within OSHA Categories I, II, or III, is so broad as to be virtually meaningless; all that one could readily conclude from assignment to such a category would be that the substance is not found in United States workplaces. While there would be no objection to OSHA's merely communicating with EPA so as to be alerted if anyone should propose to import or manufacture within this country a material as to which there was some, unevaluated, information of potential carcinogenicity, it would be reasonable to rely upon EPA's premarket notification scrutiny to provide appropriate warning of such a potential development.

I. Avoidance of controversy, uncertainties, and mistakes concerning substitutes.

Unlike the OSHA proposal, the following proposal would not call for OSHA to decide whether substitutes are available for a chemical (in one or more uses or processes) being regulated as a carcinogen, and would not call for a zero-exposure limit (generally, a ban of the substance) where substitutes are thought to be available.

First, the banning of any substance is beyond OHSA's legal authority. As noted above, standards must be feasible, and Congress did not intend OSHA to protect workers by adding them to the unemployment rolls. The OSHA Act, with its feasible-standard authorization, stands in sharp contrast with the Toxic Substances

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Control Act, which does specifically authorize EPA to ban manufacture or use of a substance where certain conditions are met. Any effort to read the authority to ban a substance into the general language of the OSHA Act would raise serious questions as to the ~~constitutionality~~ legality of such an expansive delegation of legislative authority. But even as a policy matter, OSHA should not concern itself with substitutes.

One policy objection to the OSHA proposal on substitutes is that it is largely unnecessary where good substitutes are -- or subsequently become -- available. Industry experience demonstrates that materials discovered to be carcinogenic have generally been replaced, over time, by other materials. The incentives to make such shifts include health factors, as well as avoidance of the expenses of complying with carcinogen regulation.

It should be noted here that the six months that the OSHA proposal contemplates as the maximum rulemaking period will generally not provide adequate time for OSHA to determine whether substitutes are presently available. Substitution can be a very complex question for a given use of a chemical; where as is common the uses are quite varied, the difficulties of deciding about substitutes becomes much greater. In addition, the rulemaking could not anticipate subsequent development of substitutes, and thus could never do a complete job. Neither could a rulemaking anticipate future new uses for the chemical, which could be quite beneficial -- but impossible because it had been banned.

Another objection is that OSHA might, under the pressure of the six months limits and other pressures, err in deciding that

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adequate substitutes are available. It is all well and good for someone to say ban a material or use a substitute. Unfortunately, those who glibly make such statements are often unaware of what is entailed in finding suitable substitutes. Compositions must generally be tested for stability and functionality. Processing equipment, shipping containers and users' processes must also be evaluated. In addition, before any substitution is made, extensive testing is necessary to insure that the substitute is safer than the original product. Such testing would generally include, for example, an evaluation of carcinogenic potential and other toxic potentialities, and such physical/chemical properties as reactivity and flammability. All this takes time, ranging from months to years. Thus, while it may be easy to say substitute, it may be difficult to accomplish. The consequences of such errors could be very substantial, for consumers and employees as well as employers.

Further, very substantial controversy would generally attend OSHA's rulemakings if substitutes were at issue, unnecessarily taxing the limited personnel resources which OSHA hopes to utilize better by the current proposal.

J. Decreased resort to emergency temporary standards.

The OSHA proposal would require, in every case of a Category I classification within its scheme, automatic invocation of the Emergency Temporary Standards approach that is authorized by Section 6(c) of the Act. The following alternate proposal would be more selective, for several reasons. First, the ETS route is authorized only when there really is a "grave hazard." This term has a connotation of immediacy of injury that generally is not presented

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by low-level exposure to a suspect or potential carcinogen; it is the possible immediacy of the injury that warrants the extraordinary step of bypassing the normal rulemaking process.

This is not to say that serious consequences including death could not result in the long term. This, however, is true of most industrial hazards. It is true of many in the short term; for example, sulfuric acid can have dire results, depending on the degree of contact. We think it clear, however, that the ETS approach was authorized by Congress only when immediate action was needed to avert serious short-term injury hazards. The ETS approach thus is generally not warranted where a suspect or potential carcinogen is involved.

As a policy matter, the ETS approach seems undesirable whenever complex factual issues are involved, and must be resolved in a permanent rulemaking to be instituted and completed within only six months from the promulgation of an ETS. This is particularly so when controversy may be expected, as would generally be the case considering the ~~stringent~~ inflexible controls and far-reaching implications that attend a carcinogenic rulemaking. These reservations are all supported by OSHA's prior uses of the ETS approach to substances being regulated only because of carcinogenic potential.

K. Provision for exclusion of mixtures.

The OSHA proposal is silent on exclusion of mixtures containing very low concentrations of the material being regulated. Given the recently greatly increased sensitivity of analytical methods, with parts per billion and even per trillion not uncommon, the failure to provide for exclusions of mixtures has great potential

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for economic disruption, adverse environmental impact, and employment dislocation. On the other hand, there will often be no discernible health benefit from the application of a costly (or prohibitive) regulation to a mixture containing very low concentrations of the substance being regulated. Examples can readily be produced, for example, of maximum airborne concentrations emanating from commercially very important mixtures in the parts per billion, examples drawn from OSHA's own regulatory experience (e.g., the "14 carcinogens" rulemaking) and otherwise.

L. Expert performance of categorization function.

Unlike the OSHA proposal, the following proposal would rely upon a scientific body separate from federal regulatory authorities to make the essential scientific judgment or decision as to the appropriate categorization of a particular chemical substance with respect to carcinogenic potential. There are a number of reasons for separating these functions. One is simply efficiency and consistency throughout the regulatory agencies, all of which, it is proposed, should accept the results of classifications made by the proposed Classification Panel. Another is to separate the scientific process of classification from the 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. A further reason would be to improve the expertise of those making the categorizations. 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

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needed to provide only a single classification panel, rather than such a panel or similar authority for each of a variety of regulatory agencies. The activities and decisions of the Panel would be governed by the Administrative Procedure Act.

III. Tentative Nature of Endorsement of Categorical Approach.

A. Regulation of individual chemicals.

OSHA should expedite its formulation of occupational health standards for individual chemicals known or suspected to be carcinogens. In doing so, OSHA should develop regulatory priorities based on such matters as the strength of the evidence implicating the chemical as a carcinogen, the carcinogenic potency of a chemical, the number of employees exposed, the extent of exposure, and the likelihood of a carcinogenic event.

OSHA could readily expedite individual rulemakings for chemicals with known or suspected carcinogenic potential by applying accepted principles of risk assessment and hazard evaluation in conjunction with expanded manpower resources. These modifications could be readily implemented without a simplistic, unrealistic categorization scheme and simultaneously solve the concerns expressed by OSHA in the preamble to the proposed generic standard: specifically,

1. OSHA's problem of relitigating certain issues in each and every rulemaking could be eliminated by a complete risk assessment which would resolve such questions in a practical manner and establish priorities for regulation.

2. The taxing of witnesses through repetitive public hearings would be relieved by complete risk assessment prior to rulemaking, and/or by adoption of general principles, such as the

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use of mammalian test data, to be followed except where counter-vailing evidence was presented to the Classification Panel or during an OSHA rulemaking.

3. Continuity of approach in regulating carcinogens would be achieved by basing proposed regulations on the results of substance-by-substance hazard evaluations. These evaluations would review such factors as chemical and physical properties, conditions of use in the workplace, extent of production, nature of the processes, etc.

4. OSHA should petition Congress for additional manpower resources to effectively regulate materials with carcinogenic potential. Additional manpower would be far less costly to the nation than would OSHA's proposed categorization and model standard scheme, which would often impose enormous cost increments not related to incremental enhancement of health.

5. OSHA can avoid futile rulemaking by proposing regulations based on valid risk analysis and hazard evaluation, rather than utilizing a non-specific generic approach.

B. Need for flexibility and excercise of judgment in each case; doubts as to regulatory efficiency.

The following proposal does not proceed on the basis of agreement with OSHA's assertions of a compelling need to simplify science and facts by categorization. Accordingly, the following proposal is only a conditional endorsement of a categorical approach, an endorsement that depends in material respects upon greater flexibility and potential for individual consideration of particular chemical substances than would be afforded by the general approach of the OSHA proposal.

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Similarly, the following proposal does not proceed on the basis of agreement with OSHA's assertion that its proposal would result in significant savings of time and effort in carrying out its regulatory mandate. Such efficiencies are asserted to be principal reasons for OSHA's categorical approach. It is, however, quite questionable whether these efficiencies will indeed be achieved, when the total regulatory process, which includes enforcement proceedings and judicial review or the opportunity for judicial review thereof, are considered. Initially, it may be ventured that even if the pending OSHA proposal is adopted, subsequent rulemaking proceedings on individual chemicals will surely be controversial, on matters such as whether a chemical has been correctly categorized and whether OSHA has accurately or validly ascertained feasible exposure limits, a matter which can vary quite significantly with different uses of the same chemical.

It also seems reasonable to anticipate that such future rulemakings will not be entirely self-enforcing, and that individual enforcement proceedings through citations and adjudications before the Review Commission will be necessary. In such Review Commission proceedings, the economic feasibility of standards would be at issue. Moreover, in judicial review proceedings, aggrieved employers would be entitled to judicial consideration not only of the standards for individual chemicals but also of the categorical standard that OSHA now proposes. Since in many cases several years would have elapsed between OSHA's adoption of the present proposed categorical standard, "freezing" the science and shutting off consideration of information developed in the future, and such an enforcement pro-

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ceeding arising under a particular rulemaking promulgated in implementing the categorical approach, it seems reasonable to anticipate that there would be litigation not only before the Review Commission but also the courts as to the propriety of the issues that OSHA now seeks to put at rest by a categorical rulemaking approach. In brief, the supposed efficiencies may well prove to be illusory; OSHA's efforts to shortcut debate may be counterproductive. By providing more flexibility to consider (and attribute significance to) all evidence available at the time of a rulemaking on any given substance, the following proposal may be more efficient from an overall regulatory standpoint than would the OSHA proposal, which seems to assume that the process terminates with promulgation of a standard in the Federal Register.

IV. Appropriate Timing and Scope of Assessment of Economic and Environmental Impacts.

The following 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 the following proposal, it should be appropriate to assess those impacts in the regulation of individual chemical substances; indeed, the following proposal contemplates that the results of such impact analyses would play a major role in shaping the regulation, particularly the permissible exposure level. However, because of the rigidity of the OSHA proposal, it seems clear that to the maximum extent currently possible, the economic and environmental impact of implementation of that proposal should have been assessed before the OSHA proposal had proceeded to the

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current regulatory phase. Such impacts are likely to be enormous if indeed not catastrophic, and much further study than has been essayed so far is clearly warranted to inform decision-making at OSHA before any further movement is made toward implementation of the pending proposal.

Morover, OSHA's proposal to assess economic and environmental impacts only after it has adopted a rigid framework -- rigid both as to substance and procedure -- and only in the context of individual-substance rulemakings implementing its categorical approach, would make such assessments futile exercises. Why assess impacts, when no regulatory choice remains? The point here is obvious; OSHA's pending proposal renders nugatory any assessment of economic or environmental impact.

V. Laboratories.

In general, regulations appropriate for the industrial workplace are not appropriate for laboratories, whether quality-control, pure research, or some admixture of both. Probably a single work-practices oriented regulation for laboratories would be sufficient; there clearly should be separate regulations for laboratories.

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CLASSIFICATION PANEL

Determination of carcinogenicity is a scientific, not a regulatory question. This determination should be made:

1. Outside of regulatory authorities such as OSHA.
2. Based on the critical, scientific evaluation of all available data.
3. By a panel of appropriately qualified and experienced scientists.

A Classification Panel would be established by Executive Order issued pursuant to the Reorganization Act of 1977, 5 U.S.C. § 901 et seq. The Panel's determination of carcinogenicity classification would be administratively final (subject to appropriate judicial review.) OSHA and other regulatory agencies would then proceed to assess occupational health hazard, etc., and define necessary controls or priorities for regulation based on the Panel's determination and the agency's hazard assessment.

The Panel would consist of nine members, representing a cross-section of expertise in toxicology, pharmacokinetics, cancer research and therapy, epidemiology, occupational medicine, etc. Candidates would be proposed on the basis of scientific expertise and professional qualifications by relevant professional groups such as:

National Cancer Institute

The Society of Toxicology

American Academy of Occupational Medicine

American Academy of Veterinary Pathologists

American Occupational Medical Association

American Cancer Society

American Academy of Industrial Hygiene

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Panelists would be selected from the candidate list by the National Academy of Science. They would serve with staggered appointments for terms from two to four years. The Panel would have a staff; the Panel and staff would be housed within the National Cancer Institute.

The Panel could revise the Classification Categories and criteria from time to time, upon public notice and opportunity to be heard.

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Categorization

The Classification Panel shall assign a chemical substance to one of the following categories. Such assignment shall be accomplished as soon as possible following receipt of information, by petition or otherwise, that the Panel judges warrants consideration of making an initial categorization or of changing an existing categorization.

In deciding the order in which to categorize various chemical substances, including those listed in the NIOSH subfile of suspect carcinogens, the Panel shall give priority to ones alleged or appearing to be known human carcinogens or highly potent confirmed animal carcinogens, and shall consider the total available literature and industrial history for the substance.

The Panel shall use the criteria listed below in categorizing chemical substances. The Panel may from time to time revise the categorization scheme or revise the criteria, in light of scientific advancements, additional information, or experience with the categorization scheme, provided that reasonable notice of intended changes and an opportunity to comment are afforded to the public.

CATEGORY I. Known Human Carcinogen.

A. Potent carcinogens.

B. Intermediate carcinogens.

C. Weak carcinogens.

Criteria: A substance shall be classified as a known human carcinogen on the basis of valid epidemiological data. Such data should be evaluated in light of:

1. The magnitude of the association between exposure and excessive age-standardized

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risk (as measured by relative risk analysis or Standard Mortality Rate) and the statistical confidence limits.

2. The size of a study population and the number of cases of cancer.

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-exposure 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.

Potency shall be determined on the basis of (1) epidemiological data where exposure data are available or where exposure intensities can reasonably be estimated, (2) mammalian bioassay data where dose-response data are available, or (3) by both kinds of evidence when both are available.

Where epidemiological evidence shows that exposure under in-use conditions has increased the age-standardized risk of development of any form of cancer by a factor of 10-fold or more, the agent shall be regarded as a potent carcinogen. Examples here include heavy cigarette smokers, occupational exposure a few decades ago to beta-naphthylamine and to nickel plating operations.

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Where such an increase is by a factor greater than 2-fold but less than 10-fold, the agent shall be regarded as an intermediate potency carcinogen. Examples here include chrome worker exposures.

Where such an increase is by a factor of 2-fold or less, the agent shall be regarded as a weak carcinogen. Examples here include exposure to coke oven emissions.

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

CATEGORY II. Confirmed Animal Oncogens.

Criteria: Well documented results of adequate mammalian bioassays in at least two different species showing a statistically significant increase in tumors in test animals over that occurring in negative 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. A number of the terms used in this general criterion are more fully stated below. The general criterion does not differentiate between malignant and benign tumors observed in bioassays, hence the term "oncogen". This does not signify that they are the same, but rather reflects present uncertainty on this matter and prudence in protecting employees. The general criterion also accepts, as prudential, use of mammalian test results as guides to carcinogenic risks to man. This is accepted despite very substantial scientific complexities and uncertainties about extrapolating from

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animals to man; in exceptional cases those uncertainties may be so formidable as to preclude such extrapolation.

B. Excessive doses. The criterion accepts as valid the judgment of the American Conference of Governmental Industrial Hygienists that no substance is to be considered an occupational carcinogen of any practical significance on the basis of having reacted oncogenically by the following routes above the following doses.

1. Dosage exceeds via the respiratory route, 1,000 mg/m^3 for the mouse and hamster or 2,000 mg/m^3 for the rat.

2. Dosage exceeds, by the dermal route, 1,500 mg/kg for the mouse and hamster or 3,000 mg/kg for the rat.

3. Dosage exceeds, by the gastrointestinal route, 500 mg/kg/d for a lifetime, equivalent to about 10 g. T.D. for the mouse and hamster, and 100 g. T.D. for the rat.

C. Appropriate routes of administration. Appropriate routes of administration are respiratory, skin application, and gastrointestinal.

D. Adequacy of bioassay for evaluating oncogenic potential.

The following factors,[1/] among others, shall be considered in assessing the adequacy of the protocols, conduct, and results of a bioassay:

-- the experimental design and its conformity to accepted protocols

-- the appropriateness of the method of exposure

1/ Many of these factors are discussed in "Guidelines for Carcinogen Bioassay in Small Rodents", NCI Carcinogenesis Technical Report Series No. 1, February, 1976, by James M. Sontag, Norbert P. Page, and Umberto Saffiotti.

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-- the appropriateness of the route of exposure

-- the appropriateness of the animal species and strain used

-- whether test populations were randomized

-- size of each dosage group

-- adequacy of concurrent controls

-- character and type of animal housing; type of bedding if any; number of animals per cage

-- non-tumor responses to test agents; influence on tumor yield

-- duration of exposure

-- schedule of intercurrent sacrifice

-- experiment termination date

-- metabolic and pharmacokinetic data, if available

-- number, type and site of tumors

-- number of animals developing tumors

-- temporal pattern of tumor appearance

-- the quality of the pathology

-- method of statistical analysis and statistical significance of positive results

-- dose response relationships

-- adequacy of reporting of the bioassay

E. Relative potency. The 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 in their "TLVs, Threshold Limit Values," is reasonable and sensible. The additional relationship of latency period (time from first contact to the appearance of tumors) is also applied in the definitions of industrial substances

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of high, intermediate, or low potency as the result of experimental mammalian studies. Accordingly, agents for which adequate bioassay results of statistically significant tumor occurrence are available shall be categorized by potency in light of the following guidelines for bioassays of the hamster, mouse, or rat.

1. Respiratory route exposure.

A. Potent.

(1) Inhalation exposure 6 to 7 hours per day, five days per week, for a major portion of a lifetime, to dosages below 1 mg/m^3 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;

B. 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/m^3 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 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 volume.

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C. Weak.

(1) Inhalation exposure to 6 to 7 hours per day, five days per week, for a major portion of a lifetime, with dosages greater than 10 mg/m^3, but non-excessive, with an excess of tumors appearing at any time during the study;

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

(3) Exposure to intratracheally administered (non-excessive) dosages totaling more than 10 mg of particulate or liquid per 100 ml or more of animal minute respiratory volume.

2. Skin application exposure.

A. Potent. Exposure by repeated skin application with tumors appearing in 6 months or less.

B. Intermediate potency. Exposure by repeated skin application with tumors appearing within 6 to 18 months.

C. Weak. Exposure by repeated skin application with tumors appearing after 18 months.

3. Gastrointestinal exposure.

A. Potent.

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

(2) Exposure by repeated peroral dosing of any non-excessive dosage with tumors appearing in 12 months or less.

B. Intermediate potency.

(1) Exposure by repeated peroral dosing at dosage between

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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. Weak.

(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. Possible Animal Oncogens.

Criteria:

A. Mammalian bioassays that do not satisfy Category II requirements but that do show statistically significant increases in tumors.

CATEGORY IV. "Cleared" List.

A. Criteria. Completion of adequate mammalian testing or epidemiological studies with no statistically significant evidence of carcinogenicity in the particular testing or study results.

It is not contemplated that where more than one valid bioassay report is available and some reports are negative and others positive a substance would be placed in this category. The controversiality of the reports would, however, be considered by OSHA in assessing risks.

In some cases, however, epidemiological studies showing no increased incidence of cancers could warrant categorization here, despite positive bioassay reports, for example where substantial metabolic differences were shown.

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RECATEGORIZATION

It is recognized that some, perhaps most, chemical substances will be categorized on the basis of less than definitive data, and that subsequent scientific advancements as well as additional data may suggest that a prior categorization was erroneous and should be reconsidered. Accordingly, any interested party may petition for reclassification of a chemical on the basis of significant data or scientific learning that were not considered at the time of the prior classification. Depending on the information and its assessment during the categorization process, a substance could be reclassified to a higher or a lower category. Where such reclassification results, OSHA shall promptly consider modification of its standards.

OSHA Regulatory Response to Classification

A. Category I classification.

1. Emergency temporary standard. Upon classification of a substance as a known human carcinogen, 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 the epidemiological data; animal experimental factors, where available, such as dose-response relationships, metabolism, duration and amount of exposure, route of exposure) and (b) evaluation of actual hazards (e.g., physical and chemical properties, degree of occupational exposure, likelihood of a carcinogenic event).

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Upon completion of such a determination, OSHA shall immediately commence 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, hazards, costs 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 an acceptable level of risk. In deciding upon such a level, OSHA shall perform analyses of risks, hazards, benefits and costs in accordance with Subpart C below, to the extent such analyses can be very promptly performed. Where the available epidemiological 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 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 may vary from chemical to chemical, depending upon the analyses of risks, hazards, costs and

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benefits.

(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 can be immediately achieved through a practical combination of readily available engineering and administrative controls and personal protective equipment.

(c) The ETS shall exclude mixtures containing less than specified percentages of the substance being regulated. Such percentages may differ for different uses or mixtures, and shall be determined in light of analyses of risks, hazards, and costs and benefits, performed in accordance with Subpart C below, to the extent such analyses can be promptly performed.

2. Permanent Standard.

(a) Where an ETS has specified an acceptable exposure level reflecting data sufficient to quantify risks to employees, the permanent standard shall require achievement or maintenance of that limitation.

(b) Where an ETS not based on data sufficient to quantify risks has been issued, and such data becomes available during the maximum statutory life (six months) of the ETS, a regular permanent standard shall issue to require achievement of an acceptable exposure level derived in part from such data. OSHA shall also consider, in setting permissible exposure levels, the analyses of risks, hazards, costs and benefits. Different levels may be set for different

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chemicals. Compliance with the permissible exposure limits shall require use of engineering controls to the extent technically and economically feasible, augmented by administrative controls and personal protective equipment as necessary.

(c) Where an ETS not based on data sufficient to quantify risks has been issued and such data does not become available within six months, an interim permanent standard similar to the ETS shall be issued, to be in effect no longer than three years. If during that three years' period such data become available, a regular permanent standard shall 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 does 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 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. Such percentages may differ for different uses or mixtures and shall be determined in light of analyses of risks, hazards, benefits, and costs performed in accordance with Subpart C below.

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

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of such a rulemaking proceeding, OSHA should advise the ITC of the desirability of dose-response data if it does not exist. Permissible exposure levels should be established in the same manner as called for in the preceding subparagraphs (a) through (d).

3. Provisions of Standards Other than Ones Related to Permissible Exposure Levels.

[To be developed; some degree of uniformity seems desirable, but some flexibility to accommodate particular circumstances of a given chemical seems necessary.]

B. Category II Classification. OSHA shall consider issuance or non-issuance of an ETS in the same manner as provided above for the regulatory response to a Category I classification. Similarly, OSHA shall prepare analyses of risks, hazards, benefits and costs, as called for there, and shall consider them in establishing permissible exposure levels and other regulatory provisions. Also, OSHA shall proceed to promulgate permanent standards, or to consider such action, according to the provisions for response to a Category I classification.

Permissible exposure levels may vary from chemical to chemical, depending on the analyses of risks (including the strength of the evidence of carcinogenic potential), hazards, costs and benefits. Such exposure levels need not correspond with permissible exposure levels, or the range of such levels, that may be specified for Category I substances, and could be higher or lower.

C. Analyses of Risks, Hazards, Benefits, and Costs for for Category I and Category II Substances.

In establishing permissible exposure levels, OSHA shall analyze risks, hazards, benefits and costs and shall state in writing the

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manner in which each of the factors listed below has been considered.

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

(a) evidence of carcinogenic potency, whether epidemiological or experimental animal evidence;

(b) dose-response relationships and associated metabolic and pharmacokinetic data, if available;

(c) where only experimental animal evidence tends to implicate a chemical substance, evidence of epidemiologic experience with the substance. It is recognized that while epidemiological evidence cannot conclusively show that a substance is not carcinogenic to humans, favorable epidemiological evidence would be relevant and could be material in assessing risks (under established or prior conditions of use);

(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;

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

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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 include:

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

(b) the number 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, and/or (2) at proposed permissible exposure levels.

(e) the physical and chemical properties of the substance, and inherent warning properties;

(f) non-carcinogenic toxic properties of the substance;

(g) the foregoing factors, as applicable to workplaces where the substance is present in other substances in contaminant or trace amounts;

(h) statistical or other methods of quantifying the likelihood of a carcinogenic event in light of the foregoing factors;

(i) hazards of use of likely substitutes for the substance being regulated;

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(j) comparisons with hazards of other contemporaneous activities, occupational and non-occupational.

3. Benefits. As used herein, benefits include health benefits of reductions in actual employee exposures to the substance and benefits of continued use of the substance or mixtures containing the substance. An analysis of benefits shall include consideration of the following factors:

(a) benefits of reductions in actual employee exposure to the substance being regulated, including health benefits, reductions in costs of health care, reductions in lost employment, psychological and emotional benefits to employees and their families and friends;

(b) economic benefits of production and use of the substance, including volume and dollar amount of sales, number of employees, competiveness of domestic industry, and cost advantages or benefits to consumers of products made from or with the substance being regulated; balance-of-payments advantages; enhancement of productivity; improvement of cost effectiveness; reduction of waste; retardation of deterioration.

(c) "quality of life" non-economic benefits of production and use of the substance, including

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any safety or health benefits, e.g., prolongation of productive life, reduction of loss of life, limits and health; reduction of other burdens; increases in knowledge; cultural values; uniqueness, vis-a-vis likely or possible substitutes.

4. Costs. As used herein, costs include environmental and economic consequences of compliance with regulation, including adverse aspects of shifts to, and use of, substitutes that might result, as a by-product or otherwise, from imposition of regulation. Cost factors include:

(a) increases in energy or other raw material requirements, due to compliance with regulation or shifts to substitutes, and adverse environmental impacts of any resulting need to exploit additional natural resources or to exploit existing resources more aggressively;

(b) economic feasibility of compliance with regulation;

(c) technological feasibility aspects of compliance with regulation;

(d) employment dislocation resulting from responses to the other costs of regulation, including direct local increases in unemployment and related economic and psychological effects;

(e) indirect adverse economic effects of any reduction in direct employment.

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In considering costs, particular importance should be attributed to incremental costs, in comparison with incremental benefits. Generally, the incremental costs of reducing employee exposure will increase exponentially as zero is approached, but there will not be substantial data to indicate any significant health benefit increment would be achieved by further reductions.

Consideration of costs will also include the social costs of increased economic concentrations that may result in response to regulatory action. Only with reluctance should costs be imposed that can be borne only by the largest corporations, or that will be somewhat less severe but still have harsh impacts upon small businesses. The appropriateness of these considerations in this area is suggested by the Toxic Substances Control Act, which recognizes the desirability of avoiding imposition of unnecessary regulatory burdens on small businesses, and the desirability of preserving an economic system with diversity of size.

[Comment: It is recognized that benefits could be expressed as costs (reductions), and vice versa. It may be desirable, however, to suggest risk/risk, benefit/benefit, cost/cost analyses of the substance being regulated versus substitutes, for refined analyses and to avoid unwarranted appearances of advocating a simplistic trade-off of health benefits versus economic costs.]

D. Category III Classification.

1. Reference to ITC for possible further testing.

2. Within 60 days OSHA may issue a notice of proposed rulemaking to establish permissible exposure limits at (1) the present

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OSHA standard or (2) where none exists, an appropriate level based on acute or chronic effects of exposure to the toxic substance other than carcinogenicity or (3) where acute or chronic effects indicate that the present OSHA standard is inadequate, the exposure level shall be lowered to the level found appropriate by the Secretary. [Basically Section 1990.122 of proposed standard.]

E. Category IV Categorization.

No regulatory action is to be taken other than classification (or reclassification) as "cleared". It is recognized that a substance may subsequently be removed from this category, in the light of additional information.

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