SEQUENCE OF THE ACGIH TLV FOR ASBESTOS

Year	Listing
1946 - 1961	MINERAL DUSTS Asbestos - 5 mppcf
1962 - 1967	MINERAL DUSTS Silicates (less than 1% crystalline silica) Asbestos - 5 mppcf
1968 - 1969	MINERAL DUSTS Silicates (less than 1% crystalline silica) **Asbestos - 5 mppcf **NOTICE OF INTENDED CHANGES Asbestos - 12 fibers/ml > 5 μ in length,[J] or 2 mppcf[K] J) As determined by the membrane filter method at 430X phase contrast magnification. K) As counted by the standard impinger, light-field count technique.
1970	MINERAL DUSTS Silicates (less than 1% crystalline silica) **Asbestos, all types - 5 mppcf **NOTICE OF INTENDED CHANGES Asbestos (all types) - 5 fibers/ml > 5 μ in length[K] K) As determined by the membrane filter method at 430X magnification phase contrast illumination. Concentrations > 5 fibers/ml, but not to exceed 10, may be permitted for 15-minute periods each hour up to five times daily.
1971	MINERAL DUSTS Silicates (less than 1% crystalline silica) **Asbestos, all types Note: A value was not listed, however, it should have been listed as 5 mppcf. **NOTICE OF INTENDED CHANGES MINERAL DUSTS Asbestos (all types) - 5 fibers/ml > 5 μ in length[J] J) As determined by the membrane filter method at 400-450X magnification (4 mm objective) phase contrast illumination. Concentrations > 5 fibers/ml, but not to exceed 10, may be permitted for 15-minute periods each hour up to five times daily.

Year	Listing
1972	MINERAL DUSTS Silicates (< 1% quartz) **Asbestos, all types Note: A values was not listed, however, it should have been listed as 5 mppcf. **NOTICE OF INTENDED CHANGES MINERAL DUSTS Asbestos (all types) - 5 fibers/ml > 5 μ in length;[n)] Ala Ala: Appendix A. Carcinogens 1a. Human Carcinogens - Substances known to be occupational carcinogens with an assigned TLV. Asbestos, 5 fibers/cc > 5 μm in length. Note: Appendix A on Notice of Intended Changes n) Same as J) for 1971.
1973	MINERAL DUSTS Silicates (< 1% quartz) ** Asbestos, all forms Note: A value was not listed, however, it should have been listed as 5 mppcf. **NOTICE OF INTENDED CHANGES MINERAL DUSTS Asbestos, all forms† - 5 fibers/cc > 5 μ in length;[n)] Ala Ala: Appendix A - Carcinogens 1a. Human Carcinogens - Substances recognized as occupational carcinogens with an assigned TLV: Asbestos, all forms, 5 fibers/cc > 5 μm in length. n) As determined by the membrane filter method at 400-450X magnificaiton (4 mm objective) phase contrast illumination. †A more stringent TLV for crocidolite may be required.
1974	MINERAL DUSTS Silicates (< 1% quartz) *Asbestos, all forms† - 5 fibers/cc > 5 μm in length;[n)] Ala *1974 Addition †A more stringent TLV for crocidolite may be required. n) As listed for 1973. Ala: As listed for 1973.

Year	Listing
1975 - 1976	As 1974 except for Appendix A now defined as: Occupational Carcinogens. 1a. Human Carcinogens. Substances, or substances associated with occupational processes, recognized to have carcinogenic or cocarcinogenic potential, with an assigned TLV. Asbestos, all forms* - 5 fibers/cc, > 5 μ in length. *Cigarette smoking may substanially enhance the incidence of bronchogenic carcinoma from this and others of these listed substances or processes.
1977	As 1975-1976 except Appendix A adopted.
1978 - 1979	MINERAL DUSTS Silicates (< 1% quartz) **Asbestos, all forms (5 fibers/cc > 5 μm in length; m) A1a) m) Same as n) for 1973. **Notice of Intended Changes Asbestos Amosite..... 0.5 fiber/cc, A1a Chrysotile..... 2 fibers/cc, A1a Crocidolite..... 0.2 fiber/cc, A1a Tremolite..... 0.5 fiber/cc, A1a Other forms..... 2 fibers/cc, A1a A1a. Human Carcinogens. **Asbestos, all forms* (5 fibers/cc, > 5 μm in length) **See Notice of Intended Changes *Cigarette smoking can enhance the incidence of respiratory cancers form this and other of these substances or processes.
1980	MINERAL DUSTS Silicates (< 1% quartz) *Asbestos Amosite..... 0.5 fiber > 5 μm/cc, A1a Chrysotile..... 2 fibers > 5 μm/cc, A1a Crocidolite..... 0.2 fiber > 5 μm/cc, A1a Tremolite..... 0.5 fiber > 5 μm/cc, A1a Other forms..... 2 fibers > 5 μm/cc, A1a Note: Footnote 1) should have been carried for asbestos values. 1) Same as n) for 1973. *1980 Addition.

Year	Listing
1980 (con't)	Ala. Human Carcinogens. ††Asbestos Amosite..... 0.5 fiber > 5 μm/cc Chrysotile..... 2 fibers > 5 μm/cc Crocidolite..... 0.2 fiber > 5 μm/cc Tremolite..... 0.5 fiber > 5 μm/cc Other forms..... 2 fibers > 5 μm/cc ††1980 Adoption
1981	MINERAL DUSTS Silicates (< 1% quartz) Asbestos Amosite..... 0.5 fiber > 5 μm/cc, Ala Chrysotile..... 2 fibers > 5 μm/cc, Ala Crocidolite..... 0.2 fiber > 5 μm/cc, Ala Other forms..... 2 fibers > 5 μm/cc, Ala Note: Footnote 1) should have been carried for asbestos values. 1) Same as n) for 1973. Ala. Human Carcinogens. Asbestos Amosite..... 0.5 fiber > 5 μm/cc Chrysotile..... 2 fibers > 5 μm/cc Crocidolite..... 0.2 fiber > 5 μm/cc Other forms..... 2 fibers > 5 μm/cc
1982	MINERAL DUSTS Silicates (< 1% quartz) Asbestos Amosite [12172-73-5] 0.5 fiber > 5 μm/cc, Ala Chrysotile [12001-29-5]..... 2 fibers > 5 μm/cc, Ala Crocidolite [12001-28-4]..... 0.2 fiber > 5 μm/cc, Ala Other forms..... 2 fibers > 5 μm/cc, Ala Note: Footnote 1) should have been carried for asbestos values. 1) Same as n) for 1973. Ala. Human Carcinogens. Same as 1981

ADVANCES IN INDUSTRIAL TOXICOLOGY FOR THE YEAR 1955

Herbert E. Stokinger, Ph.D.
Occ. Health Field Hdqs.
USPHS

In the brief space allotted to review recent findings in the field of industrial toxicology, I have selected those subjects that have appeared to be of interest, either because of their novelty, their basic value or their indications of future importance to industrial health. From the vast field from which to choose it is obvious that other selections might equally well have been made.

New Compounds Presenting Serious Hazards. Acrylamide, CH_2=CH-$CONH_2$, a chemical intermediate of great potential usefulness for the formation of polymers and copolymers, plasticizers, dispersants and other purposes, has the unusual property of being insidiously neurotoxic at relatively low levels of intake, while at the same time showing unremarkable toxicity from acute doses (oral LD_{50}, 170 mg/kg) (1). Acrylamide is toxicologically remarkable in other ways. 1. It shows practically no species variation; effective doses for the cat, dog, and rat were essentially the same. 2. Its physiologic effects are produced by any route, oral, skin or eye. 3. A definite quantity of acrylamide will produce the characteristic central nervous system syndrome of disturbed gait, postural tremors, visual and auditory halucinations and muscular atrophy irrespective of the dosage schedule used. 4. There is an anamnestic response, in that following cure, lesser amounts of acrylamide recalls the syndrome. Apparently the effects are reversible, although in severe cases this may amount to a matter of years (in man).

Acrylamide represents an interesting demonstration of our current inability to predict the grave physiologic consequences from chemical structure; the closely related amine, propionamide ($CH_3CH_2CONH_2$), is used as an animal feed supplement. Here, again is another striking case of the addition of a second double bond in the molecule to form a conjugated system with conference of remarkable toxicity. Another well-known example is the 44-fold greater toxicity of crotonaldehyde compared with its saturated analogue butyraldehyde (Skog, Acta Pharm. Tox. 6,299, 1950). Less well known, but equally striking is the highly lacrimatory power of conjugated unsaturated nitrocompounds such as 1 nitroisobutylene compared with the unsatured but not conjugated isomer, 1-nitroisobutyl-2-ene which has no marked lacrimatory powers. The potent irritating capacity of the diisocyanates discussed below are other examples of the effects of conjugated unsaturated compounds. Examples could be multiplied almost endlessly.

Diisocyanates. As a new group of nonomeric substances used in foam rubber, lacquers and for other purposes, the aromatic diisocyanates, especially 2, 4-diisocyanotoluene, 1,5-diisocyanonaphthylene, and 1,4-diisocyanobenzene present interesting toxicologic properties. Although extremely inert in polymeric forms, and possessing a very low oral toxicity 1-8 g/kg, (2) these aromatic isocyanates, particularly the naphthalene derivative, are exceedingly irritating to the upper respiratory tract, producing histologic changes in animals at 0.09 ppm and death at 1 ppm upon repeated inhalation exposures. Man also responds at exceedingly low concentrations with evidences of sensitivity such as asthma at air levels well below 1 ppm. Peculiarly sensitive

individuals may show sensitivity responses below 0.1 ppm, which is below the odor threshold of toluene diisocyanate for many individuals. A level of 0.5 ppm of TDI produces throat irritation. The tentative threshold limit has been set for TDI at 0.1 ppm. In our present state of knowledge it is believed that the upper respiratory tract is first involved following inhalation of low concentration of the isocyanates, pulmonary edema occurring only at far higher concentrations (TDI). Also, all evidence to date indicates no other type of systemic involvement from the isocyanates if the respiratory tract itself is free of involvement. Moisture greatly reduces the toxicity of 1, 4 diisocyanobenzene presumably by hydrolysis and destruction of the unsaturated conjugated system.

Boranes. Three boron hydrides, diborane, pentaborane and decaborane have received considerable toxicologic and pharmacologic study (3-6). Used as high-energy fuels these boranes are highly hazardous by all practical routes of entry into the body. Diborane, a gas at room temperature (b.p. 92.5C) differs from the others in toxicologic action in possessing no neurotoxic properties presumably because of its ease of hydrolysis; it is however, acutely, subacutely and chronically injurious to the lungs, producing congestion, edema and hemorrhage in higher doses and in the kidneys it leads to the production of tubular casts. The threshold limit of exposure has been tentatively set at 0.1 ppm; this is considerably below its odor threshold of from 2-4 ppm.

Pentaborane (B_5H_9) is the most hazardous of the 3 boranes. A liquid (b.p. 58C) whose vapor in a 2-hour exposure at 14 ppm results in immediate death of mice at lower concentrations, produces symptoms of weakness and tremors indicative of central nervous system involvement but without the lung involvement seen with diborane. Cumulative effects are seen with low repeated doses. Skin absorption is a possible contribution to the over-all toxicity. On the basis of hazard from the vapor and its severely toxic effects, a tentative threshold limit has been set for this compound of 0.01 ppm. No medical preventive or therapeutic effective agent for this compound has yet been developed; complete protection is afforded by airline gas-masks or a mask cartridge layered with soda lime, silica gel and activated carbon (7).

Decaborane. ($B_{10}H_{14}$) presents a toxicity picture similar to, but slightly less than that of pentaborane but as it is a solid, it presents less of a hazard than pentaborane; accordingly its tentative threshold limit has been set at 0.05 ppm. The cardiovascular actions of decaborane in animals have been reported (8).

It is recognized that the boranes are but additional examples of non-metal hydrides such as phosphine, arsine, stibine, hydrogen sulfide, etc., which are characterized by their exquisite toxicity.

A LOOK AT NEW INDUSTRIAL CANCERIGENS

There would seem to be small solace in attempting escape by the common argument that, if a compound is carcinogenic in animals, this does not necessarily prove its carcinogenicity in man; a more proper argument is that all animal carcinogens should at least be considered potentially carcinogenic in man.

Beryllium. Sufficient work seems now to have been done in one laboratory (Saranac), at least, by Vorwald, Schepers and Scheel [9] to establish beryllium as a carcinogen in the rat. Inhalation of beryllium sulfate for several months produced what was interpreted as an adenocarcinoma of the lung. The cancer has been successfully transplanted subcutaneously in rats, whence it metastasized to the lung and the lymph nodes of the mediastinum. Inhalation of beryllium phosphor (13% Be) produced in 3 to 6 months lesions in the lungs which appear to be squamous cell carcinoma. The beryllium cancer has not been produced by other workers although it is not rat-strain dependent in the hands of the Saranac workers. Alkaline phosphatase inhibition appears to be the first step in the physiologic process leading to tissue changes. It is believed that the $Be(OH)^{+}$, a form through which all beryllium compounds pass in the fluids of the body, initiates the reaction. The lack of success of other workers elsewhere to reproduce beryllium cancer opens the intriguing question of locality-dependent cancer.

Asbestos. Doll[10] has found that the incidence of lung cancer among 105 English asbestos workers employed more than 20 years was tenfold that in the normal population. Cartier[11] studying over a 9-year period 4000 asbestos miners in Canada, involving 128 cases of asbestosis, 40 of them with autopsies, found 6 of these have bronchogenic carcinoma. One might be inclined therefore to associate lung cancer with asbestosis were it not for the fact that 7 cases of lung cancer were found among asbestos miners with no asbestosis. If one inclines to the view that asbestos may produce lung cancer, one might admit the occurrence of this disease from asbestos inhalation without the production of asbestosis. On the other hand one might equally well question whether the ten-fold increase in incidence of lung cancer among asbestos workers is statistically significant in view of the small number of cases involved. According to Lanza[12] investigators both here and abroad are now less certain than formerly that lung cancer is associated with asbestosis. It is most difficult to determine the causative agent of a disease whose time of onset may be delayed two decades or more from the start of exposure. Before a final decision is reached it would seem well to wait until a more impressive number of cases have been documented. Moreover it seems to this author that the question of the nature of the asbestos in different localities and the associated minerals such as chromium and nickel seem to have been too little considered. Asbestos is a fibrous form of several different species of minerals, a point commonly disregarded.

Hydrocarbon Products of Incomplete Combustion. Carcinogenic hydrocarbons have now been shown to be present amont the exhaust products of Diesel and gasoline engines [13], and in the air of English [14] and American cities [15]. These products have been shown furthermore to produce skin tumors in mice. Although these findings were made in connection with air pollution studies, it is pointed out that the diesel and gasoline engine is becoming a significant factor in many industrial operations. Efficient and innocuous operation of a diesel engine from an atmospheric pollution view has been pointed out as possible, moreover, without costly engine redesign[13]. The fact that human lung cancer has not yet been proven to arise from the inhalation of these hydrocarbon products should not act as a deterrent to an active program to reduce the air contamination of working areas from this source.

Bladder Cancer from Aromatic Amines. 4-Amino diphenyl has now been repeatedly found to produce carcinoma of the urinary bladder of dogs fed this substance (16-18), the last of these confirming reports being that of Deichmann in 1956. The cancer was predominantly squamous in type and was produced from total doses ranging from 30g (English workers) to 113g, 3 to 10 g/kg (American workers). The British investigators consider 4-Amino diphenyl as a more effective bladder carcinogen than either benzidine or 2-acetyl amino fluorene, and at least as potent as beta naphthylamine.

A resurvey of the British chemical dye industry (19) produced statistical evidence that bladder tumors are associated with the manufacture of the dyes auramine or magenta, (amino diphenyl-and aminotriphenylmethane dyes) but do not necessarily arise from contact with the finished dyes themselves. Aniline, however, has been definitely excluded as a causative agent in bladder tumors, at least in the British chemical industry over the years 1910-1952.

Skin Cancer from Cutting Oils. Straight-run distillates (20) and higher boiling point fractions of catalytically cracked petroleum (21) may contain numerous carcinogenic hydrocarbons. A relationship between exposure to these substances and high incidence of occupational skin diseases other than cancer has been reported (22) and tests in animals with cutting oils have implicated them as possible carcinogenic agents. More recently cutting oils with a sulfonated mineral-oil base have been connected definitely with squamous cell carcinoma of the skin among Canadian metal cutters (23). 6 cases of skin cancer and one papilloma case have been reported among workers with an average exposure period of about 20 years. Although most of the lesions appeared on the forearms, one case involved the scrotum of a worker on whom oil splashed continually in the region of his lower abdomen, giving a clear definition to the relation between exposure and response from this type of oil. On the other hand, no skin cancer or precancerous manifestations have appeared to date among a group of 60 shale-oil workers in this country studied over a period of the past 6 years (24). The group will remain under continued observation, however.

TOXIC THERMAL DECOMPOSITION PRODUCTS

The toxicity of the degradation products of a large number and variety of plastics, synthetic hydraulic and lubricating fluids and fire extinguishants has been determined chiefly by Treon and associates (25). The importance of the studies is the finding that the over-all toxicity of the thermally degraded products from each substance was more toxic by a large factor than the substances from which they originated. The substances studied thus far include Teflon, Kel-F, Fluorolube FS, (all fluoro or fluorochloro-organic polymers), silicones, Gafite, (a chlorinated methacrylate), a paraffinic hydrocarbon lubricating oil, Skydrol, Pydraul F-9, Arochlor 1248, tricresyl phosphate, adipate and sebacate esters and Freon F13B1. In a few instances the toxic factors have been partly identified. As might be expected, the amount, nature and toxicity of the products was dependent upon the temperature of decomposition; in general, greater toxicity was experienced with increasing decomposition temperatures until a maximum was reached at a temperature characteristic of the substance. Temperatures above 500°F generally produced the more important amounts of toxic products from most polymers. Another interesting finding was a marked decrease in toxicity of the thermal decomposition products of Freon F13B1 in the presence of moisture. The mechanism by which this is brought about is being studied.

Bibliography

CLAIMED PRIVILEGED BY OCF

1. Golz, H. H., Toxicity of Acrylamide, Lecture delivered at Kettering Laboratories, Cincinnati, O., March 1956.

2. Treon, J. F., Zapp, J., et al., Toxicity of the Diisocyanates, discussed at Kettering Laboratories, Cincinnati, O., Feb. 1956.

3. Krackow, E. H., Toxicity and Health Hazards of Boron Hydrides, AMA Arch. Ind.Hyg. 8, 335, 1953.

4. Svirbely, J. L., Subacute Toxicity of Decaborane & Pentaborane Vapors. AMA Arch.Ind.Hyg., 10, 305, 1954.

5. Svirbely, J. L., I. Acute Toxicity Studies of Decaborane. AMA Arch.Ind. Health, 11, 132, 1955.

6. Svirbely, J. L., II. Effect of Repeated Doses of Decaborane for Laboratory Animals, AMA Arch.Ind.Health, 11, 138, 1955.

7. Hill, W. H., Svirbely, J. L., Gas-Mask Protection against Decaborane. AMA Arch.Ind.Hyg. 10, 69, 1954.

8. Walton, R. P., Richardson, J. A., Brodie, O. J., Cardiovascular Actions of Decaborane. J. Pharm.Expt.Therap., 114, 367, 1955.

9. Schepers, G. W. H., Beryllium Cancer in the Rat. Reported at Ind.Hyg.Ann. Meeting, Pittsburgh, Pa., Nov. 1955.

10. Doll, R., Mortality from Lung Cancer in Asbestos Workers, Brt. J. Ind. Med., 12, 81, 1955.

11. Cartier, P., Clinical Observations of Asbestosis in Mine & Mill Workers, AMA Arch.Ind.Health, 11, 204, 1955.

12. Lanza, A. J., Pneumoconiosis lecture at Kettering Laboratory, Cincinnati, Ohio, March, 1956.

13. Kotin, P., Falk, H. L., Thomas, M., Aromatic Hydrocarbons III. Carcinogenicity of Exhaust Extracts, AMA Arch.Ind.Health, 11, 113, 1955.

14. Waller, R. E., Benzopyrene Content of Town Air, Brt. J. Cancer, 6, 8, 1952.

15. Chambers, L. Private communication to author.

16. Hueper, W. C. Recent Development in Environmental Cancer, AMA Arch.Path., 58, 360, 1954.

17. Walpole, A. L., Williams, M. H. C., Roberts, D. C., Tumors of Urinary Bladder in Dogs After Ingestion of 4-Aminodiphenyl, Brt. J. Ind.Med., 11, 105, 1954.

18. Deichmann, W. B., et al., Carcinogenic Action of p-Aminobiphenyl in the Dog, AMA Arch.Ind.Health, 13, 8, 1956.

19. Woodhouse, D. L., Irvin, J. O. Composition of Straight Run Distillates. J. Hyg.(Comb.) 48, 121, 1950.

20. Smith, W. E., Sunderland, D. A., Suguira, K., Experimental Analysis of the Carcinogenic Activity of Certain Petroleum Products, Arch.Ind.Hyg., 4, 299, 1951.

21. Cruickshank, C. N. D., Occupational Exposure to Cutting Oils, J. roy. Sanit. Inst., 70, 480, 1950.

22. Gilman, J. P. W., Vesselinwitch, S. D., Cutting Oils and Squamous Cell Carcinoma, Brt.J.Ind.Med., 12, 244, 1955.

23. Case, R. A. M., Pearson, J. T., Tumors of the Urinary Bladder in Workmen Engaged in the Manufacture of Certain Dyestuff in Britain, II, Brt.J.Ind. Med. 11, 213, 1954.

24. Birmingham, D. J., Unpublished Reports, Occupational Health Field Hdqs., Cincinnati, Ohio.

25. Treon, J. F., et al., Toxicity of the Products formed by the Thermal Decomposition of Certain Organic Substances, A.I.H.A. Quart. 16, 187, 1955.

MR. DOYLE: Mr. Chairman, this completes the report of the Joint Committee on Respiratory Protection. I move its adoption.

MR. COUCHMAN: Thank you, Mr. Doyle. Is there a second to the motion?

MR. JACK BALIFF (N.Y.): Second the motion.

MR. COUCHMAN: Are there any questions? (There being none, the report was approved.)

MR. COUCHMAN: Next we will hear a report from the Committee on Worker Health Information. Dr. Christine Einert (Calif.) is the Chairman of that Committee, but is not here, so we will hear from the alternate, who will please come forward to present that report.

(No response)

Since there has been no one appointed as an alternate* to submit that report, we will then go on to the report of the next Committee, entitled, "Threshold Limits". Mr. Allan L. Coleman (Conn.) is Chairman of that Committee.

REPORT OF COMMITTEE ON THRESHOLD LIMIT VALUES

Your committee has continued to review the literature for information substantiating or indicating the need for changes in threshold limit values listed. As the result of this year's work, it is suggested that the following changes in values be made:

	Present		Suggested	
	P.P.M.	Mg./m^3	P.P.M.	Mg./m^3
Chloroform	100	490	50	240
Bromine	1	7	0.1	0.7
Chloropicrin	1	7	0.1	0.7

The reduction in the value for chloroform is suggested on the basis of results of a study of industrial chloroform exposures recently published in the British Journal of Industrial Medicine by Challen, Hickish and Bedford. The suggested reduction in the threshold limit values for bromine and chloropicrin is the result of careful review of data which has been in the literature for a longer period.

*The Committee on Worker Health Information had prepared a report which Dr. Einert asked Mrs. Tula Brocard (USPHS) to present. Mrs. Brocard unfortunately was not able to be present for this business session and the report was not presented. It is included as Appendix I, page 148.

It is also suggested that the following substances be removed from the list of tentative values and be added to the list of recommended values. These appeared for the first time on the 1957 list and it is felt that these materials should be considered for transferral to the list of recommended values.

Acetylene tetrabromide	Tertiary butyl alcohol
Beryllium	Tolylene-2,4-diisocyanate
Methyl styrene	Triethylamine
Monomethyl aniline	Vinyl toluene
Paradichlorobenzene	Xylidine
Propylene oxide	

Inquiries were received during the past year requesting information in respect to values for sulfur dioxide, cyanides, nitrogen dioxide, silicon dioxide, diglycidyl ether, Teflon, fluorine, phosphoric acid, boron trifluoride, methyl chloroform and chlorobromomethane. Source of inquiries was not confined to the United States but came from such far-away places as Australia and New Zealand.

Information developed by the committee is getting wider circulation. The list published in the 1958 issue of the A.M.A. ARCHIVES was reprinted in the INDUSTRIAL HYGIENE DIGEST, in the GUIDE OF THE AMERICAN SOCIETY OF HEATING & AIR CONDITIONING ENGINEERS, and by the Mine Safety Appliances Company. Permission was granted in response to request from the British Embassy to publish the list in a table to be included in a new publication of the British Department of Safety, Health & Welfare. The National Safety Council is also considering republication of the recommended values.

It is gratifying to your committee to see this wide interest but it would be more meaningful to see greater evidence of the proper application and interpretation of these values. The use of the values listed as the only basis for the selection of a less hazardous material for an industrial operation is one of the greatest violations of the purpose of the table. Its improper use as the sole basis for the diagnosis of suspected disease is another. Comparison of values with the results of one or two atmospheric determinations taken over a very short sampling period with a spot or grab sampling instrument is another. Your committee has taken great care to explain that this information has been developed for use in the field of industrial hygiene as a guide in the detection and evaluation of health hazards in industry and that it should be used and interpreted by persons trained and experienced in this field. Membership of our conference could be of real assistance by further explaining the purpose of threshold limit values to those who use them in evaluation or control work. Your committee has spent a great deal of thought and time on the introduction which precedes the listing and its contents should be read and understood thoroughly before referring to values in the table.

Suggestions have been made by Conference members and others that various characteristics of solvents, such as vapor pressure or evaporation rate, and the threshold limit value be expressed as a product, which would be known as a "toxic hazard index," "relative safety index," "relative toxicity hazards," etc. Experienced persons in the field of industrial

hygiene know that volatility of a solvent at room temperature is only one of the factors which must be considered in the appraisal of the extent of the health hazard presented by the use of solvents, that many materials containing solvents are sprayed in the open or in poorly ventilated areas and, also, that there are operations using external sources of heat which make vapor pressure considerations useless. People in our profession also realize that exposure to many of the organic solvents used in industry produce insidious types of poisoning which result from continued or repeated exposure to very low concentrations, while others produce only slight irritation of the eyes, nose and throat at relatively high vapor concentrations and that the knowledge of such specific properties of solvent vapors determines how threshold limit values should be interpreted and applied. Long and careful observations on the effects of exposure to solvent vapors and other toxic materials encountered in industry enable us to decide whether threshold limit data should be interpreted strictly or freely and shows us that it is unwise to use threshold limits alone or even in combination with one or two other properties such as vapor pressure or evaporation rate as a basis for comparing toxicities.

While threshold limit values and evaporation-rate data are useful in evaluating an industrial health hazard, they should be used in conjunction with other important criteria such as the duration and frequency of exposure and the type of injury which may result. These criteria used together with the careful evaluation of exposure, using dependable field sampling and laboratory methods, and the periodic evaluation of the health status of exposed persons are all essential to the intelligent application of threshold limit values. Moreover, the threshold limit values have, included within them, safety factors which vary from substance to substance so that relative toxicities cannot be obtained by comparing one threshold limit value with another. Accordingly, arithmetic manipulation employing these values will result in a meaningless number.

During the coming year, your committee plans to request information from the various governmental industrial hygiene units to determine which of the threshold limit values appearing on the list have been used in evaluating exposures over a period of perhaps five years. Data obtained from such a questionnaire, together with information on methods used in these environmental studies, could be of great value to this committee and your Committee on Recommended Analytical Methods in the development of future programs.

Work on editing and rewriting of material documenting the threshold limit values has progressed during the past year, though not as rapidly as was hoped. If all goes as planned, the finished material will be available by the time of our next meeting.

The committee wishes to thank members of the Conference for their interest and cooperation in the past and looks forward to their continued support.

Allan L. Coleman, Chairman
William L. Ball — Keith H. Jacobson
W. Clark Cooper — W. H. Reinhart
Hervey B. Elkins — H. E. Stokinger

GENERAL JOINT MEETING WITH A.I.H.A. AND S.O.T.
MAY 7, 1963 - 1:45 P.M.

THE SECOND INTERNATIONAL SYMPOSIUM ON PERMISSIBLE LIMITS FOR AIR PARIS, APRIL, 1963
PHARMACODYNAMIC, BIOCHEMICAL, AND TOXICOLOGIC METHODS AS BASES FOR AIR QUALITY STANDARDS

Herbert E. Stokinger, Ph.D.
Division of Occupational Health
U.S.P.H.S.

I would like to express my deep gratitude to Professor Rene Truhaut, Chairman of the Symposium, for making it possible for me to present here some of the methods we employ to get acceptable toxicologic information for the recommendation of air quality standards for workplaces.

I would like to make it clear at the outset, that although my discussion is to center on pharmacodynamic, biochemical, and toxicologic methods that may serve as bases for permissible limits for the air of industrial workplaces in the U.S.A., no one principle, technic or data source are relied upon. Rather, recommendations for permissible limits for air are based on worker experience, if such exists in sufficient detail, exactness, and duration. This of course presupposes careful and precise evaluation (monitoring) of the workroom atmosphere and detailed medical supervision of the exposed workers. Because information from this source has not in the past always possessed the desired completeness, data from long-term animal toxicity studies are most commonly used. Frequently data from both sources combined are used when such information is available. In instances where applicable (irritants) human sensory (organoleptic) data form the basis of a recommendation. Thus data from all sources involving all methods and technics of the biologic and medical sciences may be utilized in arriving at recommended limits. One further important principle must be emphasized that is involved in developing hygienic standards for air in the U.S.A., namely we are attempting to an increasing extent to 'tailor' our procedures and technics according to the toxicologic requirements of the substances under study, i.e., to employ specially selected or sometimes unique procedures for specific receptor sites. This is not to imply that 'tailored' technics completely replace standard and routine methods of testing that have been effectively used in the past; rather we use particular and special technics to supplement, extend and refine information obtained from standard procedures.

Nature of U.S.A. Limits. I would like to say also at the start that I speak as Chairman of the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists; the methods I describe however, are largely those from U.S.P.H.S. laboratories. This Committee has, since 1943, been recommending, revising and more recently publishing annually, limiting values for the air of industrial workplaces. These values are called Threshold Limit Values (1) which with some recent exceptions, are the time-weighted average concentrations of chemical substances that apply to repeated, daily, 8-hour exposure periods throughout a worker's lifetime. All values are substantiated by a justification for their choice documented with references to the technical literature (2). The Threshold Limit Values, TLV's, are practical values. They are intended to provide an effective means of protecting the worker against significant effects, not only on health, but comparative freedom from irritation, discomfort and nuisance in his occupation. In short, Threshold Limit Values are intended to maintain optimal work efficiency and minimize accident proneness. In many industries in the U.S.A. currently, the

major application of the Threshold Limit Values is not toward protecting health, but toward providing comfort, freedom from irritation and nuisance and improvement of general work efficiency; as a result of many years of application of TLV's, health problems in many industries are no longer the primary concern. The Threshold Limit Values are considered as guides in the control of health hazards, and are not to be regarded as fine lines between safe and dangerous concentrations. For this reason, practically all threshold limits contain a factor of safety. They are derived on practical bases and applied practically and directly in industry. They do not represent ideal goals for compliance by industry hopefully at some future date. They are applicable when recommended. The Threshold Limit Values are not intended to be legally mandatory, but are voluntarily accepted by industry as a whole as working standards.

These are the characteristics of the threshold limits of the U.S.A. to which the following methods of pharmacodynamics, biochemistry, and toxicology may be applied (and which I have been assigned to discuss).

PHARMACODYNAMIC METHOD. The basis for using a pharmacodynamic approach (which according to our usage is the study of certain phases of the pharmacologic action of a toxic substance) is that all toxic agents may be considered to produce a stress at some threshold concentration. According to the generally accepted hypothesis of Selye (3) this stress is part of a General Adaptive Syndrome, the first phase of which is an Alarm Reaction. This is followed by an Adaptive Phase. Both phases (responses) have specific and nonspecific components, largely mediated by the endocrines and their associated and interrelated hormones. On these grounds it should be possible to select a specific function of one of the endocrine glands and to relate the change in this specific function to a threshold level of an absorbed substance (the stressing agent). We recognize, however, it may not be enough to determine only this simple relation - of just significant stress response to a concentration experienced for a defined period of time, and in turn use this concentration as the limiting one for workers' protection. One further and much more difficult step may be required, namely evaluation of the significance of the response to the over-all physiologic economy of the body (adaptation). If it is determined, for example, that there is no detectable alteration from normal body function to be expected from continued repetition of the threshold response, then the exposure concentration giving rise to this stress response is not limiting, but one at some higher level.

As far as we are aware, application of this particular pharmacologic concept of measuring specific endocrine function as a basis for air quality standards is novel. Accordingly the following example may appear crude and imperfect in the light of later developments in this area. The example has, however, we believe, general application to a broad range of inhaled stressing agents.

I^{131} Release Rates as a Measure of Toxic Stress - Alarm Phase. The basis of this particular pharmacodynamic method as developed by Fairchild and Graham (4) is the alteration in the rate of iodine released by the thyroid gland when the host is exposed (by inhalation) to a stressing agent; its practical application to selection of a threshold limit value for air is provided by the precise determination of a threshold concentration experienced for a given time interval and which corresponds to an altered response at its threshold of significance. Compared with recognized toxicologic procedures, this pharmacodynamic method appears

to have much to commend it; the entire method is relatively simple, objective, and by comparison with commonly employed toxicologic procedures, is probably capable of greater precision and is far less time-consuming.

In this present case, the agent is the respiratory irritant, ozone, the exposed subjects, rats. Iodine release is measured as gamma radioactivity of I^{131} in the thyroid glands at varying periods after intraperitoneal injection of I^{131}, compared with the corresponding radioactivity of the glands of the unexposed control animals.

Figure 1 provides detailed radioactivity data on excised thyroids of groups of 6 to 10 rats sacrificed at 24, 48, 96, 192, and 384 hours, compared with I^{131}-injected controls not exposed to ozone. Figure 1 shows the comparative results for rats exposed to 4 ppm ozone for 5 hours (CT = 20 ppm-hours); 2 ppm ozone for 5 hours (CT = 10 ppm-hours); 1 ppm ozone for 5 hours (CT = 5 ppm hours). It is seen that the thyroid release of I^{131} was significantly inhibited ($P < 0.0.$) at 24 hours and at all subsequent periods by 4 ppm ozone; i.e., significantly more iodine remained in the gland than in those of the controls at all periods tested. At a concentration of 2 ppm O_3, however, the I^{131} content of the gland at 24 hours was at the borderline of being statistically different than controls, but was significantly different at all other periods. At 1 ppm there was no statistically significant difference in thyroidal iodine at the 24-hour period, compared with that of controls, but were so at all other periods measured. The 1 ppm ozone level thus gives indication of approaching borderline or threshold concentration for pharmacodynamic effect for the alarm phase of the general syndrome. This may be interpreted to mean that the threshold concentration for a continuous, 5-hour exposure to ozone lies somewhere below 1 ppm ozone. The radiomimetic character of ozone with its characteristic irreversible effect, eliminates the need for evaluating the significance of this phase of the response in terms other than the direct stress response measured; radiation-like effects are believed to have no threshold.

I^{131} Release Rate Method in Adaptive Phase. The borderline concentration giving rise to the first phase of the General Adaptation Syndrome, the Alarm Reaction, has thus been determined by the thyroidal I^{131} release rate method; the second and more important part of the response is the determination of the critical concentration limits of the Adaptive Phase of the syndrome, i.e. to what degree the host may have adapted to the stress as initiated by the Alarm Reaction. Without such evaluation, the determination of the threshold concentration producing the Alarm Reaction may be of no significance. (O_3 and similar edemagenic agents are particularly good agents to test host-adaptation; a protective tolerance against fatal pulmonary edema is produced immediately upon exposure; this tolerance endures for several weeks or months, depending upon its method of production)(4b).

Fig. 2 shows the effect on I^{131} release from the thyroid of rats given 2 preexposures of O_3 at 2 ppm for 5 hours each and then challenged with 4 ppm O_3 for 5 hours. Controls were not given the preexposure but did receive the single challenge exposure to O_3 at 4 ppm for 5 hours. All exposures were thus at a CT of 20 ppm-hours. Fig. 2 indicates that the rats have adapted to the initial stress of O_3 exposure that causes inhibition of I^{131} release (O_3C histograms) by actually reversing I^{131} metabolism of the thyroid in these animals (O_3 P & C histograms); I^{131} release-rates now exceed normal. In a similar study (not shown in Fig. 2) a simi-

9. Mountain, J. T., Stockell, F. R., Jr., Biochemical Effects Related to Ozone and Nitrogen Dioxide Injury and Tolerance in Laboratory Animals. Public Health Service and California State Department of Public Health, Los Angeles, Calif., December 6, 1961. (Conference on Motor Vehicle Exhaust Emissions and Their Effects.)

10. Simon, F. P., Potts, A. M., Gerard, R. W., Metabolism of Isolated Lung Tissue, - Normal and in Phosgene Poisoning. J. Biol. Chem. 167, 303, (1947).

11. Scheel, L. D., Dobrogorski, O. J., Mountain, J. T., Svirbely, J. L., and Stokinger, H. E., Physiologic, Biochemical, Immunologic and Pathologic Changes Following Ozone Exposure, J. Appl. Physiol. 14, 167 (1959).

12. Beutler, E., "Drug-induced Hemolytic Anemia" in "Metabolic Basis of Inherited Disease," J. B. Stanbury, J. B. Wyngaarden, D. S. Fredrickson, Eds. McGraw-Hill, New York, 1960; Scheuch, D., Kahrig, C., Ockel, E., Wagenknecht, C., Rapoport, S. M., Role of GSH and of a Self-Stabilizing Chain of SH-enzymes in the Metabolic Regulation of Erythrocytes, Nature 190, 631, (1961).

13. Unpublished results, Toxicology Section, Occup. Health Res. Facility, Cincinnati, Ohio.

14. Kasbekar, D. K., Lavate, W. V., Rege, D. V., Sreenwasan, A., A Study of Vitamin B_{12} Protection in Thyrotoxicosis in the Rat, Biochem. J., 72, 374, (1959).

15. Dinman, B. D., Fox, C. F., Frajola, W. J., Rabor, A., Serum Enzyme and B_{12} Changes in CCl_4 Hepatoxicity, Arch. Environ. Health, 4, 168, (1962).

16. Jonderko, G., Diagnostic Value of the Determination of the Blood Glutathione Level in Chronic Lead Poisoning in Human Subjects, Pol. Arch. Med. Wewn. 31, 647 (1961).

17. Mountain, J. T., Delker, L. L., Stokinger, H. E., Reduction in Cystine Content of Rat Hair following Vanadium Exposure, Arch. Ind. Hyg., 8, 406, (1953).

18. Mountain, J. T., Stockell, F. R., Jr., Stokinger, H. E., Fingernail Cystine as an Early Indicator of Metabolic Changes in Vanadium Workers, Arch. Ind. Health 12, 494, (1955).

19. Reiner, M., and Sullivan, M. X., Cystine in Human Serum Protein, Clin. Chem. 2, 65 (1956).

20. "Exposure Chambers for Research in Animal Inhalation: Fraser, D. A., Bales, R. E., Lippmann, M., Stokinger, H. E., Pub. Health Monograph No. 57, U. S. Govt. Print. Off. 1959.

21. "Principles and Procedures for Developing Experimental Animal Data for Threshold Limits Committee, Am. Conf. Govt. Ind. Hyg., 1014 Broadway, Cincinnati, Ohio, 1962.

22. Stokinger, H. E., Wagner, W. D., Wright, P. G., Studies on Ozone Toxicity 1. Potentiating Effects of Exercise and Tolerance Development, Arch. Ind. Health, 14, 158, (1956).

23. "Detoxication Mechanisms," R. T. Williams, 2nd Ed. 800 pp. John Wiley & Sons, Inc. New York, 1959.

24. Walkley, J. E., Pagnotto, L. D., Elkins, H. B., The Measurement of Phenol in Urine as an Index of Benzene Exposure, Am. Ind. Hyg. Assn. J., 22, 362, (1961).

25. Cohen, A. E., Paulus, H. J., Keenan, R. G., Scheel, L. D., Skin Absorption of Carbon Disulfide Vapor in Rabbits, Arch. Ind. Health 17, 164 (1958).

26. Schepers, G. W. H., The Mineral Content of the Lung in Chronic Beryllicosis, Dis. Chest. 42, 600 (1962).

27. Schepers, G. W. H., Tetraethyllead and Tetramethyllead - Comparative Experimental Pathology, Presented at Lead Symposium, The Kettering Laboratory, Univ. Cincinnati, Feb. 26, 1963.

28. Cohen, A. E., Scheel, L. D., Kopp, J. F., Stockell, F. R., Keenan, R. G., Mountain, J. T., Paulus, H. J., Biochemical Mechanisms in Carbon Disulfide Poisoning, Am. Ind. Hyg. Assn. J., 20, 303 (1959).

29. Vigliani, E. C., Pernis, B., An Immunochemical Approach to Silicosis, J. Occup. Med. 1, 319 (1959).

30. Unpublished results, Scheel, L. D., Killens, R. L., Stokinger, H. E.

31. Stokinger, H. E., Scheel, L. D., Ozone Toxicity - Immunochemistry and Tolerance-Producing Aspects, Arch. Environ. Health 4, 327, (1962).

COMMENTS FOLLOWING PAPER BY DR. STOKINGER AT THE AMERICAN INDUSTRIAL HYGIENE CONFERENCE, MAY 7, 1963

W. Clark Cooper, M. D.
Chief, Division of Occupational Health
U. S. Public Health Service

I am Dr. W. Clark Cooper, Chief of the Division of Occupational Health of the U. S. Public Health Service.

I think it is important for the record for me to re-emphasize some of the circumstances surrounding this Symposium on Permissible Limits. I feel that this may allay the concern of some who may feel that we are moving too rapidly into the complex field of international standard setting. I would like to make three points:

First, I think the sponsorship of the meeting needs clarification. As I understand it, the Paris Symposium was arranged by the Subcommittee on Permissible Limits of Toxic Substances in Industry, under the permanent International Committee on Occupational Medicine which, as you know, sponsors the Triennial International

MR. BAIER: All we know is that it's statistically valid.

MR. LYNCH: The origin of that, I think, came from the problem of background, that in impingers we are going to get about a million or so background if we took a sample out in the city street, but by the same token we will on the membrane count also.

MR. SHEINBAUM: This is not true. I have been counting on membrane filters now for about two years with asbestos, and find the method quite satisfactory. We do not get the background count.

MR. LYNCH: I am entirely in favor of the membrane filter method of counting asbestos. We have two methods, we have the impinger method which has been standard in this country, we have the membrane filter count that the English use. At this point we seem to be introducing a third method which I don't think we have a great deal of experience with. I would like to see us stick to the two million particles per cubic foot by impinger, which is a lowering of the T. L. V., which I think was the Committee's intention. Admittedly, the impinger is difficult to operate down at that range, so we give an alternative of 10 or 12 fibers per ml. and fiber count by membrane filter, which is the English method, and we have covered all bases in that regard.

Now, introducing a third method seems to be adding unnecessary confusion.

SECRETARY HOSEY: In the interest of saving time, may I suggest, as Dr. Stokinger has requested on numerous occasions, that you communicate with him concerning any comments on these T. L. V. changes. (See Appendix D for list of changes.)

REPORT OF COMMITTEE ON THRESHOLD LIMIT VALUES

The first meeting of the plenary committee of FY '68 was held in Cincinnati at the O. H. P. facility with Mr. Wagner as Recording Secretary. Dr. Mastromatteo was unavoidably unable to attend. During the two days of meetings the "Notice of Intent" changes were developed for promulgation among various associations and agencies. Sixteen (16) substances were on the list for revision, 6 new substances for addition and 12 others for possible addition pending receipt of adequate substantiating data. Prominent among the revisions was a change in the asbestos limit, changes in several petroleum hydrocarbons, as well as Stoddard solvent, and a request for reviewing of the air limits for tetraethyl and tetramethyl lead. Following the meeting copies of the "Notice of Intended Changes" were sent to the Manufacturing Chemists' Association, American Industrial Hygiene Association, the Industrial Hygiene Foundation and the A. C. G. I. H. for distribution among the membership, with the request that comments on these intended changes be received by the Chairman by March 15, 1968. A flood of communications commenting variously on several of the intended changes was received by the Chairman within a few weeks after the announcement had been distributed. As a result, Dr. deTreville of the Industrial Hygiene Foundation sponsored a 1-1/2-day meeting at Kettering Laboratories in Cincinnati for discussion of the T. L. V. s; the second day being devoted to a discussion by the representatives of the membership of I. H. F. of the intended changes. Prominent among the discussants was Dr. Stanley Roach, representing the British Occupational Hygiene Society, London,

DR. STOKINGER: Has everyone a copy of the intended changes? If not, hold your hand up and we can supply you with one.

Before we give consideration to the adoption of these intended changes, I might just make a few comments on some omissions that have been made and some announcements of what progress we're making in the revision. This is the second revision of the documentation.

Going along, I can say we are well over 50 percent of the revisions, and I would think that by the end of this year that this would be available.

SECRETARY ROSE: We will give it a try.

CHAIRMAN KEY: Let's say it will be ready to be printed.

DR. STOKINGER: Yes.

I'm happy to announce also that our last meeting of the plenary session of the Threshold Limit Committee has nominated, or appointed, a subcommittee to consider appropriate excursions for individual and specific substances. The issue was just brought out this morning. Those of you who were here in the morning session noted that the rule of thumb, the present rule of thumb, suggestions for permissible excursions, does not fit appropriately the substance carbon monoxide where peak excursions have little significance.

According to this rule of thumb we have, you are only permitted to go to 75 parts per million over the suggested limit, whereas, it is on good authority and evidence it's possible to go as high as 400 parts per million without any pain for 15 minutes.

Now we might consider the more formal matter of adopting the 14 revised limits that you all have now in front of you, and the 8 new limits in the Notice of Intended Changes for 1970.

Among the more important changes--and this will be all I will have time for--is the one for asbestos. Those of you who attended the morning session heard in some detail about the large amount of consideration that was given to this substance and the need for change, which is listed here from 12 fibers per cc greater than 5 microns in length to 5 fibers per milliliter greater than 5 microns in length with, however, a 10 fiber per milliliter ceiling. This applies to all form of asbestos, and should be, of course, measured according to the stipulated methods and specified procedures.

The other major change that we wish to call your attention to is the one on "Inert" or Nuisance Aerosols limits, a reduction from the long-standing 15 milligrams per cubic meter to 10. This we felt is in the interest of the national environmental climate. In other words, what was satisfactory or accepted a quarter of a century ago, when this limit was clamped on to nuisance dust, now seems to be less appropriate.

This change in the inert dust limit automatically requires a slight adjustment in the formulae for quartz which we inserted here, because of the tendency that any form of change, however small, has got to be listed in the intended changes. You can see here, appropriately listed, the necessary arithmetical changes to fit this curve that is derived for the TLV for quartz.

Similarly, the mass sampling limits for total dust should be out of there. Some gremlin put it in there when I wasn't looking at it, I guess. Also, it would be more appropriate to footnote: "This revision automatically reduces all other particulates listed as 15 mg/m^3."

Now as to the more important additions on the other side of the page, the addition of bituminous and respirable coal dust was given the limit of two milligrams per cubic meter, because this is the one that's set in the Coal Safety Bill.

Another important limit is that of rosin fumes. We feel particularly proud about this one because this was a limit that was requested by a number of individuals, and we could find no information that was firm enough to derive a limit, and one of our Committee members not only set about the task of preparing this limit, but he identified through mass spectrographic analysis all the toxic components of this complex mixture, and then set up a human volunteer study of repeated duration and came up with a figure, strangely enough, that was already decided from what little information was in the literature. It shows you that sometimes these educated guesses aren't as bad as some people like to make them out.

The other important addition was subtilisins, the last listing, which is representative of the number of proteolytic enzymes which is now appearing in almost all laundry soaps. This is a very potent allergenic material and, as you can see, the limit reflects this. It is a half a microgram in a whole cubic meter of air. This is to indicate it's nothing to be played around with by industrial workers.

One of our men, that was doing some work with animals, was taken to the hospital in an ambulance, breathing oxygen and with severe respiratory distress from doing nothing more than handling the animals after they had been exposed for five or six hours, and the chamber had been shut down, there were no circulating particulates there. He was in a bad state of health for a considerable period.

As I said, this limit that we set here attempts to reflect this. It is a very tentative limit because of the lack of progress in the development of essential information, but it's the best guess we can get at this present time.

I guess we might put it up for adoption by the Conference.

CHAIRMAN KEY: This would be an appropriate time for discussion and eventual vote on acceptance of the recommended changes and new additions. Is there any discussion? I have several hands. Stand up and identify yourself.

MR. CHAMBOW: I am Milt Chambow from New York State. I notice on the asbestos you're proposing to drop the two parts per million completely, or is this an error? Is there no counting whatsoever as far as this is concerned on asbestos?

DR. STOKINGER: That's right. The reason being, as I understand it, that when you get down to five fibers per cc, you're going to come down around a little bit below one million particles per cubic foot, and then extraneous dust becomes such a factor. Isn't that true, Howard?

MR. AYER: Yes.

DR. STOKINGER: You cannot get any reliable counts.

MR. KUSNETZ: Howard Kusnetz, Public Health Service. There is a bit of confusion,

The principle of excursions has been adopted also by another standard-setting body, ANSI.[4] Three limits for each substance are commonly used to control industrial air concentrations: "Acceptable Time-weighted Average," "Acceptable Ceiling Concentrations," and "Acceptable Maximum for Peaks" above the acceptable ceiling for an 8-hour workday. These excursions recognize the hour-to-hour variations that occur in most industrial operations and are so designed in magnitude and duration as to incur no rish to health. The ANSI excursions differ from the rule-of-thumb excursions of the TLVs in that their magnitude is tailored to the specific toxicologic responses of the substance. For example, the ANSI peak excursion for CO is 1000 ppm for 10 minutes once per day; by the TLV rule-of-thumb, 75 ppm (1.5 x 50 ppm), thus showing TLV rule-of-thum is not appropriate in some instances.

Unquestionably, the greatest value of the TWA concept is that it brings to the attention of the factory inspector and judicial bodies alike that small deviations in concentration above the designated limit are not ipso facto evidence of the existence of a health hazard.

Why such excursions are possible stems from the fact that all TLVs (with the exception of some 30 substances bearing "ceiling" values) have built-in safety factors, or zones of "no-effect" above the prescribed TLV.

As with all generalities, there are exceptions, the exceptions in this case being the 30 or so TLVs bearing the "C" designation, a ceiling or maximal permissible limit below which all air concentrations must fluctuate. Ceiling limits are placed on those substances which, in an exposure period of 15 minutes or less, may result in (a) intolerable irritation, (b) chronic or irreversible change, or (c) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency.[3]

Misuse of TLVs. In parallel with guidelines for proper use of TLVs, should go cautions against their misuse. The Committee has identified five areas of improper use.[1] The TLVs are not intended for use, or by modification, for use:

a. As a relative index of toxicity. Chemical salesmen tend to use this ploy to point out to their customers that the lower TLV of the competitor's products makes them less safe to use than theirs with the higher TLV. This is certainly an instance of misapplication, simply because the bases of the TLVs for the compared products can differ widely. Consider the case of ethyl benzene, TLV, 100 ppm, vs methyl chloroform, TLV, 350 ppm. To say that methyl chloroform is safer than ethyl benzene on the basis of comparative TLVs is erroneous. The basis of the TLV for methyl chloroform is protection against narcosis; that for ethyl benzene, irritation. Furthermore, safety of a product involves hazard; the hazard of the two differ. Only when the metabolism of two substances is similar, can TLVs be used as a relative index of toxicity; this is generally not known.

b. The TLVs should not be modified for use in the evaluation or control of air pollutants for a number of reasons, the most important of which are that the population at risk differs and the exposure times differ.

c. In estimating the toxic potential of continuous, uninterrupted exposures, the TLVs do not serve as appropriate guides even by factorial modification, for the simple reason that the proper factor cannot be determined a priori.

d. Nor should TLVs be used as proof or disproof of an existing disease or physical condition. Attempts have been not infrequently made to use, in court as evidence, that a disease was caused simply because a TLV was exceeded. As previously pointed out, the safety factors incorporated in TLVs permit reasonable excesses above the stated limit without the incurrence necessarily of any health penalty.

e. Other countries should not indiscriminately adopt TLVs. Over the years, several non-iron curtain countries have adopted without modification the American TLVs, despite warnings to the contrary.[1] A typical instance of an American TLV proving unsuitable for foreign adoption is the Japanese use of the Cadmium TLV.[5] A medical environmental survey of smelter workers in cadmium-silver alloys indicated that the American TLV for cadmium should be halved for the protection of Japanese workers from proteinuria and anemia.

This concludes a brief summary of "do's and don'ts" if the intent of the American TLVs is to be fulfilled. To what extent this fulfillment occurs, you will learn from the succeeding speakers.

Summary. The main point that I hope comes out loud and clear: In testing industrial air environments for compliance with the TLVs, whoever evaluates the air concentration data should be keenly aware that excesses above the stated TLV are permissible, that they vary in magnitude in accordance with the nature of the substance, that in many cases the magnitude of the excursions can be determined by consulting the documentation or ANSI limits. If neither has this information, apply TLV rule-of-thumb.

References

1. Threshold Limit Values of Airborne Contaminants and Intended Changes Adopted by A.C.G.I.H. for 1970, p. 2, P.O. Box 1937, Cincinnati, Ohio 45201.

2. Ibid, p.1.

3. Ibid., Appendix C, p. 26.

4. American National Standards Institute, 1430 Broadway, N.Y. 10018.

5. Tsuchiya, K., Proteinuria of Workers Exposed to Cadmium Fume, Arch. Environ. Hlth., 14, 875 (1967).

DOCUMENTATION OF THE THRESHOLD LIMIT VALUES FOURTH EDITION 1980

CINCINNATI, OHIO

AMERICAN
CONFERENCE
OF
GOVERNMENTAL
INDUSTRIAL
HYGENISTS
INC.

ARSINE

AsH_3

TLV, 0.05 ppm (≈ 0.2 mg/m³)

Arsine is a colorless gas with a disagreeable garlic odor. It has a molecular weight of 77.93, specific gravity of 2.695, melting point of -113.5° C, boiling point of -55° C, a vapor pressure of ≥ 1 atmosphere and decomposes at 230° C. It is soluble in water, slightly soluble in alcohol and alkalies.

It is used in organic synthesis; as a military poison gas; doping agent for solid state electronic compounds.

Most cases of arsine poisoning do not result from the manufacture or use of the gas itself; rather they come from formation of arsine as a byproduct of a chemical reaction involving, in most instances, a base metal, an arsenic impurity, and an acid, or, rarely, a strong alkali.

The extreme acute toxicity of arsine is well known; 250 ppm for 30 minutes is fatal, and 3 to 10 ppm can cause poisoning symptoms in a few hours.[1] Nau[2] found that animals exposed three hours a day to concentrations between 0.5 and 2 ppm developed blood changes in a few weeks.

Published reports of occupational and other poisoning from arsine describe some 310 cases, 74 of them fatal, through 1959.[3] Several reports since 1960 record 28 cases, with two deaths, in this country[4-7] and abroad.[8-10] Typical cases resulted in hemoglobinuria, jaundice and hemolytic anemia.

While data on the actual concentrations causing acute intoxication are lacking, post event concentrations of 70 to 300 ppm (Morse and Setterlind, fatal cases.[11] 5 ppm Kipling and Fothergill[8] and 0.5 ppm Elkins[3] were reported. When urine samples were analyzed at early stages concentrations of arsenic ranging from 0.5 to 2 mg/L were the rule, but occasionally much higher values were found.

Bulmer *et al*[12] reported a number of cases of chronic poisoning, with severe anemia. Urinary arsenic levels averaged 2.3 mg/L, dropping to 0.66 mg/L three days later. Greig *et al*[13] recorded three relatively mild chronic cases with arsenic in urine levels of 0.5 mg/L.

In an extensive clinical study of 14 simultaneous cases of arsine poisoning,[14] tissue arsenic levels, determined by neutron activation analysis, indicated a total body content of arsenic one-third to one-half the lethal dose (300 mg), if one "assumes" that the poisoning action of the hydride follows to some extent that of the trioxide. None of the cases were fatal, but ranged from mild to very severe. Hemolysis and renal damage typified the toxic responses. The most severely poisoned had oliguria for 40 days and required hemodialysis 10 times, but hemolysis disappeared in a few days in all others. In four cases, renal function was impaired for a long time, but was finally restored.

Since arsenic appears to be excreted rather freely in the urine,[15] the levels found in the urine of intoxicated workers could have resulted from inhalations of concentrations below 1 mg/m³ or 0.25 ppm. The recommended TLV of 0.05 ppm (0.2 mg/m³) is the same as that of other inorganic arsenic compounds, which are considered substantially less toxic.

Other recommendations: Cook (1945) 1 ppm; Smyth (1956) and Elkins (1959) 0.05 ppm; USSR (1966) 0.1 ppm; Czechoslovakia (1969) 0.06 ppm.

References:

1. **Henderson, Y., Haggard, H.W.:** *Noxious Gases*, Reinhold, NY (1943).
2. **Nau, C.A.:** *South. Med. J. 41*:341 (1948).
3. **Elkins, H.B.:** *Chemistry of Industrial Toxicology*, p. 64, Wiley & Sons, NY (1959).
4. **Konsen, J.L., Dodson, V.N.:** *J. Occup. Med. 8*:540 (1966).
5. **Elkins, H.B., Fahy, J.P.:** *Ind. Med. & Surg. 36*:747 (1967).
6. **Teitelbaum, D.T., Kier, L.C.:** *Arch. Env. Health 19*:133 (1969).
7. **DePalma, A.E.:** *J. Occup. Med. 11*:582 (1969).
8. **Kipling, M.D., Fothergill, R.:** *Brit. J. Ind. Med., 21*:74 (1964).
9. **Kambara, T., Nohara, Y., Ikegama, K., Nakamura, T., Kajiwara, T.:** *J. Sci. Labour 42*:454, Japan (1966).
10. **Fallentin, B., Frost, J., Grut, A.:** *Ugeskrift for Laeger 129*:544 (1967).
11. **Morse, K.M., Setterlind, A.N.:** *Arch. Ind. Hyg. & Occup. Med. 2*:148 (1950).
12. **Bulmer, F.M.R., Rothwell, H.E., Polack, S.S., Stewart, D.W.:** *J. Ind. Hyg. & Tox. 22*:111 (1940).
13. **Greig, H.B.W., Bradlow, D.A., Harrison, C., Dalton, M.B.:** *So. Af. Med. J. 32*:101 (1958).
14. Arsine Poisoning in a Metal-Refining Plant. B. Nielson, ed., *Acta Med. Scand. Suppl.*
15. **Elkins, H.B.:** *Am. Ind. Hyg. Assoc. J. 28*:305 (1967).

ASBESTOS

TLV, Appendix A1a— Recognized Carcinogen

0.5 fiber > 5 μm/cc — Amosite
2.0 fibers > 5 μm/cc — Chrysotile
0.2 fiber > 5 μm/cc — Crocidolite
2.0 fibers > 5 μm/cc — Other forms

According to recent authoritative mineralogical definitions,[1] asbestos is "1) A collective mineralogical term encompassing the asbestiform varieties of various minerals; 2) An industrial product obtained by mining and processing primarily asbestiform minerals."

For the purpose of considering a recommendation for a threshold value of asbestos dust in the workplace, only the second definition above is applicable. Although there are four types of natural mineral fibers that have been in industrial use, only three have been used in the United States: chrysotile, amosite, and crocidolite. The fourth, anthophyllite, is mined and used in Finland. Of the three types of asbestos that have been used in North America, Canadian chrysotile has formed 95% of all natural mineral fibers used, with amosite and crocidolite (both imported from South Africa) constituting the other 5%. It should be noted that chrysotile is classified as a serpentine mineral, whereas the other three types of asbestos are amphiboles.

It is now generally recognized that excessive inhalation of asbestos dust causes chronic inflammations of lung tis-

sue and pleural membranes as well as cancers. Whereas identification of asbestos dust as a cause of fibrosing inflammation of lung tissue occurred as early as 1907,[2] it was not until 1930 that a more definitive study by Merewether and Price[3] resulted in the regulations which greatly improved hygienic conditions in asbestos factories in the United Kingdom. The development of lung cancer in asbestos workers, first reported by Wood and Gloyne[4] in the U.K. in 1934 and by Lynch and Smith[5] in the U.S. in 1935, was not firmly established until 1955 by the publication of Doll[6] of a study of workers in an English asbestos textile factory, and in the United States by the paper of Selikoff *et al*[7] in 1964 concerned with cancers in insulation workers. In 1960 the relationship between the inhalation of asbestos dust and mesothelioma was demonstrated by Wagner *et al*.[8]

Asbestosis is a diffuse but nonuniform fibrosis of the lungs that is generally most severe in the basilar portions. As a result of the fibrosis some of the airspaces (alveoli) are not perfused with blood and alveoli that are perfused with blood may not be adequately ventilated because of stiff, thickened alveolar walls. The fibrosis makes the lungs less compliant, thereby increasing the energy requirement of breathing. There is increasing impairment in diffusion of gases leading to increasing breathlessness.

It is not uncommon to find thickening of the visceral pleura, sometimes very severe, by extension of the parenchymal inflammation. This causes an additional increase in the effort of breathing.

The parietal pleura may show patches of severe thickening, particularly over the diaphragm and the lower portions of the chest wall — resulting in the so-called pleural hyaline plaques. These may become visible in X-ray films of the chest — particularly, if they become impregnated with calcium salts. Such pleural plaques may develop from asbestos exposure in the absence of asbestosis. They cause no symptoms.

A study of the members of an asbestos insulators union revealed that deaths from lung cancer in this population was much greater than expected.[7] A later investigation by Hammond and Selikoff of a much larger number of these workers (17,800) showed that nearly all cancers occurred in cigarette smokers.[9] The conclusion of these authors was as follows:

> *"It seems clear, then, that lung cancer is uncommon among asbestos insulation workers who have no history of cigarette smoking, and that if the risk is increased such an increase is not great."*

The total lung cancer rate in this cohort of workers was 4.8 times the expected. The asbestos insulators who had a history of cigarette smoking had a lung cancer rate 5.4 times the expected rate; but compared to the lung cancer rate of the nonsmoking workers, the smoking insulators' lung cancer rate was 14 times greater.

All types of asbestos are known to cause the inflammatory changes in the lungs and pleurae described above and lung cancer. However, there is experimental and epidemiologic evidence that there may be differences in the potential of the different asbestos types to produce disease. Thus, it has been suggested that crocidolite has the greatest potential to *produce* disease; chrysotile, the smallest; with amosite occupying an intermediate position.[10] In a study of 1348 retirees from the asbestos industry by Enterline and Henderson,[11] the respiratory cancer rate of men exposed only to chrysotile was 2.4 times the expected, whereas this rate was 5.3 times the expected for men who had been exposed to a combination of chrysotile and crocidolite. In the asbestos cement industry a similar difference was observed. Workers exposed only to chrysotile and cement (shingles and sheets) had a respiratory cancer rate of 1.4 times the expected, whereas workers exposed to both, chrysotile and crocidolite and cement (asbestos cement pipes), had a respiratory cancer rate 6.1 times the expected.

Mesotheliomas are rare, usually rapidly fatal cancers that originate from the surface lining the chest or abdominal cavity. From 1960 through 1975, 4539 mesotheliomas have been reported worldwide.[12] The vast majority of these cancers were in people exposed to crocidolite alone or in combination with other types of asbestos. McDonald and McDonald[12] tabulated those reports of mesothelioma where the type of asbestos exposure was known. Although the number of such cases is small, where the exposure was to crocidolite alone or in combination with other types of asbestos, death from mesothelioma constituted 6.1% of the deaths from all causes, with a range of 2.42% to 16.07%. In contrast, deaths from mesothelioma in workers exposed only to chrysotile constituted only 0.3% of the deaths from all causes, with a range of 0.24% to 0.87%. An even greater contrast is found in the Finnish statistics of workers exposed to anthophyllite. Meurman *et al*[13] investigated 216 deaths that occurred among approximately 900 miners and millers of anthophyllite during the 32-year period 1936-1967 and found not one case of mesothelioma.

Not all mesotheliomas result from asbestos exposure. There is a background of "naturally" occurring mesotheliomas that has been estimated to be about ten for males and four for females per million persons aged 45 years and older.[12] Furthermore, it is not uncommon in the various epidemiologic studies reported that 15% or more of the mesothelioma cases have no history of ever having been exposed to asbestos. Perhaps the most important indication that mesotheliomas may result from causes other than asbestos exposures; in this instance, also environmental, comes from a report by Baris *et al*[14] who described a mesothelioma incidence of 2.3% in 1974 in the village of Karain in Turkey (population, 604). This population has been exposed for many generations to dust from the soil that contains kaolin, mica, and vulcanic glass particles, but no asbestos.

A small excess of deaths from gastro-intenstinal cancers have been noted in several epidemiologic studies of asbestos workers.[9,15] An association of laryngeal cancer with asbestos exposure has been claimed. Pancreatic cancers and lymphomas have also been mentioned in this connection. However, conversion of the association to a causal relationship rests, as yet, on an insecure basis.

Whether or not there is a dose-effect relationship associated with asbestos dust has been answered affirmatively by a number of epidemiological surveys.[15-19] Whereas this relationship is clear-cut with regard to asbestosis and lung cancer, it is less well-marked with regard to mesothelioma, but it is, nevertheless positive. McDonald[20] points to a case-control analysis based on seven cases of mesothelioma at Thetford Mines that includes no case with less than

30 mppcf-years exposure and which suggests that the risk increases with exposure. McDonald further points out that, although fiber-equivalents for the dust concentrations in mppcf are difficult to estimate, there is evidence for believing that the conversion factor cannot be less than two. The data of Newhouse and Berry[21] demonstrates a doubling of the incidence of mesothelioma for males who had severe exposures as compared to that of the workers who had light or moderate exposures. This was equally true for those employed less than two years. In all of the other investigations of mesothelioma incidence, the degree of dust exposure was not indicated, thereby preventing the determination of any dose-effect relationship.

The only reliable exposure data from the asbestos industry on which a recommendation for a threshold limit of asbestos exposure can be based, stem from England.[19,22] Using the presence of persistent high-pitched rales in the basal portions of the lungs as criterion for the diagnosis of asbestosis, it was determined from a population of asbestos textile workers that less than 100 fiber-years of exposure (2 fibers/cc over a 50 year working period or 4 fibers/cc over a 25 year period) would cause the development of asbestosis in no more than 1% of the workers.[22] This departure from the previous dust standard of 5 mppcf was in recognition of the variability of the asbestos fiber content of factory dust and that the disease was related to the number of asbestos fibers inhaled and not to the amount of nonfibrous dust particles. Also, it was specified that the counted fibers were to be longer than 5 μm.

The size limit placed on the counted fibers (longer than 5 μm) was because it was not practical to count shorter fibers with an optical microscope (400 to 450 x magnification under phase-contrast illumination, with a 4MM objective). It is recognized that for every asbestos fiber longer than 5 μm, there may be as many as 100 or more fibers shorter and thinner that are not visible under the optical microscope. However, there is considerable experimental evidence to indicate that asbestos fibers shorter than 5 μm are not pathogenic.[23]

A recent publication by Gillam *et al*[24] indicated that the present limit of 2 asbestos fibers/cc longer than 5 μm set by OSHA is inadequate to protect workers against nonmalignant as well as malignant respiratory disease. This conclusion was based on a study of 440 hard rock gold miners who had been exposed to an asbestiform mineral (cummingtonite-grunerite). These investigators found 10 respiratory cancer deaths (including a carcinoma of the maxillary sinus and a mediastinal carcinoma) when only 2.74 such deaths had been expected. Five deaths from nonmalignant respiratory diseases other than influenza and pneumonia when 1.85 death from these causes had been expected. These deaths included those from silicosis (the respirable dust contained 13% free silica!).

It is of interest that although the diagnosis of asbestosis was not mentioned in the paper, Gillam *et al*[24] emphasized the finding taht the ambient air in the gold mine contained an average of 4.82 fibers/cc, 80 to 80% of which were fibrous amphiboles, *"and 60 to 70% of the latter were fibrous grunerite (amosite)."* Fibers longer than 5 μm, averaged 0.36 fibers/cc; and approximately 94% of the airborne fibers were less than 5 μm long, averaging 0.13 in diameter and 1.1 μm in length.

McDonald *et al*[25] investigated the records of the same gold mine as Gillam *et al*, but their cohort consisted of 1321 men who had completed 21 years service with the mining company (in contrast to the cohort of 440 men studied by Gillam *et al*).[24] The following is a summary of their findings:

> *"All but 10 of the men were traced to the end of 1973 when 651 were still living; cause of death was ascertained for 657 of the 660 who had died. The numbers of deaths observed in various diagnositc categories, with 'expected' figures in parenthesis, were as follows: — respiratory cancer — 17 (16.5); abdominal cancer — 39 (35.1); other malignant diseases — 37 (39.0); pneumoconioses — 39 (0); respiratory tuberculosis or silico-tuberculosis — 39 (3.6); heat disease — 264 (232.5). Silicosis was given as the cause in 37 of the 39 pneumoconiotic deaths and mentioned on the certificate in 28 of the 264 coded to heart disease. The occurrence of deaths ascribed to pneumoconiosis, tuberculosis and heart disease was in each case related directly to dust-exposure category, whereas deaths coded to respiratory, abdominal and other cancers showed no such relationship. The pattern of mortality of men with long employment in this industry indicates a serious pneumoconiotic hazard characteristic of hard rock miners but not of cancer."* (See Table 1.)

It would appear from the McDonald *et al* study[25] that there is no basis for the claim made by Gillam *et al*[24] that the OSHA standard of two fibers longer than 5 μm/cc is inadequate to protect the health of workers, or that asbestos fibers shorter than 5 μm produce deleterious health effects.

In an 8 year follow-up of the same population of asbestos workers from which the 100 fiber-years exposure was derived as a reasonably safe level, it was found that mortality was increased for lung cancer.[19] There were 31 deaths from this cause whereas only 19.3 had been expected. From non malignant respiratory disease, there were 35 deaths, where 25.0 had been expected. In addition, there were five deaths from pleural mesothelioma.

It was determined that the mean dust level of the workers had been below 5 fibers/cc only in the last decade. In 1951 the mean dust level was 10.8 fibers/cc and 89% of the men had been exposed to mean levels above 5 fibers/cc. In 1972, the mean dust level was 2.9 fibers/cc and only 3% of the men were exposed to a mean level greater than 5 fibers/cc, 65% were exposed to a mean level between 2 and 5 fibers/cc and 32% to a mean level below 2 fibers/cc.

Because there is a delay of 15 or more years between first exposure and any resulting cancer, the authors consider that the increased mortality demonstrated does not reflect the effects of working conditions over the last 15 or 20 years. They therefore propose to continue the follow-up on workers entering scheduled areas since 1951. In terms of the 100 fiber-year or 2 fibers/cc standard suggested by the British Occupational Hygiene Society (B.O.H.S.), it is apparent that the excess mortality reported above can be attributed to asbestos exposures considerably above this level.

The workers in the asbestos textile factory, from which the B.O.H.S. standard of 2 fibers/cc was derived, have been

studied by highly qualified investigators whose reports were published in 1955,[6] 1965,[16] 1968,[26] and 1977.[19] These workers represent the only cohort of asbestos workers in the world in which health effects have been correlated with definitive exposure data defined as fibers per cc. It would be premature and ill advised to change the present OSHA standard of 2 fibers longer than 5 μm/cc for chrysotile without indications from this study population of the advisability for such change. The same TLV is assigned to other forms of asbestos not specifically named herein.

The exposure level of crocidolite and amosite, particularly of the former, must be sharply lower than that of chrysotile because of their greater potential for disease production. In view of the lack of accurate information of the dose-effect relationship pertaining to these two types of asbestos, the arbitrary assignment of 0.5 fiber/cc longer than 5 μm appears reasonable and prudent for amosite. Since crocidolite may be more pathogenic than amosite, a TLV of 0.2 fiber/cc longer than 5 μm is recommended, as well as the A1a, proven carcinogen, designation for all types of asbestos.

Tabulation of Significant Findings in Two Epidemiologic Investigations of Workers in the Same Hard Rock Gold Mine

		McDonald et al[25]		Gillam et al[24]	
Size of Cohort		1321		440	
Number of Deaths		Observed	Expected	Observed	Expected
Respiratory Cancer		17	16.5	10	2.74
Nonmalignant	Pneumoconiosis	39*	0		
Respiratory	Respiratory TBC Silico-TBC	39	3.6	5	1.85
	Other Nonmalignant Respiratory Disease	?	?		

*37 of the 39 deaths were ascribed to silicosis.

References

1. **Campbell, W.J., Blake R.L., Brown L.L., Cather E.E., Sjoberg J.J.:** Selected Minerals and their Asbestiform Varieties: Mineralogical Definitions and Identification-Characterization. *Bureau of Mines Information Circular 8751*, p. 14 (1977).
2. **Murray, M.:** *Report*, Department, Commission on Compensation of Industrial Disease. Cd. 3496, pp. 127-128, London, H. M.S.D. (1907).
3. **Merewether, E.R.A., Price, C.W.:** *Report on Effects of Asbestos on the Lungs and Just Suppression in the Asbestos Industry*, London, H.M.S.O. (1930).
4. **Wood, W.B., Gloyne, R.S.:** *Lancet* 2:1383-1385 (1934).
5. **Lynch, K.M., Smith, W.A.:** *Am. J. Cancer* 24:56-64 (1935).
6. **Doll, R.S.:** *Brit. J. Ind. Med.* 12:81-86 (1955).
7. **Selikoff, I.J., Churg, J., Hammond, E.C.:** *J.A.M.A.* 188:22-26 (1964).
8. **Wagner, J.C., Sleggs, C.A., Marchand, P.:** *Brit. J. Ind. Med.* 17: 260-271 (1960).
9. **Hammond, E.C., Selikoff, I.J.:** Relation of Cigarette Smoking to Risk of Death of Asbestos-Associated Disease Among Insulation Workers in the United States, *I.A.R.C. Sci. Pub. No. 8*, pp. 312-317 (1973).
10. **Wagner, J.C., Gilson, J.C., Berry, G., Timbrell, V.:** *Brit. Med. Bull.* 27:71-96 (1971).
11. **Enterline, P.E., Henderson, V.:** *Arch. Evn. Health* 27:312-317 (1973).
12. **McDonald, J.C., McDonald, A.D.:** *Preventive Med.* 6:426-446 (1977).
13. **Meurman, L.O., Kivilioto, R., Hakama, M.:** *Brit. J. Ind. Med.* 31:105-112 (1974).
14. **Baris, Y.I.** *et al: Kanser* 5:1-14, Finland (1975).
15. **McDonald, J.C.** *et al: Arch. Env. Health* 22:677-686 (1971).
16. **Knox, J.F., Doll, R.S., Hill, I.D.:** *Ann. N.Y. Acad. Sci.* 132:526-535 (1965).
17. **Newhouse, M.L.:** *Brit. J. Ind. Med.* 26:294-301 (1969).
18. **Newhouse, M.L., Berry, G., Wagner, J.C., Turock, M.E.:** *Brit. J. Ind. Med.* 29:134-141 (1972).
19. **Peto, J., Doll, R., Howard, S.V., Kinlen, L.J., Lewinsohn, H.C.:** *Brit. J. Ind. Med.* 34:169-173 (1977).
20. **McDonald, J.C.:** Exposure Relationships and Maglignant Mesothelioma, Opening paper for Session V., *Asbestos Symposium*, Johannesburg, So. Africa (October 3-7, 1977).
21. **Newhouse, M.L., Berry, G.:** *Brit. J. Ind. Med.* 33:147-151 (1976).
22. **British Occupational Hygiene Society:** *Ann. Occup. Hyg.* 11:47-69 (1968).
23. **Gross, P.:** *Arch. Env. Health* 29:115-118 (1974).
24. **Gillam, J.D., Dement, J.D., Lemen, R.A.** *et al: Ann. N.Y. Acad. Sci.* 271:336-344 (1976).
25. **McDonald, J.C., Gibbs, G.W., Lidell, F.D.K., McDonald, A.D.:** Mortality after Long Exposure to Cummingtonite-Grunerite. To be published. Abstracted in *Am. Red. Resp. Dis.*
26. **Knox, J.F., Holmes, S., Doll, R., Hill, I.D.:** *Brit. J. Ind. Med.* 25:293-303 (1968).

DOCUMENTATION OF

THRESHOLD LIMIT VALUES

1962

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS

COMMITTEE ON THRESHOLD LIMIT VALUES

Copies of this publication may be obtained from:

Secretary-Treasurer
American Conference of Governmental Industrial Hygienists
1014 Broadway
Cincinnati 2, Ohio

Price per copy $4.00
Make checks payable to American Conference of Governmental Industrial Hygienists

References
1. Sayers, R.R.; Am. Stds. Assn. Z37, No. 9, 1943; Cook, W.A.: Ind. Med. 14, 936, (1945).
2. Pinto, S.S.: Communication to Committee Member (1961).

ARSINE

0.05 ppm (Approximately 0.2 mg/m^3)

The extreme, acute toxicity of arsine is well known; 250 ppm for 30 minutes is fatal to man and 3-10 ppm can cause poisoning symptoms in a few hours (1). Nau (2) reported the conditions of an arsine exposure that indicated the previous limit of 1 ppm was too high. Elkins (3) reported a case of severe, but nonfatal, arsine poisoning that resulted from an exposure averaging 0.5 ppm. Elkins has concluded that 0.05 ppm arsine is not an unreasonable low limit on the basis of a study of chronic arsine exposures of Bulmer, et al. (4). Urinary As varied from 0.7 to 4 mg. in men showing toxic signs of exposure of jaundice and anemia. Assuming 75% of the As is excreted in the urine 1 mg. As/l corresponds to 1.33 mg. intake, or 0.133 mg. As/m^3 air if 10 m^3 air is taken as the average amount of tida air inhaled during a working day. This corresponds to 0.033 ppm arsine, and suppo the recommended limit of 0.05 ppm arsine.

References
1. Henderson, Y., Haggard, H.W.: Noxious Gases, Reinhold Publishing Co., N.Y. (1943).
2. Nau, C.A.: South. Med. J. 41, 341 (1948).
3. Elkins, H.B.: Chemistry of Industrial Toxicology, Wiley & Sons, N.Y. (1959).
4. Bulmer, F.M.R., et al.: J. Ind. Hyg. & Tox. 22, 111 (1940).

ASBESTOS

5 mppcf

Asbestos is a generic term applying to a number of mineral silicates that are incombustible in air and can be separated into filaments. The most widely used in industry is chrysotile, a magnesium silicate from serpentine. Other types include amosite (an iron magnesium silicate) crocidolite (a sodium iron silicate), tremolite (a calcium magnesium silicate) and anthophyllite (also an iron magnesium silicate).

Miller and Sayers (1) showed that intraperitoneal injection of amosite, chrysotile and crocidolite in guinea pigs produced the reaction of an inert dust. Vorwald et al. (2) confirmed this for short fibers (under 3μ) but observed that long fibers produced a fibrous reaction. Continuing unpublished work by Gardner, these workers demonstrated that long fibers (20 microns and above) produced peribronchiolar fibrosis in lower animals, and developed evidence that this resulted from mechanical rather than chemical action. Asbestos dust containing 0.6 per cent fibers longer than 10 microns, in concentrations of 138 mppcf (or 0.8 million "long" fibers per c.f.), was capable of producing experimental asbestosis in guinea pigs. When the concentration was 6.7 per cent fibers over 10 microns, 40 mppcf, (equivalent to 2.7 million "long" fibers per c.f.), the reaction developed in approximately half the time.

That exposure to asbestos is associated with development of a potentially disabling pneumoconiosis in man has been amply demonstrated by industrial experience (3,4,5,6,7,8,9,10,11). The present threshold limit relates to the prevention of asbestosis. It was recommended by Dreessen et al. (8), after study of 541 employees in three asbestos textile plants using chrysotile. Only three

doubtful cases of pneumoconiosis were found in those exposed to dust concentrations under 5 mppcf, whereas numerous well-marked cases were found above 5 mppcf. Counts were from impinger-collected samples in ethyl alcohol and distilled water. Both fibrous and non-fibrous particles were counted, but the latter greatly predominated. While chemical analyses of collected samples of airborne dust corresponded to those of settled dust samples, it is believed that dust counts of particulates by conventional methods can be expected to give only an indirect measure of the risk of asbestosis because of the great relative importance of long fibers.

References

1. Miller, J.W., Sayers, R.R.: Pub. Health Rept. 56, 264 (1941).
2. Vorwald, A. J., Durkan, T.M., Pratt, P.C.: Arch. Ind. Hyg. 3, 1 (1951).
3. Merewether, E.R.A.: J. Ind. Hyg. 12, 198, 239 (1930). Pneumoconiosis Abstracts, 1926-1938, Vol. I, p. 128.
4. Wood, W.B., Gloyne, S.R.: Lancet, Dec. 22, 1934, pp. 1383-1385.
5. Fulton, W.B., Dooley, A., Matthews, J. L., Houtz, R.L.: Penn. Dept. Labor and Ind. Bull. 42 (1935).
6. Lanza, A.J., McConnell, W.J., Fehnel, J.W.: Pub. Health Rept. 50, 1 (1935).
7. Donnelly, J.: J. Ind. Hyg. & Tox. 18, 222 (1936).
8. Dreessen, W.C., DallaValle, J.W., Edwards, T.I., Miller, J.W., Sayers, R.R.: Pub. Health Bull. No. 241. Wash., D.C., (1938).
9. Lynch, M.: Arch. Ind. Health. 11, 185 (1955).
10. Smith, K.W.: Arch. Ind. Health 12, 198 (1955).
11. Cartier, P.: Arch. Ind. Health 11, 204 (1955).

BARIUM (and Compounds)

0.5 mg/m^3

The clinical entity "baritosis" has been reported in the industrial hygiene literature sporadically since 1934 when Leschke (1) described a case with almost fatal outcome in a baryta worker who had apparently inhaled ample quantities. Other reports of industrial exposure to barium compounds with or without exposure to lithopone have described pulmonary nodulation with or without decrease in lung function, such as dyspnea on exertion (2,3). More soluble forms of barium, as the carbonate, oxide and nitrate, tend to be more injurious, particularly acutely. Dusts of barium oxide are considered potential agents of dermal and nasal irritation (4).

The pharmacologic action of barium is well known (5); chief among the actions of barium is its effect on muscle, particularly cardiac, increasing its excitability. Skeletal, arterial, intestinal, and bronchial muscle are all affected by barium. In addition, effects on the hematopoietic system have been noted, as well as on the cerebral cortex.

Fazekas, et al. (6) have reported that subcutaneous injection of an aqueous solution of barium chloride at a dosage of 5 mg/kg caused acute toxicity with death after 2-2.5 hours. Chronic poisoning was achieved by the injection of solutions at 10, 5, and 2 mg/kg. Rabbits in this series were killed at 98 to 193 days. Effects on the central nervous system are described.

The present limit of 0.5 mg Ba/m^3 air was suggested by Hyatt (7), who employed this limit for a number of years at the Los Alamos Laboratories with satisfactory results for the control of exposure to barium nitrate. It is not known what degree of added safety this limit incorporates.

DOCUMENTATION OF THE THRESHOLD LIMIT VALUES

for Substances in Workroom Air

WITH
SUPPLEMENTS FOR THOSE SUBSTANCES
ADDED OR CHANGED
SINCE 1971

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS

Third Edition 1971

3RD PRINTING 1976

While data on the actual concentrations causing acute intoxication are lacking, post event concentrations of 70 to 300 ppm (Morse and Setterlind, fatal cases(11), 5 ppm (Kipling and Fothergill(8)) and 0.5 ppm (Elkins(3)) were reported. When urine samples were analyzed at early stages concentrations of arsenic ranging from 0.5 to 2 mg/liter were the rule, but occasionally much higher values were found.

Bulmer et al.(12) reported a number of cases of chronic poisoning, with severe anemia. Urinary arsenic levels averaged 2.3 mg/1, dropping to 0.66 mg/1 three days later. Greig et al.(13) recorded three relatively mild chronic cases with arsenic in urine levels of 0.5 mg/1.

Since arsenic appears to be excreted rather freely in the urine (Elkins(14)) the levels found in the urine of intoxicated workers could have resulted from inhalations of concentrations below 1 mg/m^3 or 0.25 ppm. The recommended TLV of 0.05 ppm (0.2 mg/m^3) is nearly half the limit of other inorganic arsenic compounds, which are considered substantially less toxic.

Other recommendations: Cook (1945) 1 ppm; Smyth (1956) and Elkins (1959) 0.05 ppm; U.S.S.R. (1966) 0.1 ppm; Czechoslovakia (1969) 0.06 ppm.

References:

1. Henderson, Y., Haggard, H.W.: Noxious Gases, Reinhold, N.Y. (1943).
2. Nau, C.A.: South. Med. J. 41, 341 (1948).
3. Elkins, H.B.: Chemistry of Industrial Toxicology, p. 64, Wiley & Sons, N.Y. (1959).
4. Konsen, J.L., Dodson, V.N.: J. Occ. Med. 8, 540 (1966).
5. Elkins, H.B., Fahy, J.P.: Ind. Med. & Surg. 36, 747 (1967).
6. Teitelbaum, D.T., Kier, L.C.: Arch. Env. Health 19, 133 (1969).
7. DePalma, A.E.: J. Occ. Med. 11, 582 (1969).
8. Kipling, M.D., Fothergill, R.: Brit. J. Ind. Med., 21, 74 (1964).
9. Kambara, T., Nohara, Y., Ikegama, K., Nakamura, T., Kajiwara, T.: J. Sci. Labour (Japan) 42, 454 (1966).
10. Fallentin, B., Frost, J., Grut, A.: Ugeskrift for Laeger 129, 544 (1967).
11. Morse, K.M., Setterlind, A.N.: Arch. Ind. Hyg. & Occ. Med. 2, 148 (1950).
12. Bulmer, F.M.R., Rothwell, H.E., Polack, S.S., Stewart, D.W.: J. Ind. Hyg. & Tox. 22, 111 (1940).
13. Greig, H.B.W., Bradlow, B.A., Harrison, C., Dalton, M.B.: Sou. Af. Med. J. 32, 161 (1958).
14. Elkins, H.B.: Am. Ind. Hyg. Assn. J. 28, 305 (1967).

ASBESTOS (all forms)

5 fibers/ml (longer than 5μ)

Asbestos is a broad term embracing a number of fibrous mineral silicates that differ in chemical composition. The three types of greatest commercial importance are chrysotile, a hydrated magnesium silicate; crocidolite, a sodium iron silicate; and amosite, an iron magnesium silicate. Of these chrysotile is by far the most widely used in industry. Other asbestos minerals include tremolite, anthophyllite and actinite.

That exposure to asbestos is associated with development of a potentially disabling pneumoconiosis in man has been amply demonstrated by industrial experience(1, 2, 3, 4, 5, 6, 7, 8, 9). A threshold limit of 5 mppcf was recommended by Dreessen et al.(6), in 1938 after studying 541 employees in four asbestos textile plants where massive exposures to chrysotile occurred. Only three doubtful cases of pneumonoconiosis were found at the time of the study in those exposed to dust concentrations under 5 mppcf, whereas numerous well-marked cases were found above 5 mppcf. Counts were from impinger-collected samples in ethyl alcohol and distilled water. Both fibrous and nonfibrous particles were counted, but the latter greatly predominated. Although chemical analyses of collected samples of airborne dust corresponded to those of settled dust, it is believed that dust counts of particulates by impinger can be expected to give only an indirect measure of the risk of asbestosis because impinger sampling collects particulates other than asbestos.

A conference on the biologic effects of asbestos(10) in 1965 called attention to the very real probability that the 5 mppcf limit recommended by Dreessen is inadequate to give complete working-life-time protection against all forms of asbestos. Medical data on which the limits had been based were inadequate; more than half of the asbestos workers studied were under 30 years of age and thus provided an insufficient exposure time for asbestosis to develop. Of the 105 workers exposed to <5 mppcf, 82 had worked < 5 years; 101, <10 years; only 4 had >10 years exposure. Seven of 36 workers exposed to 5 - 9.9 years had asbestosis; 3 of 50 workers exposed to 10 - 19.9 mppcf for <5 years had asbestosis(6). Moreover it was a "point-in-time" study; many of the ill were missing and the dead uncounted, hence not considered in the over-all evaluation of the limit.

The asbestos conference(10) further called attention to the rising worldwide rate of increase in lung cancer among asbestos workers, particularly bronchial cancers, and also noted with alarm a widespread incidence of pleural and diffuse mesotheliomas, tumors heretofore overlooked and only recently (1959) associated with exposure to asbestos. The epidemiology of the early cases was especially revealing in pointing out the scope of asbestos exposures; many of the mesothelioma cases had no industrial association, but were "neighborhood" cases or cases traced to users of asbestos. Exposures to asbestos extend far beyond those of miners and millers of asbestos or textile weavers, and include carpenters (sawing asbestos board), insulators and pipe laggers, dockers handling asbestos cargo, brake-lining workers, rubber compounders and several others.

The Committee on Hygienic Standards of the British Occupational Hygiene Society from an evaluation of medical evidence from Great Britain and data from the U.S. Public Health Service Study(6) recommended the following criteria for limiting exposure to chrysotile asbestos assuming a 1% risk of contracting asbestos disease during a 50-year working exposure(11).

Dust Category	Chrysotile Concentration[a] Fibers/ml[b]
Negligible	<0.5
Low	0.5 - 2.0
Medium	>2 - 10
High	>10

a) Averaged during a three-month period
b) Greater than 5μ in length

From these criteria, a limit of 100 fibers/ml-years was proposed, hence a limit of 2 fibers/ml averaged over a 50-year period.

In arriving at an asbestos limit based on American experience and considerations applicable to the American industrial scene, the following facts predominated. Recent evaluation of the health experience in asbestos plants indicated that the 5 mppcf limit was not sufficiently low to protect workers exposed for 30 years, a period rarely exceeded in America. Balzer and Cooper (12) supported this review in a report of asbestosis occurring among insulation workers from levels that were deemed highly unlikely to have exceeded a time-weighted average of 5 mppcf. A retrospective investigation of the association between lung cancer in asbestos workers and smoking by Selikoff et al.(13) revealed that asbestos neoplasias were strongly associated with smokers.

From a study of asbestos fiber concentrations in six different industries in 32 plants, Ayer et al.(14) found average counts above 5 fibers/ml in 61 departments, and below 5 in 146. The highest counts generally were found in insulation, textile and friction plants. Lower levels were obtained in shingle and mill board plants and cement pipe plants, and the lowest in packing and rubber plants.

Williams and associates(15) compiled data from two Pennsylvania asbestos textile plants, going back to 1930 in one plant and 1948 in the other. Even though exposures for the most part were below 5 mppcf and in many cases below 2 mppcf, 64 cases of asbestosis were reported from the two plants. The authors concluded that a limit of 3 mppcf would provide inadequate protection and even the 2 mppcf TLV might not be substantiated.

An Ad Hoc select review committee of the Bureau of Occupational Safety and Health(16) proposed a standard of 6 fibers/ml, longer than 5 μ. This concentration has been found equivalent to 1 mppcf by the conventional light field impinger count.

Inasmuch as the particles counted by the impinger procedure often include extraneous material, a limit of 1 mppcf might be unrealistic in processes where dust other than asbestos was present, even in relatively low concentrations. A TLV of 5 fibers, longer than 5 micra (μ), per cc, as determined by collection on membrane filters and counted using phase-contrast illumination at 430X magnification(17) is recommended.

On present evidence, this interim standard should affort protection against asbestosis and reduce to an acceptably low risk the development of neoplasms. Complete elimination of risk cannot be assured at the present time from this or any other potential neoplastic agent, because of incomplete understanding of dose-response relationships of such agents.

Although some authorities believe that different varieties of asbestos have different biological effects, at this time there appears to be insufficient information to justify differentiating among them in establishing the TLV.

References:

1. Merewether, E.R.A.: J. Ind. Hyg. 12, 198, 239 (1930). Pneumoconiosis Abstracts, Vol. I, p. 128, (1926-1938).
2. Wood, W.B., Gloyne, S.R.: Lancet, pp 1383-1385, (Dec. 22, 1934).
3. Fulton, W.B., Dooley, A., Matthews, J.L., Houtz, R.L.: Penn. Dept. of Labor & Industries Bull. #42 (1935).
4. Lanza, A.J., McConnell, W.J., Fehnel, J.W.: Pub. Health Rep. 50, 1 (1935).
5. Donnelly, J.: J. Ind. Hyg. & Tox. 18, 222 (1936).
6. Dreessen, W.C., DallaValle, J.W., Edwards, T.I., Miller, J.W., Sayers, R.R.: Pub. Health Bull. #24, Washington, D.C., (1938).
7. Lynch, M.: Arch. Ind. Health 11, 185 (1955).
8. Smith, K.W.: Arch. Ind. Health 12, 198 (1955).
9. Cartier, P.: Arch. Ind. Health 11, 204 (1955).
10. Biologic Effects of Asbestos, H.E. Whipple, ed.: Ann. N.Y. Acad. Sciences 132, Art. 1 (1965).
11. Brit. Occ. Health Soc.: Report of Committee on Hygiene Standards; "Hygiene Standards for Chrysotile Asbestos Dust" (Dec., 1967).
12. Balzer, J.L., Cooper, W.C.: Ind. Hyg. News Report (Dec. 1967).
13. Selikoff, I.V., Hammond, E.C., Churg, V.: J. Am. Med. Assn. 204, 104 (1968).
14. Ayer, H.E., Oster, C.V., Ligo, R.N., Weidner, R.B., Raymond, H.W., Knight, R.M.: To be published in Am. Ind. Hyg. Assn. J.
15. Williams, H.L., Baier, E.J., Thomas, A.W.: To be published.
16. Review Committee on Asbestos, Bureau of Occupational Safety and Health: Preliminary Draft, (1970).
17. Ayer, H.E., Lynch, J.R., Fanney, J.H.: Ann. N.Y. Acad. Sciences 132, Art. 1, p. 274 (1965).

ASPHALT (PETROLEUM) FUMES

5 mg/m^3

Asphalt is a native mixture of hydrocarbons which occurs as an amorphous, brownish black solid or semisolid(1, 2). It results from evaporation of the lighter hydrocarbons from petroleum and partial oxidation of the residue. Petroleum asphalt thus is to be differentiated from tar or pitch, which results from the destructive distillation of coal. Asphalt fumes arise in the course of manufacture or from the secondary heating of asphalt. Thus asphalt fume exposure occurs not only in association with its manufacture but also in road building, roofing, and in the coating of construction metals.

Animal inhalation studies have not yielded sufficient evidence of asphalt-induced lung cancer, and only limited investigation has been done on the chemical properties and the metabolic changes

Documentation of Threshold Limit Values

1966

REVISED EDITION

COMMITTEE ON THRESHOLD LIMIT VALUES

Copies of this publication may be obtained from:

Secretary-Treasurer
American Conference of Governmental Industrial Hygienists
1014 Broadway
Cincinnati, Ohio 45202

Price per copy $4.50
Make checks payable to American Conference of Governmental Industrial Hygienists

References:

1. Henderson, Y., Haggard, H.W.: Noxious Gases, Reinhold Publishing Co., N.Y. (1943).
2. Nau, C.A.: South. Med. J. 41, 341 (1948).
3. Elkins, H.B.: Chemistry of Industrial Toxicology, Wiley & Sons, N.Y., (1959).
4. Bulmer, F.M.R., et al.: J. Ind. Hyg. & Tox. 22, 111 (1940).

ASBESTOS

5 mppcf

Asbestos is a generic term applying to a number of mineral silicates that are incombustible in air and can be separated into filaments. The most widely used in industry is chrysotile, a magnesium silicate from serpentine. Other types include amosite (an iron magnesium silicate), crocidolite (a sodium iron silicate), tremolite (a calcium magnesium silicate) and anthophyllite (also an iron magnesium silicate).

Miller and Sayers (1) showed that intraperitoneal injection of amosite, chrysotile and crocidolite in guinea pigs produced the reaction of an inert dust. Vorwald et al. (2) confirmed this for short fibers (under 3μ) but observed that long fibers produced a fibrous reaction. Continuing unpublished work by Gardner, these workers demonstrated that long fibers (20 microns and above) produced peribronchiolar fibrosis in lower animals, and developed evidence that this resulted from mechanical rather than chemical action. Asbestos dust containing 0.6 per cent fibers longer than 10 microns, in concentrations of 138 mppcf (or 0.8 million "long" fibers per cu. ft.), was capable of producing experimental asbestosis in guinea pigs. When the concentration was 6.7 per cent fibers over 10 microns, 40 mppcf (equivalent to 2.7 million "long" fibers per cu. ft.), the reaction developed in approximately half the time.

That exposure to asbestos is associated with development of a potentially disabling pneumoconiosis in man has been amply demonstrated by industrial experience, (3,4,5,6,7,8,9,10,11). The present threshold limit was recommended by Dreessen et al. (8), after study of 541 employees in three asbestos textile plants using chrysotile. Only three doubtful cases of pneumoconiosis were found in those exposed to dust concentrations under 5 mppcf, whereas numerous well-marked cases were found above 5 mppcf. Counts were from impinger-collected samples in ethyl alcohol and distilled water. Both fibrous and nonfibrous particles were counted, but the latter greatly predominated. While chemical analyses of collected samples of air-borne dust corresponded to those of settled dust samples, it is believed that dust counts of particulates by conventional methods can be expected to give only an indirect measure of the risk of asbestosis because of the great relative importance of long fibers.

References:

1. Miller, J.W., Sayers, R.R.: Pub. Health Rep., 56, 264 (1941).
2. Vorwald, A.J., Durkan, T.M., Pratt, P.C.: Arch, Ind. Hyg. 3, 1 (1951).
3. Merewether, E.R.A.: J. Ind. Hyg., 12, 198-239 (1930). Pneumoconiosis Abstracts, 1926-1938, Vol. I, p. 128.
4. Wood, W.B., Gloyne, S.R.: Lancet, Dec. 22, 1934, pp. 1383-1385.
5. Fulton, W.B., Dooley, A., Matthews, J.L., Houtz, R.L.: Penn. Dept. Labor and Ind. Bull. 42 (1935).
6. Lanza, A.J., McConnell, W.J., Fehnel, J.W.: Pub. Health Rep. 50, 1 (1935).
7. Donnelly, J.: J. Ind. Hyg. & Tox., 18, 222 (1936).
8. Dreessen, W.C., DallaValle, J.W., Edwards, T.I., Miller, J.W., Sayers, R.R.: Pub. Health Bull. No. 241, Washington, D.C., 1938.
9. Lynch, M.: Arch. Ind. Health, 11, 185 (1955).
10. Smith, K.W.: Arch. Ind. Health 12, 198 (1955).
11. Cartier, P.: Arch. Ind. Health 11, 204 (1955).

Substance	PPM*	Approx. Mg. per. Cu. M.†
Cellosolve (2-ethoxy-ethanol)	200	740
Cellosolve acetate (2-ethoxyethyl acetate)	100	540
Chlorine	1	3
(x) Chlorine trifluoride	0.1	0.4
Chlorobenzene (monochlorobenzene)	75	350
Chloroform (trichloromethane)	100	490
1-Chloro-1-nitropropane	20	100
Chloroprene (2-chloro-1,3-butadiene)	25	90
Cresol (all isomers)	5	22
Cyclohexane	400	1,400
Cyclohexanol	100	410
Cyclohexanone	100	400
Cyclohexene	400	1,350
Cyclopropane	400	690
(x) Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240
(x) Diborane	0.1	0.1
o-Dichlorobenzene	50	300
Dichlorodifluoromethane	1,000	4,950
1,1-Dichloroethane	100	400
1,2-Dichloroethylene	200	790
Dichloroethyl ether	15	90
Dichloromonofluoro-methane	1,000	4,200
1,1-Dichloro-1-nitroethane	10	60
Dichlorotetrafluoro-ethane	1,000	7,000
Diethylamine	25	75
(x) Difluorodibromomethane	100	860
(x) Diisobutyl ketone	50	290
Dimethylaniline (N-dimethylaniline)	5	25
Dimethylsulfate	1	5
Dioxane (diethylene dioxide)	100	360
Ethyl acetate	400	1,400
Ethyl alcohol (ethanol)	1,000	1,900
Ethylamine	25	45
Ethylbenzene	200	870
Ethyl bromide	200	890
Ethyl chloride	1,000	2,600
Ethyl ether	400	1,200
Ethyl formate	100	300
Ethyl silicate	100	850
Ethylene chlorohydrin	5	16
(x) Ethylenediamine	10	30
Ethylene dibromide (1,2-dibromoethane)	25	190
Ethylene dichloride (1,2-dichloroethane)	100	400

Substance	PPM*	Approx. Mg. per. Cu. M.†
(x) Ethylene imine	5	9
Ethylene oxide	100	180
Fluorine	0.1	0.2
Fluorotrichloromethane	1,000	5,600
Formaldehyde	5	6
Gasoline	500	2,000
Heptane (*n*-heptane)	500	2,000
Hexane (*n*-hexane)	500	1,800
Hexanone (methyl butyl ketone)	100	410
Hexone (methyl isobutyl ketone)	100	410
(x) Hydrazine	1	1.3
(x) Hydrogen bromide	5	17
Hydrogen chloride	5	7
Hydrogen cyanide	10	11
Hydrogen fluoride	3	2
(x) Hydrogen peroxide, 90%	1	1.4
Hydrogen selenide	0.05	0.2
Hydrogen sulfide	20	30
Iodine	0.1	1
Isophorone	25	140
(x) Isopropylamine	5	12
Mesityl oxide	50	200
Methyl acetate	200	610
(x) Methyl acetylene	1,000	1,650
Methyl alcohol (methanol)	200	260
Methyl bromide	20	80
Methyl cellosolve (2-methoxyethanol)	25	80
Methyl cellosolve acetate (ethylene glycol monomethyl ether acetate)	25	120
Methyl chloride	100	210
Methylal (dimethoxy-methane)	1,000	3,100
Methyl chloroform (1,1,1-trichloroethane)	500	2,700
Methylcyclohexane	500	2,000
Methylcyclohexanol	100	470
Methylcyclohexanone	100	460
Methyl formate	100	250
(x) Methyl isobutyl carbinol (methyl amyl alcohol)	25	100
Methylene chloride (dichloromethane)	500	1,750
Naphtha (coal tar)	200	800
Naphtha (petroleum)	500	2,000
Nickel carbonyl	0.001	0.007
(x) *p*-Nitroaniline	1	6
Nitrobenzene	1	5
Nitroethane	100	310
Nitrogen dioxide	5	9
Nitroglycerin	0.5	5
Nitromethane	100	250
2-Nitropropane	50	180
Nitrotoluene	5	30

Substance	Mg. per Cu. M.‡
Tellurium	0.1
Tetryl (2,4,6-trinitrophenylmethylnitramine)	1.5
(x) Titanium dioxide	15
Trichloronaphthalene	5
Trinitrotoluene	1.5
Uranium	
(soluble compounds)	0.05
(insoluble compounds)	0.25
(x) Vanadium	
(V_2O_5 dust)	0.5
(V_2O_5 fume)	0.1
Zinc oxide fumes	15
(x) Zirconium compounds (as Zr)	5

‡ Milligrams of dust, fume, or mist per cubic meter of air.
(x) These values appeared on the tentative list for 1955.

Radioactivity: For permissible concentrations of radioisotopes in air, see "Maximum Permissible Amounts of Radioisotopes in the Human Body and Maximum Permissible Concentrations in Air and Water," Handbook 52, U. S. Department of Commerce, National Bureau of Standards, March, 1953. In addition, see "Permissible Dose from External Sources of Ionizing Radiation," Handbook 59, U. S. Department of Commerce, National Bureau of Standards, Sept. 24, 1954.

Mineral Dusts

Substance	MPPCF§
Aluminum oxide	50
Asbestos	5
Dust (nuisance, no free silica)	50
Mica (below 5% free silica)	20
Portland cement	50
Talc	20
Silica	
high (above 50% free SiO_2)	5
medium (5 to 50% free SiO_2)	20
low (below 5% free SiO_2)	50
Silicon carbide	50
Slate (below 5% free SiO_2)	50
Soapstone (below 5% free SiO_2)	20
Total dust (below 5% free SiO_2)	50

§ Millions of particles per cubic foot of air.

TENTATIVE VALUES

The following values are suggested for further consideration before being presented for adoption as established values.

Substance	PPM‖	Approx. Mg. per Cu. M.¶
Allyl chloride	5	15
ANTU (alpha-naphthylthiourea)		0.3
(x) Butyl mercaptan	10	35
(x) Calcium arsenate		0.10
Chlorinated camphene, 60%		0.5
Chlorobromomethane ($Cl\ Br\ CH_2$)	400	2,100
Chlorodiphenyl (54% chlorine)		0.5
Chloropicrin	1	7
(x) D.D.T. (2,2-bis-[p-chlorophenyl)-1,1,1-trichloroethane)		1
Decaborane ($B_{10}H_{14}$)	0.05	0.3
2, 4-Diisocyanotoluene	0.1	0.7
Dinitrobenzene		1
Ethyl acrylate	25	100
(x) Ethyl mercaptan	250	640
Ferbam (ferric dimethyldithiocarbamate)		15
Fluoroacetates		0.1
(x) Furfural	5	20
(x) Furfuryl alcohol	50	200
HETP (hexaethyl tetraphosphate)		0.1
(x) Lead arsenate		0.15
Methyl acrylate	10	35
(x) Methyl mercaptan	50	100
Nicotine		0.5
Nitric acid	10	25
Pentaborane (B_5H_9)	0.01	0.03
(x) Perchloromethyl mercaptan	0.1	0.8
Pyrethrum		2
Rotenone		5
Strychnine		0.15
Tetrahydrofuran	200	590
Thiram (tetramethylthiuram disulfide)		5
Thallium (soluble compounds)		0.15
Warfarin (3-[α-acetonylbenzl]-4-hydroxycoumarin)		0.5

‖ Parts of vapor or gas per million parts of air by volume.
¶ Approximate milligrams of dust, fume, or mist per cubic meter of air.
(x) These values appeared on the tentative list for 1955.

Beryllium: During the past few years several papers have appeared in the literature which report a limit of 2γ per cubic meter of air for beryllium. Among these are the paper by Van Ordstrand, H. S.: Berylliosis, *A.M.A. Arch. Indust. Hyg.* 10:232-234 (Sept.) 1954 and one by Sterner, J. H., and Eisenbud, M.: Epidemiology of Beryllium Intoxication, *A.M.A. Arch. Indust. Hyg.* 4:123-151 (Aug.) 1951. Conflicting data from industrial experience have caused the Committee to postpone the suggestion of a threshold limit for this material. It is apparent that more epidemiologic work is needed for the establishment of a definite value.

William L. Ball, H. E. Stokinger, W. H. Reinhart, A. J. Vorwald
L. T. Fairhall, Ralph S. Smith, S. D. Silver, Allan L. Coleman, *Chairman*

Printed and Published in the United States of America