cance, both could have been due easily to chance alone.

A final word is in order concerning the methods for developing data by which the environment is described—the conditions of exposure. As much variability can be, and is, encountered with this function as with the methods for laboratory experimentation and in-plant clinical examinations. The accuracy and reliability of the analytical techniques, the relation of the time and site of sampling to the true exposure, the presence of other agents which might modify the single action of the toxin under study are some of the many factors which must be critically examined in the light of their usefulness for correlation with a given set of experimental or clinical findings.

It is obvious that there is no single method or pattern of methods which can satisfy the varied requirements for establishing threshold limits. It is equally obvious that even though rigid standards were described which would satisfy a discriminating jury of scientists, the available data for establishing threshold limits for all but a very few substances would fail to satisfy such limits. The real use for threshold limits, as a guide for industry in the control of exposures and as a measure for action by governmental agencies, demands a continuing improvement in the quality and quantity of the methods by which truly valid criteria may be achieved.

Prepared Discussion

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DR. STERNER has discussed the great difficulties attendant on developing adequate data for threshold limits, the many imponderables in their interpretation, and their unsatisfactory and necessarily always incomplete nature. All these considerations should certainly be thoughtfully considered and strongly stressed, because errors in judgment cannot be afforded. But lest these many considerations seem so formidable to many potential investigators as to prevent their needed contributions (which was far from Dr. Sterner's intention) or depress the more experienced contributors, it should be immediately pointed out that there are at least two practical and very helpful means of overcoming certain deficiencies inherent in the basic data. One is the safety factor, the other, the periodic re-evaluation of the threshold limit values. The safety factor has been built into most of the values in the threshold limits list.* The factors 2, 5, 10 or even greater have been applied to some values. There are, of course, some notable exceptions, such as the present value for trichloroethylene, for which the threshold limit is the absolute ceiling, but generally such instances are rare. In general, the greater the uncertainty in the data's applicability to human industrial exposure, the larger the factor applied. This lowering of the limit value by an arbitrary safety factor may at times provoke some controversy, because now the value becomes one of opinion, not fact. Be that as it may, the safety factor incorporated in the air standards gives increased assurance of safety to many doubtful values.

The re-examination of the listed values by the committee provides annually for readjustment of all values, whatever their sanctity, upon submission to the committee of new and experimentally supported findings. Repeated scrutiny and re-appraisal of this sort can lead finally only to assignment of safe values on which complete reliance can be placed. The committee welcomes all such information.**

Need for more Data

IN THIS CONNECTION another point implied in Dr. Sterner's discussion should be strengthened—namely, the need for more data substantiating the choice of safe exposure levels based on industrial experience. Much useful information is undoubtedly in the files of many plants. Indication of this was the fine evidence on six industrial sub-

*The incorporated safety factor in the threshold limit values, although added at times because of uncertainty in the value as related to human exposure, often actually provides an appreciable margin of safety. For this reason the correctness of the term "threshold limit" may be questioned; it might more properly be replaced with "air hygiene standard."

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stances derived from many years of plant experience that came to light last year at these meetings from the presentation of Herbert J. Weber.[1] Others should have similar material that should be brought to the attention of the Threshold Limits Committee. Like Weber's material, all of it need not be novel or presented to show need for changing existing limits; equally valuable are data confirming existing limits. As never before, interest in the value of the control of industrial environments is being shared by management generally. Greater numbers of industrial hygienists than ever before are being engaged by industry. Is it too much to hope that meetings such as these will orient the thinking of properly placed industrial hygienists to secure much needed plant information to aid in the choice of safe limits of human exposure?

The type of information needed may be listed as follows: (1) Air concentrations should be determined for the substances under study through a complete cycle of plant operations and with reasonable regularity in order to obtain a true picture of the range and fluctuations of exposure. (2) The data should have good accuracy. (3) The observations should be carried out over a reasonable period of time—a minimum of five years. (4) The air concentration data should be correlated with a good medical program. A pattern for such work is that of Dr. Sterner's 10-year study of workers exposure to butyl alcohol.[2]

There is a real need for more data based on industrial experience. The often-heard statement "the threshold limits are nothing but educated guesses" unquestionably reflects the wish at least that more data be firmly based on industrial experience to substantiate the choice of limits. As a member of the Threshold Limits Committee, I was concerned over the statement and took the trouble to review each substance in the threshold limit list for 1955 as to the basis for choice of the level. The results are shown in Table I. It is possible that everyone would not arrive at precisely the same figures, but I believe that their magnitude would not be much altered. Although the table shows that the educated guesses account for a relatively small number, it does confirm the often expressed feeling of the need for more solidly based levels. Table I shows a number

TABLE I.
BASIS FOR CHOICE OF THRESHOLD LIMIT VALUE*

Study Type	No. of Listings	Percent Total Listings (223)
Animal	94	42
Industry	51	23
Animal & Industry	23	10
Man	25	11
"Educated Guess"	21	9
Animal & Man	9	4
Source uncertain	3	1

*Based in part on COOK, W. A., *Ind. Med.* 14:936, 1945, and from documented material of Threshold Limits Committee A.C.G.I.H. 1953-1955.

of other interesting facts: (1) that most of the values have some sort of scientific basis; (2) that each level has been documented either by Warren A. Cook,[3] or by the Committee on Threshold Limits; (3) that the values based on animal experiments account for the largest number, 42%; but (4) that values having some industrial basis account for 1/3 of the total.

The values ascribed to the "man" category arise from two sources—that of Nelson, et al.[4] and those more recent publications of the Dow Chemical workers, Irish, Rowe, Spencer, Adams et al.

The "Educated Guess"

A FEW WORDS should be said in defense of the "educated guess." A review of the values described as guesses indicates in the instances in which sound information has later become available that the "guess" was remarkably good. Two prominent examples only will suffice—hydrogen fluoride and uranium. A safe exposure level for hydrogen fluoride was set at 3 ppm on the very limited evidence supplied by a study in animals by Ronzani in 1909.[5] Last year a report[6] culminating many years of study of fluoride exposure in the aluminum industry, involving thousands of air and urine analysis for fluoride and studies of roentgenographic changes in bone, showed without question that air levels double the accepted limit gave rise to perceptible changes in bone in only a few individuals, and only after many years of exposure, thus validating the wisdom of this "educated guess."

In the case of uranium, an engineering bench-mark had to be "guessed" at early in the days of the Manhattan Project. After a

review of the quite limited animal data on uranium then available, Dr. Stafford Warren suggested that the "safe" exposure level for uranium be the same as that for lead, 0.15 mg/cu.m. After $500,000 and many years had been spent in research, the safe levels of exposure to uranium compounds were found to bracket this value very closely.

Levels for Cancerigens

THERE is still one group of substances for which some method should be devised for establishing safe air standards—the industrial cancerigens. How shall we establish the limits for this type of substance? Thus far the question has been sidestepped completely. As a result, with one exception, nickel carbonyl, limits taking into consideration potential cancerigenicity have not been assigned. Several industrial substances are known or suspected cancerigens; many more are suspect on the basis of animal experiments. As a suggested method of approach, the following is offered: To the level judged safe for other types of systemic injury add a safety factor for carcinogenicity. The magnitude of the safety factor is suggested to be from 100 to 500. This provides at least a second power of 10, which, from the well-known dosage-response hypothesis, provides at least a fourfold longer interval before effects may be expected to occur, or conversely at least a response with ¼ the intensity. This manner of approach has been used for nickel carbonyl. A tentatively safe level for systemic effects from repeated daily exposure has been set at 0.1 ppm; one-hundredth this level, or 0.001 ppm was set for nickel carbonyl on the basis that nickel poisoning gives rise to a substantial increase in the incidence of lung cancer. It is realized that unfortunately the safe limits for all industrial cancerigens cannot be so readily resolved. This is especially true of dye intermediates, such as benzidine and naphthyl amines whose major route of entry is not commonly via the lungs but through the skin and gastrointestinal tract. These are laundry and protective equipment problems not solvable by air control.

There are undoubtedly substances to which the suggested procedure may not strictly apply, but imperfect as it may be, the suggested method is felt to be a step in the right direction and serves better to curb exposures to industrial carcinogens than considering the problem too difficult to cope with at the present time.

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Engineering and Chemical Application of Standards

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THE WHY AND HOW of threshold limits for air contaminants have been discussed by the preceding speakers. The logical next and final consideration is the use or application of these limits in preventing occupational diseases, in avoiding complaints from exposed employees, in maintaining employee efficiency, and in promoting good housekeeping.

To engineers engaged in industrial hygiene, threshold limits provide the reference line or bench mark upon which all considerations and calculations for the control of air contamination are based. It is characteristic of engineers and of others in the physical sciences to want to reduce to numbers the problems with which they deal, because only then can they be attacked in a precise man-