CHAPTER 8

PRINCIPLES AND USE OF STANDARDS OF QUALITY FOR THE WORK ENVIRONMENT

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INTRODUCTION

Rationale

Total removal of all potentially harmful agents from the work place is the only absolute method of assuring worker safety and health. Since this optimum is not always possible, exposure to potentially toxic substances is unavoidable. Accordingly, it has become necessary to define quantitatively which exposure levels are *not* attended by a risk to the worker's health or well-being.

Basic Underlying Principles

An understanding of the dose-response relationship (see Chapter 7) is a basic determinant of the feasibility of such standards. In brief, all chemical agents cause biological response as a function of the quantity absorbed and the period of time over which such absorption occurs. Thus, there should be a dose (concentration and time dependent) which does not exceed the capability of the organism to metabolize, detoxify or excrete such compounds. This dose is usually referred to as a "no effect" level.

The "no effect" level — is a puristic concept because there is always some biological or chemical alteration when the organism encounters some exogenous material.[1, 2] Whereas in the United States it is clearly understood that such responses are not deleterious *per se*, in the Soviet Union this is not explicitly recognized. Nevertheless, in the United States a "no effect" level is implied to be one which does not produce any deleterious or undesirable effect upon human health and well-being or overload the normal protective mechanisms of the body.[2]

Thus a biological accommodation, e.g., a non-specific alteration in brain waves, a decreased serum catalase (an enzyme normally present in the body far beyond stress demands), is seen as probably not having immediate or long-term effect on health. Such changes are not deleterious in and of themselves. By contrast, although exposure to H_2S at concentrations of 30-50 ppm produces no changes other than self-limited eye irritation. such concentrations are, in normal circumstances. unacceptable. This is in keeping with the WHO* definition of health which considers any encroachment upon human well-being as being ill health and, therefore, undesirable.

Problems in Definition of "No Effect Level"

It can be seen that there may be profound differences of opinion as to what constitutes a "no effect" level. The preponderant opinion in the United States holds that slight deviations within homeostatic limits of biological change are not deleterious.[2]. All necessary life processes required by living organisms are associated with perturbations of a steady state. Thus the basic processes of digestion and absorption are associated with considerable fluxes of, e.g., electrolytes, lipids, proteins, etc., at concentrations which deviate from those found between meals. With each eyelid flicker there are attendant electrical discharges along multiple nerve pathways that previously were essentially quiescent. Therefore, it should be apparent that for all bodily functions there are constant deviations from a "steady state"; such represent necessary accommodative change to environmental alteration in its broadest sense.

While such generalizations are useful, the problem becomes more difficult when one attempts to define the actual limits beyond which change becomes deleterious. Though practically *any* change is considered as being potentially detrimental by the U.S.S.R., it becomes difficult to reconcile this position with the concept of a normal range associated with homeostasis. On the other hand, the question might well be asked whether the accumulated energy expenditures required by accommodation over a lifetime do not contribute to the long-term depletion of life forces which might accelerate the process of aging.

In the strictest sense a "no effect" level does not exist; however, for operational purposes the range of biological response which exceeds homeostatic limits must be ascertained. The problems of defining the effect such stresses (within homeostatic limits) may have over a long-term should be appreciated.

Other Variables Influencing the Use of Workroom Air Quality Standards

Work-rest cycle. All quality standards make certain assumptions regarding the work-rest cycle. Basically, most standards currently utilized in the United States imply an 8-hour day within a 40-hour week.[3] Thus, each work period is followed usually by a 16-hour non-exposed period, during which restituting processes (e.g., detoxification, excretion) occur. Where more prolonged work exposure periods occur, the possibility of a greater total dose being absorbed as well as less time being available for restitution make application of the usual quality standards inappropriate. With deviations from the usual work-rest cycles (e.g., as with continuous exposure in submarines or space capsules), other environmental quality status standards must be applied.

*World Health Organization

Worker Health Status. The standards utilized depend upon an essentially healthy work force. This stems from the fact that persons with a compromised function or pathological condition may not be capable of dealing with absorbed chemicals in the expected manner. Accordingly, such individuals may not be able to completely excrete each day's burden of an absorbed agent; this can lead to a progressive accumulation of such materials.

Adverse Climate Conditions. Since adverse climate conditions place an accommodative burden upon an individual, the additional work involved in accommodating to occupational stressors may be excessive. Accordingly, in such circumstances quality standards may require modifications reflecting such additional physiologic loadings.

Special Genetic and Biological Susceptibility. Because of genetic and biological factors (e.g., glucose-6-phosphate dehydrogenase or serum antitrypsin deficiencies) specific to some few (i.e., 5-10%) individual workers, these workers may possess an undue susceptibility to agents found in the work environment. It is necessary to detect the presence of such unusual persons at special risk prior to work exposure, since quality standards are designed for the normal person and do not apply to special risk workers.[4]

Implications of the Premises Underlying Quality Standards

It becomes immediately apparent that quality standards cannot be utilized without a full understanding of the foregoing premises concerning 1) the work-rest cycle, 2) worker health status, 3) climatic conditions and 4) special susceptibilities. In addition, their use requires concomitant use of adequate environmental monitoring and medical surveillance. The former stems from the need to document the fact that these limits are not being exceeded; the latter requirement, to determine that persons with pathologic or biologic deviations are not exposed (see Chapter 17).

PRINCIPLES FOR DEVELOPING WORKROOM AIR QUALITY STANDARDS

Extrapolation by Chemical Analogy

A. *Principle*. When dealing with a new chemical, animal or human toxicity data are usually unavailable. Therefore, the prevailing principle is that the quality of response of a chemical may be assumed to be analogous to that produced by similar substances. Chemicals that are structurally similar should produce a similar biological response. Thus, as a first approximation, some *estimate* of toxic potential can be obtained. Obviously, the use of such assessments, since they are not absolute predictors of qualitative effects, may be dubious for prediction of quantitative response. Nevertheless, as of 1968, 24% of all Threshold Limit Values published by the American Conference of Governmental Industrial Hygienists were based upon analogy.[5]

B. *Limitations*.

(1) Inconsistency of qualitative effect: Not infrequently one compound in a chemical family of compounds will respond in a totally atypical manner when compared with others of that family. Accordingly, some risk may be attached to predictions of safety or toxicity based upon chemical analogy.

(2) Inconsistency of quantitative effect: as fraught with risk as is prediction of qualitative risk on the basis of chemical analogy, estimating quantitative effect is even more hazardous.

Animal Experimentation

Principles and Purposes. Before workers are exposed to any chemical agents in the workplace, it is advisable to know the toxic effect such materials possess. On this basis one can design the protective measures to protect workers and deal with medical problems caused by such materials. However, in the case of new chemicals, there is often little or no information upon which to act. Accordingly, an important method of developing such new information utilizes animal experimentation.

In some cases clinical experience does exist, but it is often fragmentary, and rarely provides the detailed information needed concerning the metabolites produced following chemical absorption. Data on metabolites is useful in estimating the degree of absorption of substances. Experimentation with an animal host which responds to substances in a manner similar to man can provide such information.

The design of animal experiments should reflect the conditions of industrial usage of the substance in question. Since agents encountered in the workplace may act systemically or locally following skin or mucous membrane exposure, skin testing for possible absorption and systemic toxicity, primary irritation or sensitization is indicated. Exposure of animals to vapors, mists, aerosols or gases for determination of pulmonary effects and uptake or systemic toxicity is extremely relevant to the industrial milieu. By contrast, experiments utilizing gastro-intestinal or subcutaneous absorption are less frequently used except for range-finding toxicity purposes.

Difficult questions revolve about the problems of extrapolation of animal information to man. As a rule, it is desirable to seek toxicological information derived from more than one animal species wherever possible. Quite frequently various species respond in differing fashions qualitatively and quantitatively. Since no one species consistently reacts as does man, one can never predict which species is most like man. Accordingly, it is an operating principle, until otherwise demonstrated, that man should be considered as responding as does the most sensitive animal species; design of control programs should be developed from that point of departure.

Another important factor concerns the number of animals of any one species which are put to test. Here again, because even within any one group of animals, biological individuality will operate, enough animals must be tested. Thus, one attempts to ensure, within a reasonable degree of probability, that even the most sensitive of the group will be tested. In this regard, statistical techniques can be utilized with a view toward determining which confidence limits attend upon animal population size choice.

One last consideration relates to dose ranges used in such experiments. Obviously, a wide range of doses is useful for different purposes. The large doses help force the question, "toxic or non-toxic?" while also providing clearcut answers as to the specific organs susceptible to damage. Likewise, a lower range of doses must be used to give a clearer estimate of thresholds of response.

Criteria of Response — Organ Change. While gross changes in structure clearly delineate the bodily organ at risk of damage, such data are of limited usefulness. This follows since all control measures must be designed so as to prevent any serious, irreversible damage. Thus, while such bodily changes delineate serious responses, satisfactory control is achieved only when exposure prevents even a minimal alteration beyond the homeostatic range. Accordingly, more important data derive from functional changes rather than pathological organ alteration.

Functional Response — Biochemical Changes. Detection of altered organ function occurring prior to structural change provides the organism with greater probability of avoiding permanent damage. Such functional changes are frequently expressed when organs of detoxification produce some metabolic alteration of the absorbed chemical agent. Insofar as such organ of detoxification is not presented with an amount of chemical which does not exceed its detoxification rate, it can continue to cope with such chemical exposures. Experimentation should be designed to define such rate limits in terms of what represents both excess loadings as well as those burdens with which the organism can successfully deal. Especially important is definition of the "break point" in detoxification rates. Such experiments help define the safe "dose"; in addition, quantitative biochemical indicators of over-exposure may also be delineated. As an example of this, one can assay how much absorption of an organo phosphorous pesticide is safe in terms of depression of red cell acetylcholine esterase, or how much lead exposure has occurred by estimation of urinary coproporphyrin or delta aminolevulinic acid. Likewise, measurement of the metabolites of trichloroethylene, e.g., trichloracetic acid, provides useful indicators of the existence and degree of absorption of that solvent.

Neurophysiologic Response. Recently, changes in nervous system function have been studied extensively as a parameter of toxic or subtoxic exposure. Largely as a result of Russian studies, investigation of neurofunctional response has been considered as possibly indicating early change. Where changes in neurologic function impair higher functions, e.g., alertness, cognition, such alterations have obvious industrial implications as regards safety and performance adequacy. However, the relation of certain measurements, e.g., nerve chronaxie, to occupational exposure is problematic. Nevertheless, such studies of higher nervous function increasingly have been undertaken to delineate man's response to his occupational environment.

Other types of response:

(1) Carcinogenesis: Obviously, given the serious implications of occupationally induced cancer, studies designed to detect such a change are of the utmost importance.

Here, the problems of dose-response relationships become extremely complex, since definition of a threshold of response is problematic. Accordingly, testing here is directed largely toward defining whether such a hazard exists; the use of animal experiments for establishing operational control is directed mainly toward defining the necessity for total isolation or substitution. In the present absence of truly effective therapy, once the malignant alteration has been induced, the value of such preclinical indicators is limited.

(2) Mutagenesis and teratogenesis: Mutagenesis is the process wherein normal cells are converted into genetically abnormal cells. The result of such alteration, particularly since it involves the genetic processes which determine normal cell growth and division, are changes in structure and function. This process may result in malignant or other aberrations. Teratogenesis refers to the process whereby abnormalities of the off-spring are generated. Such usually results from damage to embryonal structures in the first trimester of pregnancy, or because of alteration of germinal elements, i.e., ovarian cells or spermatozoan.

While these responses are extremely important — especially where women may be at a risk, the danger of mutagenesis could theoretically also affect male generative tissue. While little such testing has been undertaken with a view toward protection of working populations, serious consideration should be given to such studies in the future.

Application of Animal Data

Principles of Application:

(1) Use of the most sensitive species: because the detoxification represents in essence a genetically controlled metabolic degradation process, it follows that various animal species will respond differently to toxic chemical exposure. Unfortunately, just how any species — including man — will respond is not predictable. Accordingly, when the human quantitative response to a chemical agent is unknown, prudence would dictate that the design of environmental quality standards assume that man responds as does the most sensitive species.

(2) Application of the dose-response curve to setting standards: primarily, environmental quality standards are intended to quantitatively indicate the amount of contaminant which may be present in the workplace without causing harm to man. Obviously, experiments should be directed toward determining the concentra-

tion at which "no effect" is produced, i.e., one which is safe.

Experiments which permit the development of a dose-response curve indicate the several ranges of response. In this manner, the doses producing "no response," a minimal response and the more severe response are defined. In most circumstances, a linear relationship between these doses emerges with the use of logarithmic plots. While a dose-response curve can be estimated without data points being available in the "no response" or safe range, downward extrapolation to this area holds some risk. Problems will occur when a break occurs in such a linear response curve; this is seen particularly in the low dose range.

(3) Safety margins and their bases: because of problems inherent in interpretation of toxicological data (see above), it is desirable to have a margin of safety between the lowest effective dose and a proposed TLV. Expressed mathematically, TLV = lowest effective dose/safety factor. The safety factor depends upon the nature of the response* produced by such lowest effective dose. Where such responses consist of reversible irritation of skin or mucous membranes, safety factors between the dose producing these phenomena and the recommended TLV tend to be low. By contrast, minimal dose-related responses characterized by toxicity usually possess a greater safety margin or factor. The range of safety factors associated with A.C.G.I.H. TLV's has been estimated to extend between 0.2 and 10.[8]

A safety factor of 0.2 denotes that the Threshold Limit Value is 0.2 fold (or 20%) higher than the dose which produces a response; a factor of 10 states that the TLV is 10 fold (or 1000%) higher than the dose producing a threshold response.

While the use of safety margins as an extrapolation process for estimation of the "no response" area is useful, their limitations should be recognized. For one thing, departures from the linearity of the dose-response curve are apt to occur in such estimates of lower ranges. Furthermore, given a steep dose-response line, in the biologically reactive range, the "no effect" level tends to be estimated with a high degree of error. Finally, when dealing with agents that appear to be active at extremely low levels, i.e., 5-10 ppm, departures from linearity appear quite common; this introduces even more chance of an unrealistic standard being set if a 5- or 10-fold safety margin is applied.[7]

It is for such reasons that data in the "no effect" range are preferred by those setting work environmental quality standards.

*What constitutes evidence of a "response" varies. In the United States biochemical, physiologic or even reversible changes in organ morphology may constitute the "minimal" response. In the U.S.S.R. more credence is placed upon subtle neurophysiologic change as evidence of a deleterious alteration (see section on Functional Response).

Problems in the Use of Animal Data for the Establishment of Environmental Quality Standards

In the absence of data based upon human experience, extrapolation from animal experiments must be used in establishing environmental quality standards. But because our concerns are directed toward prevention of human harm, the limitations inherent in animal-derived data should be recognized. Whether man will respond as the most reactive or least reactive species tested frequently cannot be predicted. Further, the question as to whether the most sensitive species has been tested is frequently unanswered. Finally, whether the animal response has any parallel to human responsiveness cannot be answered. (This has occurred in the case of induction of bladder tumors by aromatic amines; unless the dog is tested — a relatively uncommon test animal — such chemicals do not ordinarily produce bladder tumors in the animals usually used in the laboratory.) For these reasons, human exposure data assume considerable importance in quality standard development, though animal-derived information may be commonly the only type in existence.

Sensitization. This type of response, sensitization, is produced with difficulty in animals. Accordingly, if animal testing is relied upon, the potential for such responses may be undetected.

Genetic Defects Peculiar to Man. A number of genetic defects found in various human "strains" have no parallel in animals. Such defects occur commonly in human populations and can deleteriously affect the mode of response to certain environmental chemicals (e.g., glucose-6-phosphate dehydrogenase defects will impede the detoxification process among persons having this aberration who are exposed to various aromatic amines). Accordingly, animal testing alone will not predict whether a chemical might cause untoward reactions in such susceptible populations.

HUMAN DATA AND INDUSTRIAL EXPERIENCE AS A BASIS FOR STANDARD DEVELOPMENT

The Necessity for Human Data

It should be readily apparent from the foregoing that animal data form a problematic basis for the development of occupational environment quality standards. While such data are highly useful in developing a broader understanding of biological response (e.g., metabolism, full range of effects), such information in itself has obvious shortcomings in setting quality standards. It is for this reason that experience based upon human exposure to the substance in question is of ultimate importance in determining standards of safety.

Such data can result from inadvertent or intentional experimental exposure. Concerning the latter, the availability of animal experiments becomes critical; only after thorough exposition of toxicity by this method is human experimentation justified.

Specific Needs Fulfilled by Human Toxicity Data

1. Irritation and nausea: since the less severe degree of irritation can only be detected by subjective means, it is obvious that animal experimentation may not provide such information in this response range.
2. Allergic response: since animals rarely demonstrate this type of response, human experience is necessary if such effect is to be detected.
3. Odor evaluation: since no quantitative measures of odor are presently practicable, this response can only be evaluated by questioning the experimental subject. Obviously, animal experiments are useless in this regard.
4. Higher nervous function effects: an important consideration in occupational safety and health revolves about environmental effects upon human performance. While animal experimentation increasingly involves measurement of neurophysiologic response, extrapolation of such test procedures for the assessment of, e.g., visual performance, manipulation of various devices leads to obvious inadequacies. Thus human testing, particularly where relevant work tasks are performed, meets a unique need in occupational safety evaluation.
5. Human metabolic pathways: while much of such information can be derived from animal experiments, ultimately application of such data for hazard assessment and control design represents an extrapolatory exercise. Thus human exposures will provide the ultimate quantitative and qualitative information regarding human metabolism of the substance in question.

The Use of Data Derived from Occupational Experience

Validity requirements:

1. Environmental sampling adequacy: in order to relate human safety or damage to environmental agents, it is necessary to have some quantitative measurement of its presence. Usually this means extensive sampling of the work environment over time and space, but especially as related to worker absorption opportunities. That is, good industrial hygiene sampling practice (see Chapter 10) is necessary to adequately assess quantitative exposure.
   In brief, in the cases of gases, vapors or dusts, samples should be taken at breathing zones. In addition, in the case of dusts, quantitative characterization of the particulates of respirable size are especially pertinent. Obviously, care should be exercised that sufficient numbers of samples are taken to represent adequately the full range as well as average of concentrations.
2. Human surveillance adequacy: for data based on human experience to be valid, the human portion of the agent-host interaction also must be characterized. Indeed, if no untoward effect is claimed, detailed medical evaluation of those exposed is required. In addition, it is possible to evaluate environmental concentrations by measurement of metabolites or of the agents themselves in biological media. Although such correlations between concentrations in biological material and the work environment may be constructed from occupational exposure situations, usually insufficient data or range of exposures mitigate against development of such a regression line. However, such measurements taken under experimental exposure conditions have been extremely useful (see below, Human Experimentation).

Problems Encountered in the Use of Occupational Exposure Data

1. Irregularity of exposure: most occupational exposures are of a fluctuating character, both in terms of duration and concentrations. Thus the need for having sufficient samples representative of the "peaks," "valleys" and mean concentrations encountered becomes essential.
2. Mixed exposures: occupational exposures to a single agent are rather uncommon. Thus, while the material in question might be specifically measured in the environment, it becomes problematic whether the human response results from exposure to that particular agent *per se*. Furthermore, the biological response can rarely be rationally apportioned as a function of the relative concentration of multiple agents. Whether such agents are acting additively, synergistically or antagonistically can markedly alter responses. Hence, since occupational exposures are mixed, this limitation on their use for occupational environmental quality standard development must be recognized. For a more detailed discussion of evaluation of mixtures, see reference (3).
   As regards the agents in such a mixed exposure, the question of the specificity of the measurement technique for the material of interest becomes significant. This is especially pertinent where mixtures of chemically similar substances are encountered; interferences may also make such measurements of the components of such mixtures non-specific.
3. Absence of long-term data: while measurements of human response over the short-term experience are readily observed, the long-term effects of such exposures are infrequently available. While drastic effects of long-term exposure may be detected — and then with difficulty, e.g., bladder tumors, subtle effects are infrequently reported or investigated.

4. Special susceptibility: unless sufficiently large populations of exposed workers are studied, the few persons who may be at special risk because of genetically determined special susceptibility will not be encountered. Such persons may be at special risk either for reasons that are well-defined, e.g., defects in metabolism, or because of poorly understood reasons (allergic sensitivity). Indeed, while such persons may constitute a small proportion of a potential population at risk, this does not constitute a reason for such effects being ignored if they could potentially be prevented.

Human Experimentation

Ethical Considerations. While it has long been recognized that each man has a moral duty to act charitably toward others, e.g., make blood or skin graft donations, some subtle and gross abuses of human experimentation have made reassessment of that practice necessary. Accordingly, a number of moral codes have been drawn up to protect the person of such subjects (Nuremberg Tribunal Code, the World Medical Association's 1964 Declaration of Helsinki, American Medical Association, etc.).

Minimally, at least four requirements should be met before experiments are considered:

1. Safety should have been extensively established in animal species;
2. Volunteers must be free of any coercion whatsoever and be fully and completely informed of all possible effects in a clearly understood fashion;
3. There must be no possibility of permanent damage, and the subject must be completely free to terminate the experiment at any time;
4. A written agreement of the volunteer to participate in the experiment which is fully described should be obtained.

Practically, it is mandatory that there be sufficient insurance coverage for each subject to compensate him voluntarily in the event of injury.

Design Requirements

1. In testing with airborne narcosis producing materials, assuming sufficiently large chambers and modalities for testing behavioral and other functional parameters, exposures are made in 3 ranges, i.e., "no effect," at borderline levels and at levels producing measureable, though minimal, narcosis in most subjects. In this manner, 3- to 4-hour exposures can aid in estimating the safety factor for human exposure, the safe limit and the rates of uptake and elimination of the agent. The latter two are determined by plotting blood concentrations against atmospheric concentrations as a function of time; such data are extremely valuable in estimating the extent of previously unknown exposure given a blood concentration at any given time after exposure.[4]
2. In testing with airborne irritants, utilizing the aid of an otolaryngologist, examinations are performed both before and after exposure in a dynamic chamber. Because of the possibility of the development of accommodation, exposures should last at least 15 minutes; such exposures should be repeated 10 times in order to establish whether — and to what degree — accommodation occurs. A repetition of these exposures after 10 to 14 days will help establish whether sensitization occurs. Further, repetition has another urgency, since experience has shown that single exposure tests usually lead to unnecessarily low limits.[5]
3. Testing cutaneous irritation and sensitization (see Chapter 34).

Measurement of Response. Since a major reason for permitting the use of human volunteers is the eliciting of data indicative of minor functional change, the criteria of response should accordingly reflect this need. Thus, functional measurement of biochemical (e.g., enzymatic, immunochemical), neurophysiologic (e.g., EEG, conditioned and unconditioned reflexes) organ activity (EKG, liver or kidney function tests) and other parameters (comfort, esthetic) should be measured at the most sensitive and systematically higher levels. While functional change may represent normal and reasonable homeostatic adaptation mechanisms rather than being deleterious, each such change must be carefully elucidated and individually evaluated for its broadest implication as regards potential human harm.

STANDARDS OF QUALITY FOR THE WORKPLACE IN COMMON USE

Quality Standards Used in the United States

United States Historical Development. In 1941 the American Conference of Governmental Industrial Hygienists (A.C.G.I.H.) established a committee of industrial hygienists for the purpose of establishing the maximal allowable concentrations (MAC) for atmospheric contaminants in the workplace. Five years later such a list of recommended MAC values was suggested for use in industry. However, certain difficulties attended this designation, MAC. For one, these values were based upon time-weighted averages (see below) and did not represent a *maximal* ceiling value inherent in the name. For another, inherent in the title was an implication that such concentrations were "allowable," and thus a certain approbation was attached to concentrations below *and up to* such concentrations. At other times and places, this latter problem was associated with the use of the designation, Maximal Permissible Concentrations, or MPC.

In order to obviate these problems, in the 1960's the term Threshold Limit Value (TLV) was substituted for MAC. This new term, TLV, did not suffer these problems; without the implications associated with "allowable," more emphasis could be given to the practice of attempting to keep ambient concentrations below any designated value to the most practicable extent.

The A.C.G.I.H. Threshold Limit Values (TLV)

Nature of the TLV of air for occupational environments — TLV values refer to airborne

concentrations of substances and represent conditions under which it is believed that nearly all workers may be exposed eight hours a day for a forty-hour week over a working lifetime without adverse effect. Because of wide variation in individual susceptibility, exposure of an occasional individual at, or even below, the Threshold Limit may not prevent discomfort, aggravation of a pre-existing condition or occupational illness.

The TLV's represent eight-hour, time-weighted averages, i.e., airborne concentrations averaged with regard to their duration, occurring over an eight-hour period.

Certain chemical agents are associated with a "c" or ceiling designation; exposure to concentrations in excess of this value should not be permitted regardless of duration. Such designations stem from the fact that such agents may provide irritation, sensitization or acute poisoning immediately, or after a short latent period, upon even short exposures. Examples of such compounds among the respiratory irritants are chlorine, formaldehyde, vinyl chloride; narcotic agents such as methyl chloride; sensitizers such as toluene-2,4-diisocyanate; or those compounds which rapidly accumulate, such as benzene.

For those substances not given a "c" designation, excursions above the TLV are permitted. These agents produce their principal effects by cumulative, repeated exposure; thus, short excursions will not necessarily produce deleterious effects. The TLV's for such substances should be considered as average values integrated in relation to time. In general, the permissible range of fluctuations depends upon: the nature of the poison in general, the intensity of concentration required to produce acute effects, the frequency with which the average maximum tolerable concentration is exceeded, the duration of such excesses, and the cumulative effects of the exposure. For such a complex of reasons, it should be apparent that expert opinion should shape the use and interpretation of the TLV's. However, the A.C.G.I.H. gives some guidance for determining how great an excess above the TLV is permissible. For substances not having a "c" designation, the following guides apply:

TLV Range ppm* or mg/M³*	Excursion TLV Factor
0 to 1	3
>1 to 10	2
>10 to 100	1.5
>100 to 1000	1.25

*Whichever unit is applicable

Thus, a substance having a TLV of 5 ppm may fluctuate above the TLV, reaching a value of 10 ppm for periods of up to 15 minutes. However, the time-weighted average for an eight-hour day should not exceed 5 ppm. It is noted that the "Excursion TLV Factor" decreases as the magnitude of the TLV increases. Not to decrease this factor and increasing TLV magnitude would permit exposure to large absolute quantities, a condition that is minimized at low TLV's. Moreover, larger factors at the lower TLV's are consistent with the difficulties in analyzing and controlling trace quantities.[3]

Where the TLV's previously were given in terms of a volume per volume basis, i.e., parts per million, the trend appears to be for statement of TLV's on the basis of mass per volume, e.g., milligrams per cubic meter (mg/M³) in addition to "ppm." Most toxic dusts are listed in terms of million particles per cubic foot and in mg/M³ of respirable dust.

Procedure for Establishment of Values. Experts in industrial hygiene and toxicology annually review a list of over 400 substances. On the basis of literature data and personal information known to committee members, TLV's are recommended. Opportunities are afforded for comment by interested persons or organizations. In the case of a new substance being added or a change in the TLV of a material on the list, such new value is listed for two years as a "tentative" value, so that such parties may submit any additional information for the committee's consideration. In addition, periodically the committee publishes a "Documentation of TLVs;" this provides a detailed review for each substance and the bases utilized in assigning the TLV's.[9]

American National Standards Institute (formerly, American Standards Association) Z-37 Committee Standards (ANSI)

Nature of ANSI, Z-37 workplace quality standards, maximal acceptable concentrations:

Time-weighted average: This Standard is essentially the same as the time-weighted eight-hour average of the A.C.G.I.H. Threshold Limit Value (TLV).

Acceptable Ceiling Concentration. The Standard establishes the maximum level allowable concentration during the period of exposure, assuming that the time-weighted eight-hour *average* concentration is not exceeded. However, excursions above this ceiling *may* be permitted under certain conditions, as in:

Maximum Acceptable Peak Concentrations. These constitute the exceptions to the ceiling level noted above. The peak concentrations noted are specified as to their concentration, the duration of such excursion(s), and the number of time(s) such peaks may occur in one eight-hour day.

Formulation Procedure. The Z-37 committee of ANSI is composed of governmental, industrial, professional society and university-based experts in industrial toxicology, hygiene and medicine. Assignments for standard development are given to committee members or others having experience with the material in question. The committee votes upon the standard which is then sent forward for other Institute approval and ultimate publication as a Standard. Maximal *acceptable* concentrations are published for a number of materials as individual documents which give the basis for such judgments. In addition, analytical and sampling methods are recommended; the Standard publication also describes the toxicity of

the material as well as its physical and chemical properties.

Federal Standards

Under the Occupational Safety and Health Act of 1970, the National Institute for Occupational Safety and Health (NIOSH) has the responsibility for developing criteria and recommended standards and the Department of Labor has the responsibility for promulgating standards.

The initial compilation of health and safety standards promulgated by the Department of Labor's OSHA was derived from national consensus standards and recognized Federal Standards. In addition to these sources there have been, and are being developed, documents by NIOSH from formulations which are reviewed by NIOSH and its consultants. Inputs from selected professional societies, other Federal agencies and such interested parties as organized labor and trade associations are also obtained. Finally, the criteria document with the recommended standard is forwarded to the Secretary of Labor. His considerations benefit from any additional review he deems appropriate.

The Secretary of Labor has the responsibility for promulgating standards. In some cases he may refer for study and review a recommended standard to an advisory committee in accordance with provisions of the Act. However, regardless of whether this step is taken, if this is a 6 b regulation, he must publish it as a proposed regulation and standard so that objections and comments can be heard before such a standard is effective.

Note: Standards promulgated under authority of Section 6 a of the Act and emergency standards under Section 6 c of the Act can be promulgated without going through the "proposed" stage.)

In addition, under the Federal Coal Mine Health and Safety Act of 1969 (P.L. 91-173) NIOSH has the responsibility for transmitting to the Secretary of Interior recommended health standards. After a similar review and hearing process such standards are promulgated by the Department of the Interior.

State Regulations and Standards

While most states have lists of in-plant Air Quality Standards, the majority have essentially adopted those of the ACGIH TLV's. Accordingly, these are all eight-hour time-weighted averages, although Pennsylvania has also developed a series of short-term limits. These latter differ from the ACGIH values in that specific exposure durations for such excursions are stated in the Pennsylvania regulations.

WORKPLACE QUALITY FORMULATIONS IN USE OUTSIDE THE UNITED STATES

U.S.S.R.

Philosophy. Standards are absolute limits that may not be exceeded during any part of the working day, regardless of lower concentration that may have existed during that day. These Standards are legally binding.

The major scientific bases utilized in setting MAC's in the U.S.S.R. derive from reactions of the higher nervous system and physiological alteration. Feasibility does not seem to be considered in the standard setting process, although there is some question as to whether such standards represent goals or working realities. Thus, because such minimal physiological or neurofunctional changes (= adaptive responses?) are considered as designating the borderline between harm and safety, and since a safety margin is then applied, the Soviet Standards tend to be lower than those found in the United States. However, close examination of these differences reveals that in actuality only relatively few cases of gross differences (more than 4-fold) exist.[10]

Formulation Procedures. Much of the work involved in establishing standards is performed by the Academy of Medical Sciences, and The Institute of Industrial Hygiene and Occupational Diseases in Moscow, as well as other institutes. The data are then evaluated by the Permanent Committee for the setting of MAC's. Ultimately, standards are promulgated as Soviet Standard 245-63 by the U.S.S.R. Ministry of Health.

West Germany

Maximum allowable concentrations (MAK-Werte) are developed by an expert commission of the German Research Association (Deutschen Forschungsgemeinschaft) and are adopted in total by the Ministry of Labor & Welfare. In essence, they reflect the values adopted by the A.C.G.I.H. with some variations. The values adopted represent legal standards. A documentation is presently in preparation.

United Kingdom

The Factory Inspection Service of the Department of Employment utilizes a list of standards which act as benchmarks for the inspectorate. The values used are essentially those of the A.C.G.I.H.

France

Although French legal codes are extremely detailed regarding precautionary measures (e.g., medical, technical) for the protection of workers exposed to toxic substances, only a very few, specific materials are given numerical values in French codes. This stems from recognition of the reality that such values *do not* represent inflexible, absolute dividing lines between safety and hazard.

Others

Eastern Bloc Nations. Legal standards specifically stated in terms of numerical values are the rule. These are then promulgated by the Ministries of Health or those relating to production and are legally binding. It is of interest to note that most frequently (except for Bulgaria) the values cited are not identical with those adopted in the U.S.S.R.

Asiatic. Several of these recommend tests of standards of air quality in workplaces. The most notable of these is Japan; the numbers recommended by the Japanese Association of Occupational Health largely reflect those published by the A.C.G.I.H.

UTILIZATION OF STANDARDS OF QUALITY FOR THE OCCUPATIONAL ENVIRONMENT

The Philosophic Basis of Their Use

Consideration of the foregoing should clearly indicate that the formulation of quality standards

has no *absolute* informational basis. The variability of biological response, the judgmental elements which enter into evaluation of environmental and biological data, the imprecise nature of the biological response — all of these imply that after such evidence is weighed, a less than absolute decision must be reached. While a numerical value is ultimately decided upon, the non-absolute nature of the data upon which it is based should suggest that such value must not be taken to represent an *absolute* boundary between the positively safe and the positively unsafe. Thus, for example, if the "safe" value is 50, this cannot be taken to mean that 49 is *always* safe or that 51 represents an unsafe area. At best, such values represent *benchmarks,* or *guides* for protective action. Within this context, if a time-weighted average of 49 is attained, this should not be understood to mean that a lower value should not be pursued. Conversely, a value of 51 does not mean that damage to the individual so exposed will necessarily ensue. Within the context of legal codes such values do indicate the boundary between "safe" and "unsafe." Application of TLV's must take into account the multiple biological considerations discussed in this chapter and elsewhere and the elements of professional judgment inherent in the formulation of such standards (see section on Principles for Developing Workroom Air Quality Standards).

Obviously, repeated excursions above an air quality standard should not be tolerated. Where "c" or ceiling values are listed (see above), such excursions may lead to health or functional impairment, e.g., for liposoluble volatile solvents with narcotic properties as trichloroethylene or carbon disulfide. With substances not having such ceiling designations, excursions above such TLV's may only be permitted consistent with the recommended level (see above discussion of A.C.G.I.H. values).

In the event that a survey indicates excursions above TLV's, the competent authority is responsible for more definitive evaluation of such situations. Thus, repeated samples of the work environment representative of temporal and spatial variations in worker exposure should be obtained, consistent with good sampling procedures (see Chapter 10).

In addition, medical biological evaluation of the workers at possible risk is indicated. The appropriate medical examinations should delineate whether health damage, actual or potential, is occurring. Samples of biological media (blood, urine, expired air, tissues such as hair) should be analyzed to determine whether undue body burdens are being taken up.

If such more definitive evaluations indicate the presence of an occupational risk to worker health and safety, appropriate control action is necessitated.

That such values represent indicators for further evaluation and control action must be clearly understood. Such values can only be properly utilized by those possessing knowledge regarding these facts as well as an understanding of health implications of the specific environmental agent concerned. Thus a considerable element of judgmental evaluation is required; *there should be no automatic, unthinking application of such values for the protection of worker safety and health.*

Appropriate Application of Standards

Health and Medical Control. Possibly the most important use of quality standards relates to their use for medical control. Since medical and clinical laboratory testing imply certain costs, judicious planning for their deployment requires some guidelines to determine the frequency and extent of medical surveillance *consistent with worker safety and health.* Thus, if threshold limit values are repeatedly exceeded, more frequent and extensive medical surveillance is indicated while and after control measures are being accomplished. Certainly, as such quality standards are exceeded, the nature of medical testing becomes quite different than if these standards are never approached. It should be clearly indicated that even if such quality standards are *not* exceeded, medical surveillance *cannot* be neglected or omitted. However, their stringency should reflect the degree to which standards are approached or exceeded. It should be emphasized that medical action becomes useless as regards prevention unless coordinated with appropriate engineering action for amelioration of workplace contamination.

Design of Engineering Controls and Practices. Given such numerical values, it becomes possible for the design engineer to ascertain that engineering control of the process is required. With a knowledge of the physical properties of the material in question, the amounts used and the possible loss from the process, one can then formulate the ventilation or enclosure requirements necessary which will capture the contaminant in question and prevent its escape to the work environment.

Good engineering practice should never permit the workplace concentration to reach the quantitative level prescribed by the standard. It should be recognized that the economic cost of controls may mount geometrically as lower levels of workplace contamination are sought. Consequently, there is decreasingly less merit in attempting to attain absolute levels of capture, nevertheless, while the lowest level feasible should be sought, it can be seen that quality standards do provide benchmarks against which performance can be measured, consistent with economic considerations.

Surveillance of Adequacy of Control and Maintenance Practices. Once such control equipment is installed, its performance should be monitored. Given accumulation of material in ducts or fans. wear and aging of equipment, the performance of such equipment will tend to deteriorate. The point at which maintenance or replacement is required — with its attendant economic cost — can be determined by monitoring the work area. Since such decisions and the attendant depreciation costs may be considerable, the benchmarks for environmental quality become useful in rational planning of maintenance and replacement.

Use for Development of Analytical Techniques. In the realm of environmental monitoring, the design of analytical methodologies requires that some specific range of sensitivity should be sought if the method is to have practical use. Thus, the analyst

can use such quality standards in ascertaining how such analysis need be carried out. For example, while wet chemical methods may be quite adequate for the measurement at the 100 ppm level, at one-thousandth of this level other techniques may be called for, e.g., gas chromatography. Thus, knowing what concentration range must be measured is of obvious value; quality standards clearly indicate such ranges.

Basis for Communication and Interaction Among the Various Specialty Disciplines in the Occupational Health Team

Misuse of Standards — Comparison of Standards with Single Environmental Determinations. Generally speaking, to properly evaluate environmental quality in the workplace, the obtaining of a short-period single determination has little or no value. Likewise, to compare such short-period sample with an 8-hour environmental quality standard represents a misuse of such standards. Since most standards represent time-weighted averages (see above), one sample probably cannot provide such an evaluation, unless it is an eight-hour sample or can be reliably related to the full-shift exposure. Even where ceiling values (see above) are exceeded, a single sample may be invalid unless it is clearly related to the worker, e.g., in relation to his breathing zone. Obviously, quality standards have meaning only when adequate industrial hygiene sampling techniques are utilized (see Chapter 10).

References

1. DINMAN, B. D. "The 'Non-Concept' of 'No Threshold': Chemicals in the Environment." *Science 175*: 495-97, 1515 Massachusetts Ave., NW, Washington, D.C. (1972).
2. HATCH, T. F. "Permissible Levels of Exposure to Hazardous Agents in Industry." *J. Occup. Med. 14*: 134-37, 49 East 33rd St., New York, N.Y. (1972).
3. *Threshold Limit Values of Airborne Contaminants and Intended Changes, Adopted by the A.C.G.I.H. for 1971.* American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio (1971).
4. STOKINGER, H. E. and J. T. MOUNTAIN. "Progress in Detecting the Worker Hypersusceptible to Industrial Chemicals." *J. Occup. Med. 9*: 537-41, 49 East 33rd St., New York, N.Y. (1967).
5. STOKINGER, H. E. "Criteria and Procedures for Assessing the Toxic Responses to Industrial Chemicals in Permissible Levels of Toxic Substances in the Working Environment." *ILO Occupational Safety and Health Series*, No. 20 Geneva, Switzerland (1970).
6. SMYTH, H. F., JR. "The Toxicologic Bases of TLV:I; Experience with TLV's Based Upon Animal Data." *A.I.H.A. J. 20*: 341-345, 210 Haddon Ave., Westmont, N.J. (1959).
7. Ibid, Reference 5, pg. 174.
8. STEWART, R. D., H. H. GAY, D. S. ERLEY, C. L. HAKE and J. E. PETERSON. "Observations on the Concentrations of Trichloroethylene in Blood and Expired Air Following Human Exposure." *A.I.H.A. J. 23*: 167-170, 210 Haddon Ave., Westmont, New Jersey (1962).
9. AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS. *Documentation of the Threshold Limit Values for Substances in Workroom Air.* Third edition, P.O. Box 1937, Cincinnati, Ohio (1971).
10. TRUHAUT, R. Reference 5, pg. 53.