AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 33:439–453 (1998)

Chemicals in the Workplace: Incorporating Human Neurobehavioral Testing Into the Regulatory Process

Robert B. Dick, PhD[1]* and Heinz Ahlers, JD[2]

In February 1996, the United Kingdom Health and Safety Executive sponsored a workshop on the role of human neurobehavioral tests in the regulation of chemical exposures in the workplace. This paper presents the review of neurobehavioral testing that was initially prepared for the workshop but has been expanded and updated for publication. Information sources for the review were drawn from "preamble to the regulation," in the 1989 air contaminants project, an attempt by the Occupational Safety and Health Administration to update the 1968 regulatory limits of workplace exposures. The scientific citations listed in the preamble provide a chemical database to review for evidence of neurobehavioral testing to support limit setting. Several conclusions emerged: 1) A wide range of nervous system effects were reported in the scientific citations for the 172 chemicals identified with effects on the nervous system; 2) Citations of studies with human neurobehavioral test results are used to support limit setting, but many are old studies primarily of acute effects; 3) There is frequently a delay of several years after publication before studies with neurobehavioral testing are cited in regulatory forums; 4) With the 1989 proposed regulatory limits never legally adopted, there has not been an update for most of the substances affecting the nervous system since 1971; 5) Investigators should be more aware of the regulatory process and submit studies reporting neurobehavioral test results to organizations that regulate and recommend workplace exposure limits; 6) Issuances in the Federal Register by the U.S. Environmental Protection Agency provide a framework for assessing neurotoxic risks that can be used by investigators to help identify and report nervous system effects using neurobehavioral testing in a more uniform fashion. Am. J. Ind. Med. 33:439–453, 1998. *© 1998 Wiley-Liss, Inc.*

KEY WORDS: nervous system; neurobehavioral; chemical exposures; regulation; limit setting

INTRODUCTION

The purpose of this paper is to briefly describe the process of chemical exposure regulation and to provide a review of the inclusion of neurobehavioral test results in the regulatory ''limit setting'' for chemicals in the workplace. This review is also intended to inform readers of the wide range of neurobehavioral tests results that are cited and to increase the ''awareness'' about how scientific results are used in the regulatory process. This compilation was originally a presentation delivered at a 1996 workshop entitled ''The Role of Human Neurobehavioural Tests in Regulatory Activity on Chemicals,'' sponsored by the United Kingdom Health and Safety Executive, February 8–9, 1996, at the Runnymede Hotel, Egham, Surrey. The paper has been expanded in response to reviewer suggestions. A major source for the review was the lengthy 655 page Book 2, of the Department of Labor, Occupational Safety and Health

[1]Division of Biomedical and Behavioral Science, Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, OH

[2]Education and Information Division, Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, OH

*Correspondence to: Robert B. Dick, Ph.D., National Institute for Occupational Safety and Health, Mail Stop C-24, 4676 Columbia Parkway, Cincinnati, OH 45226

Accepted for 10 December 1997

Administration, Air Contaminants, final rule submission which appeared in the Federal Register in 1989 [U.S. Department of Labor, 1989]. This submission contains the preamble section, subsection discussions, and health effects evidence for each chemical substance for which new or revised limits were reviewed. Attempts were made to keep the terminology in this paper consistent with the terminology used in the final rule submission. Use of the Federal Register terminology may cause some confusion to readers not familiar with the legalistic framework used in workplace regulation.

Workplace Chemical Exposure Regulation

In the United States, four Federal Agencies listed in Table I are responsible for the regulation and testing of hazardous substances. Table I also lists the law conveying authority and jurisdiction to these agencies.

The regulation of safe chemical exposures in the workplace is a complicated process with a historical record predating the legislation that established a Federal role. Prior to the Federal authority, professional organizations provided important information on safe exposure levels to chemicals and continue to do so. The Occupational Safety and Health Administration (OSHA), in the Department of Labor, is the agency that has the general authority to regulate chemical exposures in the workplace. This authority was granted under the Occupational Safety and Health Act in 1970. The same act also created the National Institute for Occupational Safety and Health (NIOSH), a research agency located in the Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Among NIOSH's many functions is the responsibility to recommend safe chemical exposure limits for the workplace to OSHA based on the best available scientific evidence [NIOSH, 1992].

In 1971, OSHA issued the first occupational exposure limits for 400 chemicals. These initial regulatory limits incorporated the pre-existing Walsh-Healy Public Contracts Act limits that were extracted from the 1968 recommended standards of two professional organizations, the American Conference of Governmental Industrial Hygienists (ACGIH) and the American National Standards Institute (ANSI). In 1987 to 1988, OSHA attempted to update (i.e., later set aside by court ruling) the 1968 regulatory limits. The final rule promulgated by OSHA was for 428 substances and appeared in the January 19, 1989 Federal Register. Scientific information submitted by ACGIH and NIOSH was used as the starting point for OSHA's analysis of new limits for 164 chemicals and revised limits for 212 chemicals. Additional information was submitted by chemical manufacturers, chemical users, and other interested parties during the rulemaking process. No changes were recommended for 52 chemicals and 160 chemicals were not re-evaluated.

Professional organizations have an important role in the limit setting process and one organization in particular, ACGIH is very active. ACGIH currently publishes recommendations for over 700 chemicals [ACGIH, 1996]. Another professional organization, the American Industrial Hygiene Association (AIHA), has published Workplace Environmental Exposure Levels (WEELs) since 1987. Although AIHA had no formal role in the 1987–1988 submission process, it has currently issued 77 WEELs [AIHA, 1997]. The WEELs are intended to be supplemental to the ACGIH-Threshold Limit Value (TLV) listings and are issued for chemicals that do not have established TLVs. Table II provides a summary list of the five organizations historically issuing workplace exposure limits and their limit setting terminology. Only the terminology for the 8-hr time weighted average (OSHA, ACGIH) or the 10-hr time weighted average (NIOSH) for the work shift (day) limits are listed in Table II. The various agencies also publish Short Term Exposure Limits (STELs), Ceiling limits, Peak Limits, skin designations, and cancer designations for several substances. Definitions for some of these additional limits are provided at the end of the Table in the Appendix.

OSHA used an avoidance of health effects by target organ/target system approach for limit setting in the 1987–1988 rulemaking. The target organ/target systems (e.g., cardiovascular, kidney or liver, respiratory, systemic) are identified as subsections in the preamble discussion of the 1989 Final Rule Submission [U.S. Department of Labor, 1989]. There are, however, some subsections which do not represent a traditional target organ/target system but a common health or toxicological effect. These subsections are physical irritation, odor, sensitization, and biochemical/metabolic. One other subsection, no observed adverse effect levels, represents substances where the research is conclusive that toxic effects will not be present below an established level. Table III lists the target organ/target system subsections. Each subsection and the accompanying Table (e.g., Tables C1-1 through C1-15 in the Federal Register), which lists the substances, is prefaced with the terminology ''Substances for which limits are based on Avoidance of.'' Table IV, which is extracted from the Federal register on page 2399, lists the types of toxicological evidence that can be introduced for establishing work place limits. Most of the toxicological evidence is based on scientific work that was designed to document lowest observed effect or no-effect levels for a variety of acute effects.

Each health effects subsection discussion in the preamble consists of an introduction, a description of health effects, a table listing the regulated substances and their

TABLE I. U.S. Government Regulatory Agencies With Authority to Regulate either Exposure To or Use Of Chemicals and Require Data on Assessment of Hazards*

Agency	Statute	Coverage
Food and Drug Administration (FDA)	Food, Drug, and Cosmetics Act	Drugs, Foods, Food additives, Cosmetics, Medical Devices, and animal drugs of medical and feed additives.
Environmental Protection Agency (EPA)	Federal Insecticide, Fungicide, and Rodenticide Act	Pesticides
	Toxic Substances Control Act	Industrial Chemicals
	Clean Air Act	Air Pollutants
	Resource Conservation and Recovery Act	Industrial Waste
Occupational Safety and Health Administration (OSHA)	Occupational Safety and Health Act	Occupational Exposure
Consumer Product Safety Commission (CPSC)	Federal Hazardous Substances Act	Consumer Products
	Consumer Product Safety Act	Consumer Products

*Adapted from Table 1.2, Federal Register, Vol. 59, No. 158, pp. 42362, 1994.

TABLE II. Agencies and Professional Organizations Involved in Work Place Exposure Limit Setting

Agency	Type	8- or 10-hr TWA limits
Occupational Safety and Health Administration (OSHA)	Government-Regulatory	Permissible Exposure Limits (PELs) 1971–88 470 PELs; 1989–212 revised and 164-new (Z-Table listings).
National Institute for Occupational Safety and Health (NIOSH)	Government-Recommend	Recommend Exposure Limits (RELs) Currently 667 RELs published.
American Conference of Governmental Industrial Hygienists (ACGIH)	Professional-Recommend	Threshold Limit Values (TLVs) Currently 700+ TLVs published.
American National Standards Institute (ANSI)	Professional-Recommend	Currently 21 PELs are from ANSI. (Z-2)
American Industrial Hygiene Association (AIHA)	Professional-Recommend	Workplace Environmental Exposure Levels (WEELs). Currently 77 WEELs.

former, proposed, and final permissible exposure limits (PELs), and a conclusion. The ''description of health effects'' provides the information related to 1) the principal toxic effects for each chemical, 2) the present permissible exposure limits, 3) the recommended limits from ACGIH, NIOSH or other interested parties, 4) the scientific citations to support limit setting, and 5) the final regulatory limit issued by OSHA. The scientific citations constituted the ''database'' for the present review. This database of citations permitted the examination of all the substances (i.e., chemicals) regulated for prevention of nervous system effects, or known to have strong effects on the nervous system. A citation usually lists the authors, date of publication, and a brief one or two sentence summary of the concentrations studied, tests used, and results. Original articles were located and reviewed if the Federal Register summary was not clear regarding the nervous system effect, the neurobehavioral testing, or the type of toxicological evidence. A key word search of the electronic version of the database was also conducted to further identify any substances where nervous system effects were cited.

Subsections identified with nervous system effects consisted of neuropathic effects, narcotic effects, sensory irritation, and odor. Sensory irritation and odor were included because the integration of cranial nerves and specialized nerve endings that convey the signals for irritation and odor produces a sensory response that often has a strong behavioral component. In addition, another subsection ''analogy to related substances,'' was examined. This subsection includes chemicals which have limited workplace exposure and toxicological information, but are occasionally used in the workplace and are structurally related to chemicals regulated for narcotic, neuropathic or sensory irritant effects. Although not a separate subsection in the 1989 submission, a classification was created to identify chemicals which are regulated for other health effects (e.g., cancer, cardiovascular, kidney, liver, biochemical/metabolic) but which also have strong effects on the nervous system. Chemicals in this last classification were identified by the keyword search of all chemicals for nervous system effects.

In total, 172 chemicals were identified as producing effects on the nervous system. These chemicals and their

TABLE III. Organ/System/Health Effects to be Avoided in the Preamble to OSHA Limit Setting, 1989*

Substances for which limits are based on Avoidance of:
(1) Neuropathic Effects;
(2) Narcotic Effects;
(3) Sensory Irritation;
(4) Liver or Kidney toxicity;
(5) Ocular effects;
(6) Respiratory effects;
(7) Cardiovascular effects;
(8) Systemic toxicity;
(9) No observed adverse effect levels;
(10) Physical irritation;
(11) Odor effects;
(12) Analogy to related substances;
(13) Biochemical/Metabolic effects;
(14) Sensitization effects;
(15) Cancer.

*Adapted from Federal Register, Vol. 54, No. 12, pp. 2402–2403, 1989.

TABLE IV. Types of Toxicological Evidence Used in OSHA Rulemaking When Establishing Workplace Exposure Limits*

Clinical Observation-	Accidents, Poisonings, Tragedies
Epidemiology Studies-	Patterns of disease or morbidity in groups of people exposed to single toxins or a group of substances. Ideally, there should be a study population versus a control population fully comparable on every variable except the single characteristic under study
In Vitro Studies-	Cell or tissue systems
Laboratory Studies-	a) Animal Toxicology studies
	b) Intervention studies conducted with human volunteers

*Adapted from Federal Register, Vol. 54, No. 12, p. 2399, 1989.

effects are summarized into the following paragraphs for each of the health effect subsections described above. The summaries outline and describe the nervous system effects for each subsection, the neurobehavioral tests used which are present in the supporting citations for each subsection, and our conclusions about the influence of neurobehavioral testing to support regulation for each subsection. Table V provides a breakdown of the toxicological evidence (e.g., laboratory studies, epidemiological studies, clinical case studies, chemicals with citations with some type of neurobehavioral testing) presented for each of the six health effects. A large table is appended which lists each substance identified in the review, the Chemical Abstracts Service (CAS) registry number, the health effects subsection that contains the substance and the principal toxic effect(s), the current and 1989 proposed Permissible Exposure Limit, and the NIOSH Recommended Exposure Limit. The ACGIH TLVs are not listed, because with few exceptions, they were the same as the proposed 1989 PELs. Since 1989 ACGIH has published TLVs for some substances that are different than the 1989 proposed PELs. These newer TLVs can be obtained directly from ACGIH. Identified in bold are the proposed exposure limits that are either new or lower than the current regulatory limits. Limits that are underlined represent recommendations from NIOSH that are lower than the OSHA 1989 proposed limits.

To include all tests reporting effects on the nervous system in adults, a broad definition for neurobehavioral tests was used. This definition included any test measuring or reporting a nervous system response that was either reversible or irreversible. Included were neurophysiological (e.g., nerve conduction, evoked potential), and neurological tests that may not be considered by some investigators as traditional neurobehavioral tests. The tests are listed in the summaries for each health effects subsection later in the text. Studies reporting results of subjective ratings of sensory irritant effects are included because they do represent indicators of nervous system response and possible behavioral change that may be distracting (e.g., coughing, wheezing, conjunctivitis, tearing) to workers and, as stated on page 2445 of the preamble, interfere with job performance and safety.

Standardized neurobehavioral testing has the advantage of providing objective definable criteria for the establishment of workplace limits that would be protective from both short- and long-term exposures [Dick, 1988]. Neurobehavioral test data have been accepted by OSHA and NIOSH since the passage of the Occupational Safety and Health Act in 1970 [OSH Act, 1970]. This act specifically required NIOSH to: 1) include psychological, behavioral, and motivational factors in researching problems of worker safety and health, and to consider these factors in developing new methods, techniques, or approaches in handling such problems (Sections 20[a][1], 20[a][4]). 2) on the basis of such research, demonstrations, and experiments, and any other information available...develop criteria dealing with the toxic materials and harmful physical agents and substances which will describe exposure levels that are safe for various periods of employment, including but not limited to the exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience (Section 20[a][3]).

Chemicals With Effects on the Nervous System

Chemicals regulated to prevent neuropathic effects.

Nineteen chemicals are listed in this subsection. These chemicals include substances such as n-butyl alcohol, dichloroacetylene, n-hexane, methyl normal butyl ketone (MnBK), manganese compounds, mercury, methyl bromide,

TABLE V. Number of Chemicals and the Types of Toxicological Evidence Cited in the 1989 OSHA Submission to Report Effects on the Nervous System

Effects	Chemicals	Laboratory studies		Epidemiological studies	Clinical case reports	Neurobehavioral testing
		Human	Animal			
Neuropathic	19	3	17	10	16	5
Narcotic	19	14	17	7	8	8
Sensory Irritation	74	38	58	15	40	15
Odor	3	2	3		1	2
Structural Analogy	35	1	34	3	15	
Other Health Effects	22	6	21	6	11	6
Total	172[a]	64[b]	140[b]	41[b]	32[b]	36[b]

[a]Total number of chemicals with citations to describe nervous system effects.
[b]Total number of nervous system citations, but the same citation may have been used for more than one chemical.

and propylene glycol dinitrate. The nervous system health effects and symptoms listed include brain lesions, nausea, vomiting, central nervous system (CNS) depression, interference with sensory and motor functions, alterations in ability to process information, drowsiness, loss of ability to concentrate, mood changes, reduced awareness, learning difficulties, unsteadiness, and auditory and visual disturbances. Also listed are exposures leading to situations where individuals are likely to hurt themselves or others in accidents caused by reduced functional capacities. A noted distinction for this subsection is that the effects are generally permanent, rather than temporary. The neurobehavioral tests used to provide evidence of neuropathic effects are standard tests of hearing and vision, manual dexterity, coordination, postural stability, visual inspection, reaction time, short-term memory, and hand tremor. Also mentioned in the citations are visual evoked responses (VERs) and full scale neurological exams. In this subsection, many occupational limits are based on experimental animal testing with some epidemiological and clinical case citations. Examination of the citations in this subsection of the Federal Register (pp 2403–2419) indicate few human studies with neurobehavioral test results cited and most of those studies are from the 1970s or older. Although OSHA stated on page 2407 of the preamble that, ''Increases in our ability to detect neurological changes at lower levels of exposure have shown that neurobehavioral changes or impairment may occur at levels previously thought to be innocuous,'' citations from the 1980s in this subsection are limited and no explanations were provided for the lack of recent scientific data.

Chemicals regulated to prevent narcotic effects.

In this subsection there are also 19 chemicals. The chemicals listed include ethyl bromide, methyl chloride, methyl chloroform, pentane, Stoddard solvent, styrene, toluene, and trichloroethylene. In this subsection, exposure to these chemicals affects health and functional capacity similar to the chemicals listed in the neuropathic subsection, but the effects are not considered to be permanent. The effects and symptoms listed include narcosis, general CNS depression, drowsiness, difficulty in concentration, mood changes, loss of coordination, increased risk of accidents, slowed reaction times, increased mistakes and errors. Tests reported to detect narcotic effects are symptom questionnaires, neurological tests (e.g., Romberg, heel-to-toe), time estimation, number inspection, electroencephalograph (EEG), VER, tremor, vigilance, monitoring, math concepts, visual acuity, postural stability, grip strength, manual dexterity, and reaction time. Eight chemicals have citations that report neurobehavioral test results.

Most chemicals regulated in this subsection are supported by both human and animal laboratory studies, with some epidemiological and clinical case citations. There are few studies cited from the 1980s, although NIOSH had submitted to OSHA studies with neurobehavioral test results (e.g., styrene, toluene) with 1980s publication dates. The proposed limits for chemicals, such as trichloroethylene and methylene chloride, which have central nervous system depressant effects and were previously regulated to prevent narcosis effects, but are now suspected of being possible human carcinogens from long-term exposures are problematic. Studies involving these chemicals listed in recent reviews [Anger, 1990; Dick, 1995] with pre-1989 publishing dates tend to be omitted in the 1989 submission in favor of more recent citations of studies with possible cancer effects. In addition, the limit setting and the NIOSH RELs for these substances appear to be much lower than necessary to prevent the nervous system effects, suggesting that the exposure limits for some chemicals are being established to prevent cancer from long-term exposures rather than narcosis, with is an acute affect. Retention of chemicals such as trichloroethylene in the ''narcotic effects'' subsection will

continue to cause confusion if the limit setting is based more on the long-term cancer potential of these chemicals. In 1997, with the recent issuance of new rule making for methylene chloride [U.S. Department of Labor, 1997] which is now regulated to avoid cancer effects, OSHA has apparently begun to address these situations.

Chemicals regulated to prevent sensory irritation.

Seventy-four chemicals are listed in this subsection. Chemicals include acetone, ammonia, bromine, methyl ethyl ketone, chlorine, ethyl benzene, ethyl ether, hydrogen fluoride, isopropyl alcohol, potassium hydroxide, tetrahydrofuran, triethylamine, and xylene. The irritant effects are listed as coughing, wheezing, conjunctivitis, tearing, irritation, and alterations in general well being. An alteration in general well being is not an easily definable health effect, but is considered relevant because workers distracted by primary irritants are more likely to have accidents and endanger themselves and others. Tests for detecting irritant effects include symptom questionnaires and questionnaires with subjective ratings of irritant effects (i.e., objectionable odor).

Many chemicals in this grouping, such as the ethers, ketones, and aromatic hydrocarbons have strong central nervous system (CNS) effects. Using sensory irritation as the basis for limit setting provides a margin of protection against acute CNS effects because the overt CNS effects (e.g., dizziness, drowsiness, incoordination) usually occur at higher concentrations than the irritant effects. Fifteen chemicals had citations of human studies with some form of neurobehavioral testing. Review of the citations shows that many of the studies are old citations which used exposed volunteers, the exposure periods were brief, and the effects measures were primarily subjective [Nelson et al., 1943; Silverman et al., 1946]. Important behavioral factors, irritant receptor factors, and experimental methods procedures essential in modern day studies were not included. Such factors include tolerance development, sensitization (e.g., perceived irritation intensity increase over time), desensitization (e.g., response fading), sensitive populations, use of naive volunteers versus chemical-exposed workers, response bias, sensory adaptation, and response differences due to chemical properties of the substances. Many studies also lacked control-air exposure conditions which is necessary in chamber exposure experiments [Johnson, 1987]. Other studies are based on observer reports of exposed volunteers or workers. In 1989, on page 2444 of the preamble, OSHA did note the need for both new human and animal evidence of sensory irritation for the substances proposed for regulation. Many substances in this subsection are probably candidates for revision using current methodologies.

Chemicals regulated to prevent odor effects.

Only three chemicals (isopropyl ether, phenyl ether, vinyl toluene) are listed in this subsection and represent substances that have obnoxious odors that cannot be tolerated for any period of time. In 1989, on page 2393 of the preamble, OSHA determined that odor effects alone do not constitute ''material health impairment,'' and that it was exceedingly rare for a ''substance'' to cause only odor effects. OSHA concluded that, generally, ''odorant chemicals'' also cause toxic effects such as sensory irritation or CNS effects. As a result, many chemicals with strong odor effects are probably more likely to be regulated to avoid sensory irritation. Intolerable odors are considered to have a strong behavioral component because workers distracted from the task at hand may be more prone to accidents and likely to experience considerable discomfort. Tests include symptom questionnaires and questionnaires with subjective ratings of irritant effects. Odor effects is a very small subsection with limited human data.

Chemicals regulated by analogy (e.g., structural) to related substances.

Thirty-five chemicals are in this subsection. Examples of chemicals include acrylic acid, calcium oxide, endosulfan, cholinesterase inhibitors (e.g., fonofos, methyl parathion, phosdrin), methyl formate, nitric acid, propylene oxide, trichloroacetic acid and several lessor known ketones (e.g., diethyl, dipropyl, methyl isopropyl), and alcohols (e.g., isobutyl, isoocytl, n-propyl). The primary health effects basis is usually analogy to chemicals causing sensory irritation, with some substances analogous to narcosis or neuropathic effects. In this subsection the human data cited are sparse. Citations of human responses are primarily clinical case reports from accidents and spills. The primary type of toxicological evidence cited comes from animal laboratory studies.

Chemicals regulated for other health effects, but having strong effects on the nervous system either directly or indirectly.

Twenty-two chemicals were placed in this classification which is not a subsection in the Federal register. These chemicals are regulated to prevent other non-nervous system health effects, but were identified in our review as having citations reporting strong effects on the nervous system. Chemicals in this category include acrylamide, methyl acetate, hydrogen cyanide, carbon monoxide, perchloroethylene, cyclohexanone, methyl iso-butyl ketone, and several pesticides (e.g., chlorpyrifos, carbofuran). One subsection included in this special classification, the avoidance of biochemical/metabolic effects, is a new subsection and lists

many chemicals that have not been previously regulated. Chemicals with evidence for three types of mechanism of action, cholinesterase inhibition, interference with oxygen carrying capacity of blood, or antabuse effects (e.g., inhibit aldehyde dehydrogenase activity), have been placed in this subsection.

Review of the citations for these chemicals indicated tests such as symptom questionnaires, subjective rating questionnaires, reaction time, dual task, tracking, neurological (e.g., Romberg, heel-to-toe), time estimation, number inspection, EEG, and manual dexterity were used to report nervous system effects. Also included in this category are chemicals such as carbon monoxide, perchloroethylene, ether, and ketones which are known CNS depressants and have been extensively studied using neurobehavioral tests. Although carbon monoxide is regulated based on biochemical/metabolic effects, the neurobehavioral effects of exposures to carbon monoxide are frequently cited to support a new lower PEL for this chemical [U.S. Department of Labor, 1989].

Rulemaking Process

The regulatory process normally followed by OSHA involves two important steps. The first is an Advance Notice of Proposed Rulemaking (ANPR) in the Federal Register which announces OSHA's intent to develop a rule on a topic and is usually, but not always put forth by the agency. The ANPR may occur several years before a proposed rule is finally announced and heralds the opening of an official OSHA docket and information gathering activity on the topic. The second is a Notice of Proposed Rulemaking (NPRM) which is mandatory and will announce the time and place of scheduled hearings and set forth the content of the proposed rule. A time schedule for hearings and the submission of additional comments and data is set up in the NPRM and is not infrequently modified. OSHA actively seeks additional scientific information in the NPRM and the preamble to the Air Contaminants rule [U.S. Department of Labor, 1989] illustrates that OSHA makes use of the information submitted.

In December, 1995, the Occupational Safety and Health Administration announced as part of the OSHA priority planning process the intention to introduce revisions of the permissible exposure limits (PELs) for workplace exposures [OSHA, 1995]. Unlike the previous 1989 submission of almost 400 chemicals for either new or revised regulation, only a limited number of high priority chemicals would be submitted for regulation. OSHA also identified solvents as a general category for special emphasis in the 1995 priority planning process. In the list of chemicals submitted for the PEL update are certain to be chemicals that have significant effects on the nervous system.

Summary and Conclusions

In the 1989 OSHA Air Contaminants project, a wide range of nervous system effects were reported in the scientific citations on the 172 chemicals identified with effects on the nervous system. The majority of the citations represented animal laboratory studies, but citations of studies with effects on humans were frequent. Citations of studies with human neurobehavioral test results were used to support the proposed limit setting, but many were old studies primarily of acute effects. For example, two frequently cited studies for several common industrial solvents [Nelson et al., 1943; Silverman et al., 1946] date to the 1940s. These studies use experimental methodology of an earlier era that would not be acceptable today. In addition, studies of long-term exposures in the workplace are needed.

The preamble to the Air Contaminants project also illustrates there is a delay of several years after publication before studies with neurobehavioral testing are cited in regulatory forums. More recent studies, which had appeared in the literature since 1980, and have investigated the long-term effects of chemical exposures on the nervous system were not frequently cited in the 1989 submission. The age of that data has become a more pronounced problem because there has not been a successful update of regulatory limits for many substances affecting the nervous system since 1971.

Examination of the documentation provided in this review shows that the current workplace limits need updating for a large number of chemicals affecting the nervous system. Including the OSHA proposed lower limits in the 1989 submission and the current NIOSH recommendations, 134 substances listed in Appendix A have lower TWA workshift (day) limits proposed than those currently in effect. Almost 10 years has elapsed since the 1989 submissions, which never went into effect because of court action (AFL-CIO vs. OSHA, 1992), a period when much more scientific evidence has become available to document limit setting.

In order to assist the agency staff in identifying recent articles appearing in peer reviewed literature, we suggest that neurobehavioral researchers become more familiar with the rule making process and the potential for investigators to participate in the process. This could include submission of published research results, reporting on either the toxicity or nontoxicity of substances on the nervous system directly to the statutory agencies (e.g., OSHA and NIOSH) that have a formal role in the limit setting process and professional organizations (e.g., ACGIH and AIHA) that are active in the regulatory arena. The means for submitting study results are available through announcements from the agencies and by responding to requests in the Federal Register. Increasing use of announcements on the INTERNET by the statutory agencies should make this process easier. OSHA maintains

an Internet site for disseminating regulatory information, http://www.osha-slc.gov/, as does NIOSH, http://www.cdc.gov/niosh/homepage.html. An assumption that only articles published in the scientific literature will be incorporated into the regulatory process in a timely fashion does not recognize the very real resource constraints placed upon Federal agencies.

Documents issued by the U.S. Environmental Protection Agency will greatly help formalize neurobehavioral testing and the use of test results for workplace exposure limit setting. The documents are the ''Principles of Neurotoxicity Risk Assessment,'' which appeared in the August 17, 1994 Federal Register, and the ''Proposed Guidelines of Neurotoxicity Risk Assessment,'' which appeared in the October 4, 1995 Federal Register. Both publications provide operational definitions for both human and animal nervous system testing that can be used to help identify and report neurobehavioral test results in a more uniform fashion.

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APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
n-Butyl alcohol	71-36-3	neuropathic	100 ppm TWA	**50 ppm Ceiling**	**50 ppm Ceiling**
Chlorinated camphene (60%)	8001-35-2	neuropathic	0.5 mg/m^3 TWA		potential occupational carcinogen
Decaborane	17704-41	neuropathic	0.3 mg/m^3 TWA	0.3 mg/m^3 TWA	0.3 mg/m^3 TWA
				0.9 mg/m^3 STEL	**0.9 mg/m^3 STEL**
Di-sec-octyl phthalate	117-81-7	neuropathic	5 mg/m^3 TWA	5 mg/m^3 TWA	**potential occupational carcinogen**
				10 mg/m^3 STEL	
Dichloroacetylene	7572-29-4	neuropathic	none	**0.1 ppm Ceiling**	**potential occupational carcinogen**
Dipropylene glycol methyl ether	34590-94-8	neuropathic	100 ppm TWA	100 ppm TWA	100 ppm TWA
				150 ppm STEL	**150 ppm STEL**
n-Hexane	110-54-3	neuropathic	500 ppm	500 ppm TWA	100 ppm TWA
				1000 ppm STEL	510 ppm Ceiling
2-Hexanone (MnBK)	591-78-6	neuropathic	100 ppm TWA	**5 ppm TWA**	**1 ppm TWA**
Iron pentacarbonyl	13463-40	neuropathic	none	**0.1 ppm TWA**	**0.1 ppm TWA**
				0.2 ppm STEL	**0.2 ppm STEL**
Manganese fume	7439-96	neuropathic	5 mg/m^3 Ceiling	**1 mg/m^3 TWA**	**1 mg/m^3 TWA**
				3 mg/m^3 Ceiling	**3 mg/m^3 Ceiling**
Manganese cyclopentadienyl tricarbonyl	12079-65	neuropathic	5 mg/m^3 Ceiling	**0.1 mg/m^3 TWA**	**0.1 mg/m^3 TWA**
Manganese tetroxide	1317-35-7	neuropathic	5 mg/m^3 Ceiling	**1 mg/m^3 TWA**	**effects at 1 mg/m^3**
Mercury (Aryl and Inorganic compounds)	7439-97-6	neuropathic	0.1 mg/m^3 Ceiling	**(0.05 mg/m^3 TWA for Hg vapor)**	**(0.05 mg/m^3 TWA for Hg vapor)**
				0.1 mg/m^3 Ceiling	**0.1 mg/m^3 Ceiling**
Mercury (organo) alkyl compound	7439-97-6	neuropathic	0.1 mg/m^3 TWA	**0.01 mg/m^3 TWA**	**0.01 mg/m^3 TWA**
				0.3 mg/m^3 STEL	**0.3 mg/m^3 STEL**
Methylacrylonitrile	126-98-7	neuropathic	none	**1 ppm TWA**	**1 ppm TWA**
Methyl bromide	74-83-9	neuropathic	200 ppm Ceiling	**5 ppm TWA**	**potential occupational carcinogen**
Pentaborane	9624-22-7	neuropathic	0.005 ppm TWA	0.005 ppm TWA	0.005 ppm TWA
				0.015 ppm STEL	**0.015 ppm STEL**
Phenyl mercaptan	108-98-5	neuropathic	none	**0.5 ppm TWA**	**0.1 ppm Ceiling**
Propylene glycol dinitrate	6423-43-4	neuropathic	none	**0.05 ppm TWA**	**0.05 ppm TWA**
Butane	106-97-8	narcotic	none	**800 ppm TWA**	**800 ppm TWA**
sec-Butyl alcohol	78-92-2	narcotic	150 ppm TWA	**100 ppm TWA**	**100 ppm TWA**
					150 ppm STEL
tert-Butyl alcohol	75-65-0	narcotic	100 ppm TWA	100 ppm TWA	100 ppm TWA
				150 ppm STEL	**150 ppm STEL**
Cyclopentane	287-92-3	narcotic	none	**600 ppm TWA**	**600 ppm TWA**
Ethyl bromide	74-96-4	narcotic	200 ppm TWA	200 ppm TWA	<200 ppm TWA
				250 ppm STEL	
Gasoline	8006-61-9	narcotic	none	**300 ppm TWA**	**carcinogen**
				500 ppm STEL	
Heptane	142-82-5	narcotic	500 ppm TWA	**400 ppm TWA**	**85 ppm TWA**
				500 ppm STEL	**440 ppm Ceiling**
Hexane isomers	No number assigned	narcotic	none	**500 ppm TWA**	**100 ppm TWA**
				1000 ppm STEL	**510 ppm Ceiling**
Isoamyl alcohol	121-51-3	narcotic	100 ppm TWA	100 ppm TWA	100 ppm TWA
				125 ppm STEL	**125 ppm STEL**

(continued)

APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL (continued)

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
Isophorone	78-59-1	narcotic	25 ppm TWA	**4 ppm TWA**	**4 ppm TWA**
Methyl chloride	74-87-3	narcotic	100 ppm TWA 200 ppm Ceiling 300 ppm Peak	**50 ppm TWA** **100 ppm STEL**	**potential occupational carcinogen**
Methyl chloroform	71-55-6	narcotic	350 ppm TWA	350 ppm TWA **450 ppm STEL**	**350 ppm Ceiling**
Octane	111-65-9	narcotic	500 ppm TWA	**300 ppm TWA** **375 ppm STEL**	**75 ppm TWA** **385 ppm Ceiling**
Pentane	109-66-0	narcotic	1000 ppm TWA	**600 ppm TWA** **750 ppm STEL**	**120 ppm TWA** **610 ppm Ceiling**
2-Pentanone (methyl propyl ketone)	107-87-9	narcotic	200 ppm TWA	200 ppm TWA **250 ppm STEL**	**150 ppm TWA**
Stoddard solvent	8052-41-3	narcotic	500 ppm TWA	**100 ppm TWA**	**350 mg/m^3 (60 ppm) TWA** **1800 mg/m^3 (310 ppm) Ceiling**
Styrene	100-42-5	narcotic	100 ppm TWA 200 ppm Ceiling 600 ppm Peak	**50 ppm TWA** **100 ppm STEL**	**50 ppm TWA** **100 ppm STEL**
Toluene	108-88-3	narcotic	200 ppm TWA 300 ppm Ceiling 500 ppm Peak	**100 ppm TWA** **150 ppm STEL**	**100 ppm TWA** **150 ppm STEL**
Trichloroethylene	79-01-6	narcotic	100 ppm TWA 200 ppm Ceiling 300 ppm Peak	**50 ppm TWA** **200 ppm STEL**	**potential occupational carcinogen** **25 ppm TWA** **2 ppm Ceiling (1-hr waste anesthetic gas)**
Acetaldehyde	75-07-0	sensory irritation	200 ppm TWA	**100 ppm TWA** **150 ppm STEL**	**potential occupational carcinogen**
Acetic acid	64-19-07	sensory irritation	10 ppm TWA	10 ppm TWA	10 ppm TWA
Acetone	67-64-1	sensory irritation	1000 ppm TWA	**750 ppm TWA** **1000 ppm STEL**	**250 ppm TWA**
Acrolein	107-02-8	sensory irritation	0.1 ppm TWA	0.1 ppm TWA **0.3 ppm STEL**	0.1 ppm TWA **0.3 ppm STEL**
Allyl alcohol	107-18-6	sensory irritation	2 ppm TWA	2 ppm TWA **4 ppm STEL**	2 ppm TWA **4 ppm STEL**
Allyl glycidyl ether	106-92-3	sensory irritation	10 ppm Ceiling	5 ppm TWA **10 ppm STEL**	5 ppm TWA **10 ppm STEL**
Allyl propyl disulfide	2179-59-1	sensory irritation	2 ppm TWA	2 ppm TWA **3 ppm STEL**	2 ppm TWA **3 ppm STEL**
Ammonia	7664-41-7	sensory irritation	50 ppm TWA	**35 ppm STEL**	**25 ppm TWA** **35 ppm STEL**
Ammonium Chloride	12125-02-9	sensory irritation	none	**10 mg/m^3 TWA** **20 mg/m^3 STEL**	**10 mg/m^3 TWA** **20 mg/m^3 STEL**
Borates (anhydrous, decahydrate, pentahydrate)	1303-96-4 1330-43-4 12179-04-3	sensory irritation	none	**10 mg/m^3 TWA**	**1 mg/m^3 TWA (5 mg/m^3 for decahydrates)**

(continued)

APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL (continued)

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
Bromine	7726-95-6	sensory irritation	0.1 ppm TWA	0.1 ppm TWA **0.3 ppm STEL**	0.1 ppm TWA **0.3 ppm STEL**
2-Butanone (MEK)	78-93-3	sensory irritation	200 ppm TWA	200 ppm TWA **300 ppm STEL**	200 ppm TWA **300 ppm STEL**
n-Butyl acetate	123-86-4	sensory irritation	150 ppm TWA	150 ppm TWA **200 ppm STEL**	150 ppm TWA **200 ppm STEL**
n-Butyl lactate	138-22-7	sensory irritation	none	**5 ppm TWA**	**5 ppm TWA**
n-Butyl mercaptan	109-79-5	sensory irritation	10 ppm TWA	**0.5 ppm TWA**	**0.5 ppm Ceiling**
Caprolactan (dust and vapor)	105-60-2	sensory irritation	none	**dust: 1 mg/m^3 TWA** **3 mg/m^3 STEL** **vapor: 0.22 ppm TWA** **0.66 ppm STEL**	**dust: 1 mg/m^3 TWA** **3 mg/m^3 STEL** **vapor: 0.22 ppm TWA** **0.66 ppm STEL**
Cesium hydroxide	213351-79-1	sensory irritation	none	**2 mg/m^3 TWA**	**2 mg/m^3 TWA**
Chlorine	7782-50-5	sensory irritation	1 ppm Ceiling	**0.5 ppm TWA** **1 ppm STEL**	**0.5 ppm Ceiling**
Chloroacetyl chloride	79-04-9	sensory irritation	none	**0.05 ppm TWA**	**0.05 ppm TWA**
Cyanogen	460-19-5	sensory irritation	none	**10 ppm TWA**	**10 ppm TWA**
Cyanogen chloride	506-77-4	sensory irritation	none	**0.3 ppm Ceiling**	**0.3 ppm Ceiling**
Dibutyl phosphate	107-66-4	sensory irritation	1 ppm TWA	1 ppm TWA **2 ppm STEL**	1 ppm TWA **2 ppm STEL**
1,3,-Dichloro-5,5-dimethyl hydantoin	118-52-5	sensory irritation	0.2 mg/m^3 TWA	0.2 mg/m^3 TWA **0.4 mg/m^3 STEL**	0.2 mg/m^3 TWA **0.4 mg/m^3 STEL**
Dichloroethyl ether	111-44-4	sensory irritation	15 ppm Ceiling	**5 ppm TWA** **10 ppm STEL**	**potential occupational carcinogen** **5 ppm TWA**
2,2-Dichloropropionic acid	75-99-0	sensory irritation	none	**1 ppm TWA**	**1 ppm TWA**
Diethylamine	109-89-7	sensory irritation	25 ppm TWA	**10 ppm TWA** **25 ppm STEL**	**10 ppm TWA** **25 ppm STEL**
Diisobutyl ketone	108-83-8	sensory irritation	50 ppm TWA	**25 ppm TWA**	**25 ppm TWA**
Epichlorohydrin	106-89-8	sensory irritation	5 ppm TWA	**2 ppm TWA**	**potential occupational carcinogen**
Ethyl benzene	100-41-4	sensory irritation	100 ppm TWA	100 ppm TWA **125 ppm STEL**	100 ppm TWA **125 ppm STEL**
Ethyl ether	60-29-7	sensory irritation	400 ppm TWA	400 ppm TWA **500 ppm STEL**	<400 ppm TWA
Ethyl mercaptan	75-08-1	sensory irritation	10 ppm Ceiling	**0.5 ppm TWA**	**0.5 ppm Ceiling**
Ethylene glycol	107-21-1	sensory irritation	none	**50 ppm Ceiling**	**<50 ppm Ceiling**
Ethylidene norbornene	16219-75-3	sensory irritation	none	**5 ppm Ceiling**	**5 ppm Ceiling**
Furfural	98-01-0	sensory irritation	5 ppm TWA	**2 ppm TWA**	**<2 ppm TWA**
Furfural alcohol	98-00-0	sensory irritation	50 ppm TWA	**10 ppm TWA** **15 ppm STEL**	**10 ppm TWA** **15 ppm STEL**
Glutaraldehyde	111-30-8	sensory irritation	none	**0.2 ppm Ceiling**	**0.2 ppm Ceiling**
Hexachlorocyclpentadiene	77-47-4	sensory irritation	none	**0.01 ppm TWA**	**0.01 ppm TWA**
Hexylene glycol	107-41-5	sensory irritation	none	**25 ppm Ceiling**	**25 ppm Ceiling**
Hydrogen bromide	10035-10-6	sensory irritation	3 ppm TWA	3 ppm Ceiling	3 ppm Ceiling
Hydrogen fluoride	7664-39-3	sensory irritation	3 ppm TWA	3 ppm TWA **6 ppm Ceiling**	3 ppm TWA **6 ppm Ceiling**
2-Hydroxypropyl acrylate	999-61-1	sensory irritation	none	**0.5 ppm TWA**	**0.5 ppm TWA**

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APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL (continued)

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
Iron Salts (soluble)	No number assigned	sensory irritation	none	**1 mg/m^3 TWA**	**1 mg/m^3 TWA**
Isopropyl acetate	108-21-4	sensory irritation	250 ppm TWA	250 ppm TWA	<250 ppm TWA
Isopropyl alcohol	67-63-0	sensory irritation	400 ppm TWA	400 ppm TWA	400 ppm TWA
				500 ppm STEL	**500 ppm STEL**
n-Isopropylamine	75-31-0	sensory irritation	none	**2 ppm TWA**	**2 ppm TWA**
Mesityl oxide	141-79-7	sensory irritation	25 ppm TWA	**15 ppm TWA**	**10 ppm TWA**
				25 ppm STEL	
Methyl 2-cyanolacrylate	137-05-3	sensory irritation	none	**2 ppm TWA**	**2 ppm TWA**
				4 ppm STEL	**4 ppm STEL**
Methyl isobutyl carbinol	108-11-2	sensory irritation	25 ppm TWA	25 ppm TWA	25 ppm TWA
				40 ppm STEL	**40 ppm STEL**
Methyl mercaptan	74-93-1	sensory irritation	10 ppm Ceiling	**0.5 ppm TWA**	**0.5 ppm Ceiling**
Methyl n-amyl ketone	110-43-0	sensory irritation	100 ppm TWA	100 ppm TWA	100 ppm TWA
alpha-Methyl styrene	98-83-9	sensory irritation	100 ppm Ceiling	**50 ppm TWA**	**50 ppm TWA**
				100 ppm STEL	**100 ppm STEL**
o-methylcyclohexanone	583-60-8	sensory irritation	100 ppm TWA	**50 ppm TWA**	**50 ppm TWA**
				75 ppm STEL	**75 ppm STEL**
Osmium tetroxide	20816-12-0	sensory irritation	0.002 mg/m^3 TWA	0.002 mg/m^3 TWA	0.002 mg/m^3 TWA
				0.006 mg/m^3 STEL	**0.006 mg/m^3 STEL**
Paraffin wax fume	8002-74-2	sensory irritation	none	**2 mg/m^3 TWA**	**2 mg/m^3 TWA**
Phosphoric acid	7664-38-2	sensory irritation	1 mg/m^3 TWA	1 mg/m^3 TWA	1 mg/m^3 TWA
				3 mg/m^3 STEL	**3 mg/m^3 STEL**
Phosphorous trichloride	7719-12-2	sensory irritation	0.5 ppm TWA	**0.2 ppm TWA**	**0.2 ppm TWA**
				0.5 ppm STEL	**0.5 ppm STEL**
Potassium hydroxide	1310-58-3	sensory irritation	none	**2 mg/m^3 TWA**	**2 mg/m^3 TWA**
Propylene glycol mono-methyl ether	107-98-2	sensory irritation	none	**100 ppm TWA**	**100 ppm TWA**
				150 ppm STEL	**150 ppm STEL**
Rosin core solder pyrolsis	Number not assigned	sensory irritation	none	**0.1 mg/m^3 TWA**	**0.1 mg/m^3 TWA**
Sodium bisulfite	7631-90-5	sensory irritation	none	**5 mg/m^3 TWA**	**5 mg/m^3 TWA**
Sodium hydroxide	1310-73-2	sensory irritation	2 mg/m^3 TWA	**2 mg/m^3 Ceiling**	**2 mg/m^3 Ceiling**
Sodium metabisulfite	7681-57-4	sensory irritation	none	**5 mg/m^3 TWA**	**5 mg/m^3 TWA**
Sulfur monochloride	10025-67-9	sensory irritation	1 ppm TWA	**1 ppm Ceiling**	**1 ppm Ceiling**
Sulfur pentafluoride	5714-22-7	sensory irritation	0.025 ppm TWA	**0.01 Ceiling**	**0.01 Ceiling**
Tetrahydrofuran	109-99-9	sensory irritation	200 ppm TWA	200 ppm TWA	200 ppm TWA
				250 ppm STEL	**250 ppm STEL**
Tetrasodium pyrophosphate	7722-88-5	sensory irritation	none	**5 mg/m^3 TWA**	**5 mg/m^3 TWA**
Thioglycolic acid	68-11-1	sensory irritation	none	**1 ppm TWA**	**1 ppm TWA**
1,2,4-Trichlorobenzene	120-82-1	sensory irritation	none	**5 ppm Ceiling**	**5 ppm Ceiling**
Triethylamine	121-44-8	sensory irritation	25 ppm TWA	**10 ppm TWA**	**<10 ppm TWA**
				15 ppm STEL	
Vanadium (V_2O_5) dust and fume	1314-62-1	sensory irritation	0.5 mg/m^3 Ceiling	**0.05 mg/m^3 Ceiling**	**0.05 mg/m^3 Ceiling**
Vinyl acetate	108-05-4	sensory irritation	none	**10 ppm TWA**	**4 ppm Ceiling**
				20 ppm STEL	

(continued)

APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL (continued)

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
VM and P naphtha	8032-32-4	sensory irritation	none	**1350 mg/m³ TWA**	**350 mg/m³ Ceiling**
				1800 mg/m³ STEL	
Xylenes	1330-20-7	sensory irritation	100 ppm TWA	100 ppm TWA	100 ppm TWA
				150 ppm STEL	**150 ppm STEL**
Zinc chloride	7646-85-7	sensory irritation	1 mg/m³ TWA	1 mg/m³ TWA	1 mg/m³ TWA
				2 mg/m³ STEL	**2 mg/m³ STEL**
			By Analogy		
Acetic anhydride	108-24-7	sensory irritation	5 ppm TWA	**5 ppm Ceiling**	**5 ppm Ceiling**
Acrylic acid	79-10-7	sensory irritation	none	**10 ppm TWA**	**2 ppm TWA**
Boron tribromide	10294-33-4	sensory irritation	none	**1 ppm Ceiling**	**1 ppm Ceiling**
n-Butyl acrylate	141-32-2	sensory irritation	none	**10 ppm TWA**	**10 ppm TWA**
Calcium hydroxide	1305-62-0	sensory irritation	5 mg/m³ TWA (respirable dust)		5 mg/m³ TWA (respirable dust)
Calcium oxide	1305-78-8	sensory irritation	5 mg/m³ TWA		**2 mg/m³ TWA**
Carbonyl fluoride	353-50-4	sensory irritation	none	**2 ppm TWA**	**2 ppm TWA**
				5 ppm STEL	**5 ppm STEL**
p-Dichlorobenzene	106-46-7	neuropathic	75 ppm TWA	75 ppm TWA	**potential occupational carcinogen**
				110 ppm STEL	
Diethyl ketone	96-22-0	narcotic effects	none	**200 ppm TWA**	**200 ppm TWA**
Divinyl benzene	108-57-6	sensory irritation	none	**10 ppm TWA**	**10 ppm TWA**
Endosulfan	115-29-7	neuropathic	none	**0.1 mg/m³ TWA**	**0.1 mg/m³ TWA**
Fonofos	949-22-9	neuropathic	none	**0.1 mg/m³ TWA**	**0.1 mg/m³ TWA**
Indene	95-13-6	sensory irritation	none	**10 ppm TWA**	**10 ppm TWA**
Dipropyl ketone	123-19-3	narcotic effects	none	**50 ppm TWA**	**50 ppm TWA**
Isobutyl alcohol	78-83-1	narcotic effects	100 ppm TWA	**50 ppm TWA**	**50 ppm TWA**
Isooctyl alcohol	26952-21	sensory irritation	none	**50 ppm TWA**	**50 ppm TWA**
Ketene	463-51-4	sensory irritation	0.5 ppm TWA	**0.5 ppm TWA**	**0.5 ppm TWA**
				1.5 ppm STEL	**1.5 ppm STEL**
Methacrylic acid	79-41-4	sensory irritation	none	**20 ppm TWA**	**20 ppm TWA**
Methyl ethyl ketone peroxide	1338-23-4	sensory irritation	none	**0.7 ppm Ceiling**	**0.2 ppm Ceiling**
Methyl formate	107-31-3	sensory irritation	100 ppm TWA	100 ppm TWA	100 ppm TWA
				150 ppm STEL	**150 ppm STEL**
Methyl iodide	74-88-4	neuropathic	5 ppm TWA	**2 ppm TWA**	**potential occupational carcinogen**
					2 ppm TWA
Methyl isoamyl ketone	110-12-3	neuropathy	100 ppm TWA	**50 ppm TWA**	**50 ppm TWA**
Methyl isopropyl ketone	563-80-4	sensory irritation, narcotic effects	none	**200 ppm TWA**	**200 ppm TWA**
Methyl parathion	298-00-0	neuropathy	none	**0.2 ppm TWA**	**0.2 ppm TWA**
Nitric acid	7697-37-2	sensory irritation	2 ppm TWA	2 ppm TWA	2 ppm TWA
				4 ppm STEL	**4 ppm STEL**
Nonane	111-84-2	narcotic effects	none	**200 ppm TWA**	**200 ppm TWA**
n-Propyl acetate	109-60-4	sensory irritation	200 ppm TWA	200 ppm TWA	200 ppm TWA
				250 ppm STEL	**250 ppm STEL**
Phosdrin	7786-34-7	neuropathic	0.1 mg/m³ TWA (0.01 ppm)	0.01 ppm TWA	0.01 ppm TWA
				0.03 ppm TWA	0.03 ppm TWA
Propargyl alcohol	107-19-7	sensory irritation	none	**1 ppm TWA**	**1 ppm TWA**

(continued)

APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL (continued)

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
n-Propyl alcohol	71-23-8	sensory irritation	200 ppm	200 ppm TWA **250 ppm STEL**	200 ppm TWA **250 ppm STEL**
Propylene oxide	75-56-9	narcotic effects	100 ppm TWA	**20 ppm TWA**	**potential occupational carcinogen**
Tributyl phosphate	120-73-8	narcotic effects	5 mg/m^3 TWA	**0.2 ppm TWA**	**0.2 ppm TWA (2.5 mg/m^3)**
Trichloroacetic acid	76-03-9	sensory irritation	none	**1 ppm TWA**	**1 ppm TWA**
Trimethylamine	75-50-3	sensory irritation	none	**10 ppm TWA** **15 ppm STEL**	**10 ppm TWA** **15 ppm STEL**
n-Valeraldehyde	110-62-3	sensory irritation	none	**100 ppm TWA** **150 ppm STEL**	**50 ppm TWA**
Isopropyl ether	108-20-3	odor effects	500 ppm TWA	**500 ppm TWA**	**500 ppm TWA**
Phenyl ether	108-84-8	odor effects	1 ppm TWA	**1 ppm TWA**	**1 ppm TWA**
Vinyl toluene	25013-15-4	odor effects	100 ppm TWA	**100 ppm TWA**	**100 ppm TWA**
			Other Primary Basis		
Acrylamide	79-06-1	cancer/neuropathy	0.3 mg/m^3 TWA	**0.03 mg/m^3 TWA**	**potential occupational carcinogen** **0.03 mg/m^3 TWA**
p-tert-Butyl toluene	98-51-1	cardiovascular/narcotic and sensory irritation	10 ppm TWA	10 ppm TWA **20 ppm STEL**	10 ppm TWA **20 ppm STEL**
Methyl acetate	77-20-9	NOAEL/narcotic and physical irritation	200 ppm TWA	200 ppm TWA **250 ppm STEL**	200 ppm TWA **250 ppm STEL**
Chlorodifluoromethane	75-45-6	NOAEL/CNS depression and stimulation	none	**1000 ppm TWA** **1250 ppm TWA**	**1000 ppm TWA** **1250 ppm TWA**
Dicyclopentadiene	77-73-6	liver and kidney/sensory irritation	none	**5 ppm TWA**	**5 ppm TWA**
Hydrogen cyanide	74-90-8	systemic/CNS effects	10 ppm TWA	**4.7 ppm STEL**	**4.7 ppm STEL**
Carbon monoxide	630-08-0	cardiovascular/CNS depression	50 ppm TWA	**35 ppm TWA** **200 ppm Ceiling**	**35 ppm TWA** **200 ppm Ceiling**
Isopropyl glycidyl ether	4016-14-2	systemic/CNS effects	50 ppm TWA	50 ppm TWA **75 ppm STEL**	**50 ppm Ceiling**
Ethanolamine	141-43-5	systemic/neuropathic	3 ppm TWA	3 ppm TWA **6 ppm STEL**	3 ppm TWA **6 ppm STEL**
o-Chlorostyrene	2039-87-4	liver and kidney/narcotic and neuropathic	none	**50 ppm TWA** **75 ppm STEL**	**50 ppm TWA** **75 ppm STEL**
Methylcyclohexanol	25639-42-3	liver and kidney/narcotic	100 ppm TWA	**50 ppm TWA**	**50 ppm TWA**
Perchloroethylene	127-18-4	cancer/narcotic	100 ppm TWA 200 ppm STEL 300 ppm Ceiling	**25 ppm TWA**	**potential occupational carcinogen**
2-Methylcyclo-pentadienyl manganese tricarbonyl	12108-13-3	analogy/CNS effects		**0.2 mg/m^3 TWA**	**0.2 mg/m^3 TWA**
Phenyl glycidyl ether	122-60-1	sensitization/CNS effects	10 ppm TWA	**1 ppm TWA**	**potential occupational carcinogen** **1 ppm Ceiling**
Tributyl phosphate	126-73-8	analogy/narcotic	5 mg/m^3 TWA	**2.5 mg/m^3 TWA**	**0.2 ppm TWA (2.5 mg/m^3)**
Ethylene dichloride	107-06-2	liver and kidney/CNS effects	50 ppm TWA 100 ppm STEL 200 ppm Ceiling	**1 ppm TWA** **2 ppm STEL**	**potential occupational carcinogen** **1 ppm TWA** **2 ppm STEL**
Ethylene chlorohydrin	107-07-3	systemic/CNS effects	5 ppm TWA	5 ppm TWA **1 ppm Ceiling**	**1 ppm Ceiling**

(continued)

APPENDIX. Table Listing Chemicals Regulated for Nervous System Effects Showing Current OSHA PEL, 1989 Proposed PEL and Current NIOSH REL (continued)

Chemical	CAS #	Primary basis	Current OSHA PEL	1989 OSHA proposed PEL	NIOSH REL
Cyclohexanone	108-94-1	liver and kidney/CNS effects	50 ppm TWA	**25 ppm TWA**	**25 ppm TWA**
Hexone (MIBK)	108-10-1	liver and kidney/CNS effects	100 ppm TWA	**50 ppm TWA** **75 ppm STEL**	**50 ppm TWA** **75 ppm STEL**
Carbofuran	1563-66-2	cholinesterase inhibition/CNS effects	none	**0.1 mg/m^3 TWA**	**0.1 mg/m^3 TWA**
Chlorpyrifos	2921-88-2	cholinesterase inhibition/CNS effects	none	**0.2 mg/m^3 TWA** **0.6 mg/m^3 STEL**	**0.2 mg/m^3 TWA** **0.6 mg/m^3 STEL**
Dimethylaniline	121-69-7	methemoglobinemia/ neuropathic	5 ppm TWA	5 ppm TWA **10 ppm STEL**	5 ppm TWA **10 ppm STEL**

*The following table is extracted from the NIOSH Pocket Guide to Chemical Hazards and compares the current OSHA PELs to the PELs proposed in the Air Contaminants Project and the current NIOSH RELs. Values in **bold** represent lower concentrations or new limits from the current OSHA PELs. Values underlined represent proposed limits different from the 1989 proposed PELs. The descriptors on the numerical limits are: TWA = Time Weighted Average concentrations that must not be exceeded during any workshift (day) of a 40 hour workweek (OSHA PEL-8-hour work shift; NIOSH REL-10-hour workday); STEL = Short Term Exposure Limit, the average exposure over a 15 minute period that should not be exceeded at any time during a workday; Ceiling = Ceiling exposure not to be exceeded during the workshift (day); PEAK = an acceptable excursion above the ceiling for a brief time period as described in 29 CFR 1900, Table Z2; NOAEL = Concentration at which no toxic effects are evident at the PEL; Carcinogen = classified as potential occupational carcinogens and for most substances 100% effective thresholds have not been identified (NIOSH recommends that exposures be limited to the lowest feasible concentration). Readers wishing more detailed descriptions should consult 29 CFR 1900, Table Z2, The ACGIH TLV Documentation, or the NIOSH Pocket Guide to Chemical Hazards.