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**TOXICOMETRIC PARAMETERS
OF INDUSTRIAL
TOXIC CHEMICALS
UNDER SINGLE EXPOSURE**

**by N.F. Izmerov, I.V. Sanotsky
and K.K. Sidorov**

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This book is intended for toxicologists, hygienists and those responsible for evaluation and control of harmful effects of chemicals to human health and the environment.

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PREFACE TO THE ENGLISH EDITION

The translation and publication of this book has been carried out at the Centre of International Projects under the State Committee of the USSR for Science and Technology in cooperation with the Research Institute of Industrial Hygiene and Occupational Diseases within the framework of the USSR—UNEP/IRPTC Project «Control of Hazards posed by Chemicals to Human Health and the Environment».

For those who are insufficiently familiar with the terminology used by Soviet toxicologists, we explain below some terms and concepts in addition to those defined in the preface to the Russian edition. These definitions do not necessarily reflect the views or official policies of UNEP.

A harmful substance is a substance human exposure to which (at work or in everyday life) may cause disease or deviation from a normal state of health detectable by currently available methods of investigation during the period of exposure or in the long term, in this or subsequent generations.

The tentative safe exposure level (TSEL) is a temporary hygienic standard specifying the level of a harmful substance in worksite air, the ambient air of residential areas, or water bodies. It is arrived at by calculation from parameters of toxicometry and physicochemical properties on the basis of regression correlations or by inter- or extrapolation in series of structurally related compounds. TSEL values are subject to approval by the USSR Ministry of Health and remain valid for a limited period of time (2 or 3 years), after which they may be replaced by maximum allowable concentrations, declared valid for another period of time, or abolished depending on prospects for the further use of the substances concerned and the available information regarding their toxic properties.

By the time of publication of this book, the USSR Ministry of Health had approved the following MACs not included in the Russian edition (these are marked by asterisk in the body of the text):

(a) Air of the working zone

| Substance | MAC, mg/m ³ | Predominant physical state | Hazard class |
|-------------------------|---------------------------|----------------------------------|-----------------|
| Benzine, solvent (as C) | 100 | vapour | IV |
| Hexamethylene diamine | 0.1 | vapour | I |
| Hydrogen fluoride | 0.05 | vapour | I |
| Nickel (metallic) | 0.05 | aerosol | I |

(b) The atmosphere of residential areas

| Substance | MAC, mg/m ³ | | Hazard class |
|----------------------|------------------------|------------------|-----------------|
| | highest mo- mentary | average daily | |
| Ammonia | 0.2 | 0.04 | IV |
| Benzene | 1.5 | 0.1 | II |
| Carbon monoxide | 5.0 | 3.0 | IV |
| Carbon tetrachloride | 4.0 | 0.7 | II |
| Nitrogen dioxide | 0.085 | 0.04 | II |

(c) Water bodies used for watersupply,
public, and/or recreational purposes
(water bodies of «sanitary-domestic uses»)

| Substance | MAC, mg/l |
|---------------|--------------|
| β-Chloroprene | 0.01 |

The Compilers, 1982

PREFACE TO THE RUSSIAN EDITION

This Handbook summarizes the data available in the Soviet literature regarding the toxicity and hazards shown after single exposure by chemicals widely employed in industry. It gives lethal and threshold doses or concentrations of more than 700 industrial toxic chemicals for laboratory animals with various routes of absorption, including inhalation, gastric intubation, intraabdominal injection, skin application, etc. The main actions of the chemicals are specified, as are the detection methods used. Where known, thresholds of irritant action on the mucous membranes of the upper respiratory tract and of the eyes and thresholds of odour for man are also given. The officially approved values of maximum allowable concentrations (MAC) of toxic chemicals for the air of workplaces and residential areas and for water bodies are presented. For a number of chemicals, tentative safe exposure levels (TSEL) are given. References to the literature used in compiling this Handbook are appended.

The Handbook is intended for a wide range of practical and research workers professionally concerned with harmful chemicals (toxicologists, occupational health physicians, hygienists, biochemists, etc.).

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INTRODUCTION

The toxicometric parameters included in this Handbook have been taken from the literature published in the USSR and partly from the material available in the Section on Establishment of Maximum Allowable Concentrations (MAC) for Harmful Substances in the Air of Working Zones of the All—Union Problem Commission on the Scientific Basis of Occupational Health. Unlike most other reference works concerned with lethal doses and concentrations, this Handbook gives also results of determination of thresholds of harmful effects, knowledge of which is considered essential for adequate validation of preventive measures. On the other hand, it was felt that a mere listing of hygienic standards (MAC) without presentation of at least some of the material on the basis of which they were derived, would reduce the usefulness of this reference book.

The Handbook presents values of lethal and threshold concentrations (doses) for more than 700 toxic industrial chemicals when these are administered by various routes — by inhalation, into the stomach, under the skin, into the abdominal cavity, intravenously, and on the skin — to laboratory animals most commonly used in toxicological studies, namely mice, rats, guinea pigs, rabbits, and cats. In most instances, precise lethal doses and concentrations for man have not been established, but the following guidelines will be helpful of extrapolation of animal data to man:

1. If the lethal doses for the four most commonly used species of laboratory rodents differ insignificantly (less than threefold), the probability is high (about 70%) that the lethal dose for man will be of the same order of magnitude (Ulanova et al., 1969).

2. An approximate lethal dose for man can be calculated by plotting a regression line using several data points in the following system of coordinates: (a) the lethal dose for a particular animal species and (b) the body weight of an adult individual of that species (Krasovsky, 1973).

For threshold values, the indices (procedures) on the basis of which these values have been established are given.

For a number of substances, single exposure thresholds for man as estimated from the irritant effect on the mucous membranes

of the upper respiratory tract and the eyes or from the effect on the organ of smell are presented. Unless otherwise stated, the data for chemicals have been obtained under standard conditions (Annex I).

To facilitate the use of this book, the material is arranged in tabular form. The chemicals are listed in alphabetical order. The names of chemicals are generally presented in accordance with the Geneva Nomenclature. In addition, the more widely used trade names are included and chemical formulas of the substances are shown as well.

The officially approved MAC values in the air of working zones are given where available, with indication of the predominant physical state (state of aggregation) of the substance concerned in the air of industrial premises and the class of hazard posed by the substance to man according to the State Standard GOST 12.1.005-76 entitled «System of Occupational Safety Standards. The air of Working Zones. General Sanitary and Hygienic Requirements». The maximum permissible values of harmful substances in the atmosphere of residential areas and in water bodies used for sanitary, domestic, and recreational purposes are presented in accordance with the Sanitary Standard SN 246-71 entitled «Sanitary Norms for the Design of Industrial Enterprises» and addenda thereto approved by the Chief State Sanitary Physician of the USSR. As regards substances for which no official MAC values exist as yet, tentative safe exposure levels (TSELs) in worksite air, the atmosphere of residential areas, and water are presented.

To make it easier for the reader to appraise the toxicometric parameters, a classification of industrial chemicals by hazard at lethal and threshold exposure levels (State Standard GOST 12.1.007-76: «System of Occupational Safety Standards. Harmful Substances. Classification and General Safety Requirements») is appended (Annex II), as is a classification of substances by toxicity with subcutaneous and intraabdominal administration (Annex III).

There is an index of chemicals included in the book and a complete list of the literature consulted in compiling the latter; this list may also serve as a source of references to the Soviet literature in the field of industrial toxicology. The information relating to toxic properties of chemical compounds has been prepared in cooperation with Dr. V. S. Pozdniakov and that relating to the detection methods used, in cooperation with Dr. L. T. Poddubnaya. The authors wish to express their gratitude to Dr. A. I. Khalepo for assistance in manuscript preparation.

In conclusion, we are well aware that this reference work is not devoid of flaws, but these were inevitable because of gaps in our knowledge concerning thresholds of harmful action of substances and experimental conditions. We will appreciate any criticisms and suggestions.

KEY TO ABBREVIATIONS AND SYMBOLS

- LD₅₀ (LD₁₀₀)** The dose of a given chemical which kills 50% (100%) of the test animals after its single administration into the stomach or abdominal cavity, application to the skin, etc. (with the exception of the inhalational route) under defined conditions and within a specified period (usually 2 weeks)¹; it is stated in milligrams of the chemical per kilogram of animal body weight (mg/kg).
- ND₅₀** The dose of a given chemical which produces narcosis in 50% of the test animals, stated in milligrams of the chemical per kilogram of animal body weight (mg/kg).
- D** The lethal dose of a given chemical¹, stated in milligrams of the chemical per kilogram of animal body weight (mg/kg).
- ND** The narcotic dose of a given chemical¹, stated in milligrams of the chemical per kilogram of animal body weight (mg/kg).
- LT₅₀** The time of exposure to a given chemical applied to the skin during which 50% of the test animals die; it is given in minutes in this handbook.
- LC₅₀ (LC₁₀₀)** The concentration of a given chemical which is lethal to 50% (100%) of the test animals with exposure by inhalation under defined conditions and within a specified period¹; it is stated in milligrams of the chemical per cubic meter of air (mg/m³); the exposure time is also indicated.
- NC₅₀** The concentration of a given chemical producing narcosis in 50% of the test animals, stated in milligrams of the chemical per cubic meter of air (mg/m³).
- LC** The lethal concentration of a given chemical¹, stated in milligrams of the chemical per cubic meter of air (mg/m³).
- NC** The narcotic concentration of a given substance¹, stated in milligrams of the chemical per cubic meter of air (mg/m³).
- Lim_{ac}** The threshold of acute effect, i. e., the lowest concentration (dose) of a given substance that causes such a change in a particular biochemical index in a whole organism which is

¹ The quantities LC₁₀₀, LD₁₀₀, LC, LD, NC, and ND have no statistical significance and are given only for guidance.

beyond the latter's capacity for physiological adaptation. The index on the basis of which this threshold has been established is designated by a figure in parentheses. The figures stand for the following indices¹:

- (1) Summated threshold index
- (2) Flexor reflex
- (3) Galvanic skin reflex
- (4) Conditioned reflexes
- (5) Electroencephalogram
- (6) Chronaxie of antagonist muscles
- (7) Respiratory rate
- (8) Oxygen consumption by whole animal
- (9) Vital staining of lung tissue
- (10) Weight coefficients of internal organs
- (11) Rectal temperature
- (12) Working capacity
- (13) Working capacity as estimated in an error correction test
- (14) Working capacity of frog gastrochemius muscle
- (15) Spontaneous motor activity
- (16) Methemoglobinemia
- (17) Blood leukocyte count
- (18) Leukocyte formula of the blood
- (19) Blood reticulocyte count
- (20) Blood catalase activity
- (21) Transferrin index of the blood
- (22) Acid resistance of erythrocytes
- (23) Number of Heinz bodies in the blood
- (24) Blood cholinesterase activity
- (25) Blood peroxidase activity
- (26) Arterial blood pressure
- (27) Morphological changes in formed elements of the blood
- (28) Hypersalivation
- (29) Lacrimation
- (30) Urinary excretion of fluorescein
- (31) Urinary level of chlorides
- (32) Change in spermatogenesis
- (33) Morphological changes in internal organs
- (34) Blood level of pyruvic acid
- (35) Phagocytic index
- (36) Blood level of sugar
- (37) Blood level of sulfhydryl groups
- (38) Urinary level of 17-ketosteroids
- (39) Blood phosphatase activity
- (40) Blood aldolase activity

¹ Only the names of the indices are listed. The specific procedures used to derive these are described in the cited literature; see also the section «How to Use this Book».

- (41) Biliary level of cholic acid
- (42) Urinary level of hippuric acid
- (43) Activity of glutamic acid decarboxylase in the cerebral hemispheres

Lim_{ir} The threshold of irritant action of a given chemical on the mucous membranes of the upper airways and eyes, stated in milligrams of the chemical per cubic meter of air (mg/m^3). The figures in parentheses denote the same indices as for **Lim_{ac}**. Values for man are based on subjective sensations for exposures lasting 1 minute unless stated otherwise.

Lim_{olf} The olfactory threshold of action of a given chemical, stated in milligrams of the chemical per cubic meter of air (mg/m^3).

MAC_{wz} The maximum allowable concentration of a harmful substance in the air of the working zone is the concentration that, in the case of daily exposure in work conditions for eight hours daily (with the exception of non-working days) or during another period, but not more than 41 hours per week, throughout the entire working life, will not cause any disease or deviations from a normal state of health detectable by currently available methods of investigation, either during the work itself or in the long term, in this and subsequent generations.

The working zone is defined as the space up to 2 m above the level of the floor or of the site which is the place where the workers are permanently or temporarily employed.

MAC_{hm} The highest momentary (single-occasion) maximum allowable concentration of a given chemical in the atmosphere of residential areas, stated in milligrams of the chemical per cubic meter of air (mg/m^3).

MAC_{ad} The average daily maximum allowable concentration of a given chemical in the atmosphere of residential areas, stated in milligrams of the chemical per cubic meter of air (mg/m^3).

MAC_w The maximum allowable concentration of a given chemical in bodies of water of «sanitary—domestic uses» (i. e., those used for water-supply, public, and/or recreational purposes), stated in milligrams of the chemical per litre of water (mg/l).

TSEL_{wz} The tentative safe exposure level of a given chemical in the air of working zones, stated in milligrams of the chemical per cubic meter of air (mg/m^3).

TSEL_{hm} The highest momentary (single-occasion) tentative safe exposure level of a given chemical in the atmosphere of residential areas, stated in milligrams of the chemical per cubic meter of air (mg/m^3).

TSEL_{ad} The average daily tentative safe exposure level of a given chemical in the atmosphere of residential areas, stated in milligrams of the chemical per cubic meter of air (mg/m^3).

TSEL_w The tentative safe exposure level of a given chemical in bodies of water of «sanitary-domestic uses» (i. e., those used for water-supply, public, and/or recreational purposes), stated in milligrams of the chemical per litre of water (mg/l).

+ The chemical is dangerous when absorbed through intact skin

v Vapour and/or gas

a Aerosol

v+a A mixture of vapour and aerosol

< This sign means that the indicated dose or concentration is not lethal to the animals. For example, in the case of intragastric administration of 4,4-azobenzenedicarboxylic acid, LD<10,000; this means that the dose of 10,000 mg/kg did not kill the animals with this route of administration.

HOW TO USE THIS HANDBOOK

In the column «Substance, MAC, TSEL, Hazard Class, Reference (s)», the chemicals are ordered alphabetically. References to the References section at the end of the book are designated by figures.

In the column «Toxicometric parameters, Test Conditions, Action(s), Method(s) of Detection» (in air), the figures in parentheses refer to the indices used in establishing threshold concentrations (doses).

Here is an example illustrating the complete description (without abbreviations and symbols) for one of the entries (see also p. 16).

Aniline (aminobenzene, phenylamine)+



The MAC for the air of the working zone is 0.1 mg/m³, vapour, Hazard class II.

The highest momentary MAC for the atmosphere of residential areas is 0.05 mg/m³.

The average daily MAC for the atmosphere of residential areas is 0.03 mg/m³.

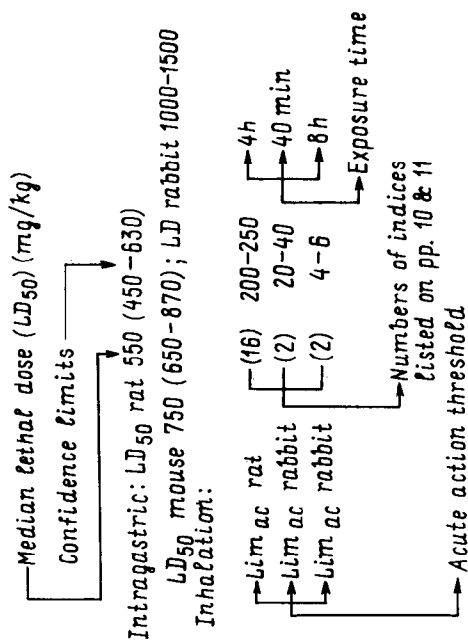
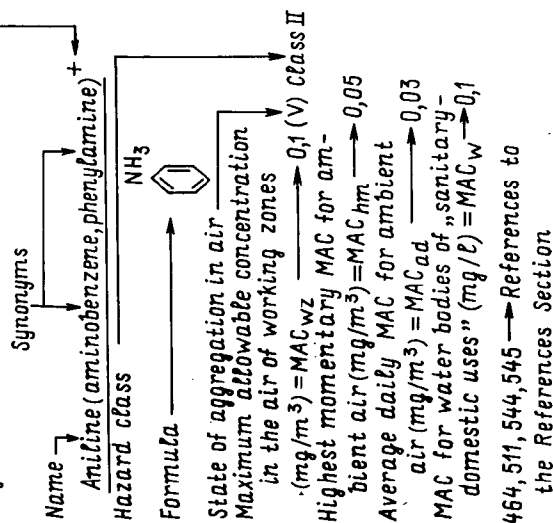
The MAC for water bodies of «sanitary-domestic uses» is 0.1 mg/l.

The figures 464, 511, 544 and 545 denote the references used

With intragastric administration, the median lethal dose is 550(450—630) mg/kg for rats and 750(650—870) mg/kg for mice; the lethal dose for rabbits is 1000—1500 mg/kg.

With exposure by inhalation, the threshold for rats is 200—250 mg/m³ with 4-hour exposure as estimated from changes in the blood level of methemoglobin; the threshold for rabbits is 20—40 mg/m³ with 40-min exposure and 4—6 mg/m³ with 8-hour exposure, and both these thresholds were estimated from changes in the flexor reflex.

This sign means that the substance is dangerous when absorbed via intact skin -



TOXICOMETRIC PARAMETERS

| Substance, MAC or TSEL, Hazard Class Reference(s) | Toxicometric Parameters, Test Conditions, Action(s), Methods(s) of Detection |
|---|--|
| <p>Acetaldehyde (acetic aldehyde, ethanal)</p> $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3 - \text{C} - \text{H} \end{array}$ <p>MAC_{wz} 5 (v), Class III MAC_{hm} 0.01 MAC_{ad} 0.2 89,465</p> | <p>Intravenous: ND mouse 350—400, ND rabbit 90—100 Has irritant properties Detection: colorimetry; detection limit 2.5 µg in analytical volume</p> |
| <p>Acetaldehyde tetramer (metaldehyde)</p> $\begin{array}{c} \text{CH}_3\text{HC} \text{---} \text{O} \text{---} \text{C} \text{---} \text{H} \\ \quad \\ \text{O} \quad \text{O} \\ \quad \\ \text{CH}_3\text{HC} \text{---} \text{O} \text{---} \text{C} \text{---} \text{H} \end{array}$ <p>MAC_{wz} 0.2 (a), Class II MAC_{hm} 0.03 MAC_{ad} 0.003 75</p> | <p>Intragastric: LD₅₀ mouse 200 (160—239)¹, LD₅₀ rat 227 (149—304)¹, LD₅₀ guinea pig 175 (101—248), LD₅₀ rabbit 290 (141—438), LD₅₀ cat 207 On skin: LD₅₀ rat 2275 Inhalation: LC₅₀ mouse 348 (182—515) 2 h, LC₅₀ rat 203 (139—270) 4 h; Lim_{ac} rat 10 4 h (6)</p> |
| <p>Acetone (propanon, dimethylketone)</p> CH_3COCH_3 <p>MAC_{wr} 200 (v), Class IV MAC_{hm} 0.35 MAC_{ad} 0.35 143, 244, 467</p> | <p>Inhalation: LC mouse 150 000 2h; Lim_a rabbit 1000—2500 40 min (2) Narcotic Detection: gas—liquid chromatography; detection limit 0.1 µg in analytical volume</p> |
| <p>Acetone cyanohydrin (CH₃)₂C(OH)CN</p> <p>MAC_{wr} 0.9 (v), Class II MAC_w 0.001 17</p> | <p>Intragastric: LD₅₀ mouse 30 Inhalation: LC₅₀ mouse 70 2h, LC₄₀ rat 185 2h Affects respiratory centre Detection: colorimetry; detection limit 0.1 µg in analytical volume</p> |

¹ Technical — grade product

| Substance, MAC or TSEL, Hazard Class Reference(s) | Toxicometric Parameters, Test Conditions, Action(s), Method(s) of Detection |
|--|---|
| Acetonitrile (methyl cyanide) $\text{H} \backslash$ $\text{H}-\text{C}=\text{C}=\text{N}$ $\text{N} /$ MAC _{wz} 10 (v), Class III MAC _w 0.7 312 | Intragastric: LD ₅₀ mouse 1670 (1450—1890), LD ₅₀ rat 5900 (4580—7220) Subcutaneous: LD ₅₀ mouse 4480 (3520—5400), LD ₅₀ rat 3500 (2560—4440) Intraabdominal: LD ₅₀ mouse (2950—3410), LD ₅₀ rat 1100 (700—1500) Intravenous: LD ₅₀ mouse 612 (278—946), LD ₅₀ rat 2800 (2450—3150) Inhalation: LC ₅₀ mouse 15 300 (13 900—16 300) 2h, LC ₅₀ rat 22 000 (20 300—23 700) 4h, LC ₅₀ cat 18 000 (13 700—22 300); Lim _{ac} rat 340 4h (4) Affects respiratory centre Detection: colorimetry; detection limit 0.003 µg per 10 ml of solution |
| Acetophenone (methyl phenyl ketone) $\text{C}_6\text{H}_5-\text{CO}-\text{CH}_3$ MAC _{wz} 5 (v), Class III MAC _{hm} 0.003 MAC _{ad} 0.003 MAC _w 0.1 222, 264 | Intragastric: LD ₅₀ mouse 1350 (1030—1510), LD ₅₀ rat 2650 (1850—3780) Inhalation: mouse, LC mouse <250 2h, Lim _{ac} rabbit 100—150 40 min, (2), Lim _{ir} man 35 Has irritant action Detection: colorimetry; detection limit 1 µg in analytical volume |
| Acetopropyl acetate $\text{CH}_3\text{COCH}_2\text{CH}_2\text{CH}_2\text{OCOCH}_3$ MAC _{wz} 5 (v), Class III 321, 469 | Intragastric: LD ₅₀ rat 6080 (5333—6931) Inhalation: Lim _{ac} rat 150 4h (1,8) Narcotic |
| Acetopropyl alcohol $\text{CH}_3\text{COCH}_2\text{CH}_2\text{CH}_2\text{OH}$ MAC _{wz} 10 (v), Class III 321 | Detection: colorimetry; detection limit 10 µg in analytical volume Intragastric: LD ₅₀ rat 6750 (4410—9280) Inhalation: Lim _{ac} rat 300 4h (8, 11) Narcotic |
| Acrylic acid $\text{CH}_2=\text{CHCOOH}$ MAC _{wz} 5 (v), Class III MAC _w 0.5 15, 465 | Intragastric: LD ₅₀ rat 33.5±4 Inhalation: LC ₅₀ mouse 5300±500 2h; Lim _{ac} mouse 300 40 min (1); Lim _{ir} man 40 Has irritant action Detection: colorimetry; detection limit 1 µg in analytical volume |
| Acrylonitrile+ $\text{CH}_2=\text{CHCN}$ MAC _{wz} 0.5 (v), Class II MAC _{ad} 0.003 MAC _w 312, 536 | Intragastric: LD ₁₀₀ rat 150 Inhalation: LC ₁₀₀ mouse 800 1h, LC ₁₀₀ rat 5300 1h Blocks respiratory enzyme; paralyzes respiratory and vasomotor centres Detection: colorimetry; detection limit 0.3 mg/m ³ |