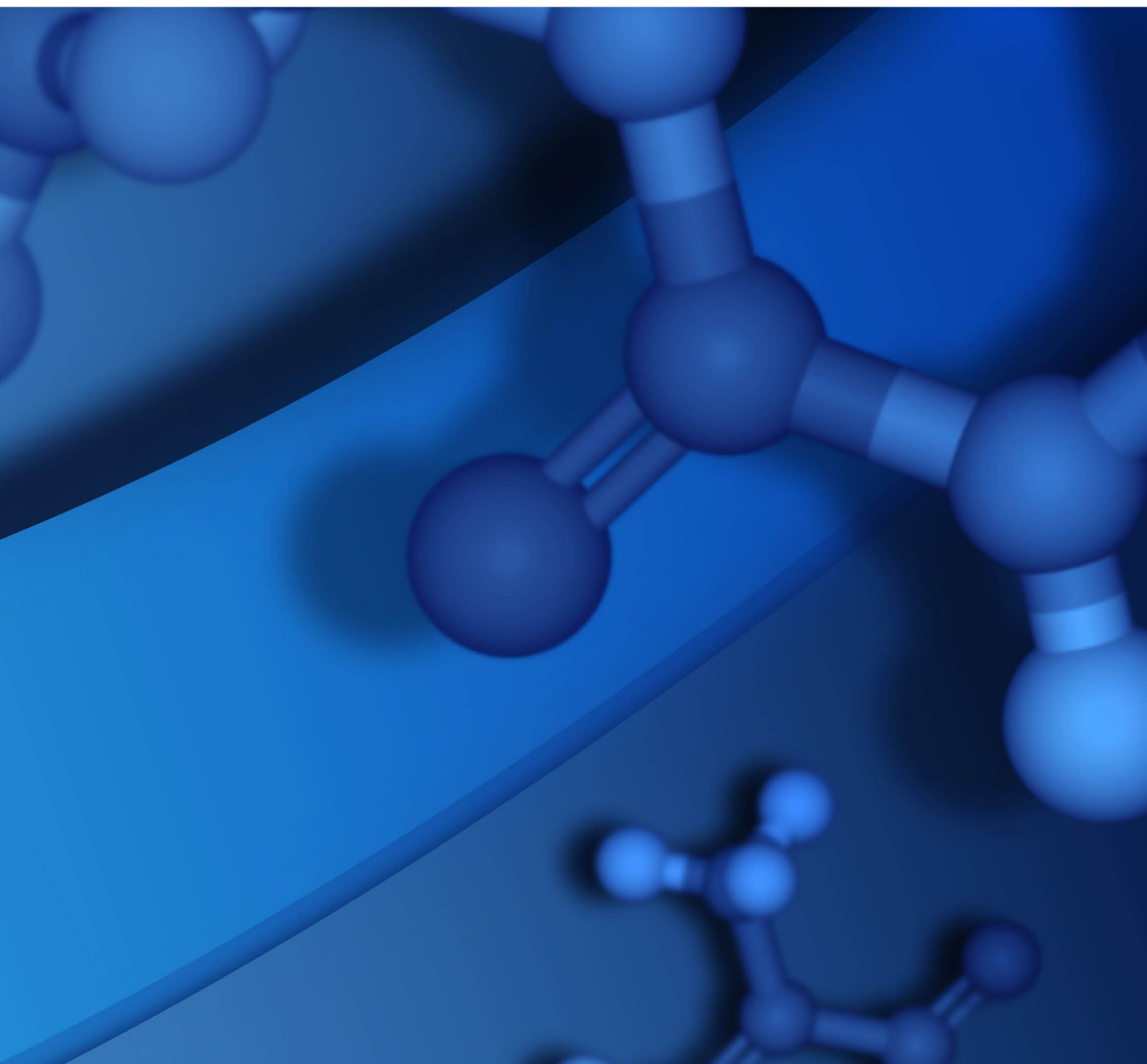


# COMPREHENSIVE GUIDE

BIOVIA REGISTRY OF TOXIC EFFECTS OF CHEMICAL  
SUBSTANCES



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# Contents

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<b>Introduction</b> .....	<b>1</b>
RTECS Data Selection, Evaluation, and Use .....	1
General Comments .....	2
<b>Detailed File Description</b> .....	<b>3</b>
Substance Selection .....	3
Format .....	3
Substance Prime Name (Data Type A) .....	4
Update (Data Type E) .....	4
Chemical Registry Number (Data Type D) .....	4
RTECS Number (Data Type G) .....	4
Molecular Weight (MW) (Data Type H) .....	5
Molecular Formula (MF) (Data Type F) .....	5
Wiswesser Line Notation (WLN) (Data Type J) .....	5
Synonyms (Data Type L) .....	5
Compound Descriptor Codes (Data Type N) .....	6
Tumorigen (C) .....	7
Reproductive Effector (T) .....	7
Mutagen (M) .....	7
Primary Irritant (S) .....	7
Human Data .....	8
Other Descriptors .....	8
Skin and Eye Irritation Data (Data Type P) .....	8
Primary Skin Irritation .....	8
Primary Eye Irritation .....	10
Species Exposed .....	10
Mutation Data (Data Type Q) .....	10
Mutation Test System .....	11
Test Species .....	12
Units of Exposure .....	13
Reproductive Effects Data (Data Type R) .....	14
Reproductive Effects Code .....	14
Route of Exposure or Administration .....	14
Species Exposed .....	14

Type of Exposure .....	14
Dose Amounts and Units .....	15
Time and Duration of Treatment .....	15
Multigenerational Studies .....	16
Tumorigenic Data .....	16
Acute Toxicity Data (Data Type T) .....	18
Toxic Effects .....	18
Route of Exposure or Administration .....	19
Species Exposed .....	19
Description of Exposure .....	19
Units of Dose Measurement .....	20
Duration of Exposure .....	21
Frequency of Exposure .....	21
Other Multiple Dose Toxicity Data (Data Type U) .....	22
Toxicity Data Summary .....	22
Cited References .....	23
Reviews (Data Type V) .....	23
Threshold Limit Value (TLVs) .....	23
IARC Cancer Reviews .....	24
Toxicology Reviews .....	26
Standards and Regulations (Data Type W) .....	27
NIOSH Standards Development and Surveillance Data (Data Type X) .....	30
ATSDR, EPA, NIOSH, NTP and OSHA Status (Data Type Y) .....	33
The Agency for Toxic Substances and Disease Registry (ATSDR) .....	33
Environmental Protection Agency (EPA) .....	33
The National Institute for Occupational Safety and Health (NIOSH) .....	34
National Toxicology Program (NTP) .....	34
Occupational Safety & Health Administration (OSHA) .....	36
<b>Table I. RTECS Abbreviations .....</b>	<b>37</b>
<b>Table II. Toxic Effects Codes (TEC) .....</b>	<b>44</b>
Position 1 - Organ, Tissue, or Functional System .....	44
Positions 2 and 3 - Damage Codes, Two Digits .....	45
A. Brain and Coverings .....	45
B. Spinal Cord .....	45
C. Peripheral Nerve and Sensation .....	45

D. Sense Organs and Special Senses .....	46
Olfaction .....	46
Eye .....	46
Ear .....	47
Taste .....	47
E. Autonomic Nervous System .....	47
F. Behavioral .....	48
G. Cardiac .....	49
H. Vascular .....	49
I. Aquatic Organism Effects .....	50
J. Lungs, Thorax, or Respiration .....	50
K. Gastrointestinal .....	51
L. Liver .....	52
M. Kidney, Ureter, and Bladder .....	52
N. Endocrine .....	53
P. Blood .....	54
Q. Musculoskeletal .....	55
R. Skin and Appendages .....	55
Skin .....	55
Other .....	56
S. Immunological, including Allergic .....	56
Allergic (Multiple organ involvement) .....	56
U. Nutritional and Gross Metabolic .....	57
Gross Metabolite Changes .....	57
Changes in Chemistry or Temperature .....	57
V. Tumorigenic .....	57
X. In Vitro Toxicity Studies .....	58
Y. Biochemical .....	58
Enzyme inhibition, induction, or change in blood or tissue levels .....	58
Effect on specific coenzyme .....	59
Metabolism (intermediary) .....	59
Neurotransmitters or modulators (putative) .....	60
Z. Related to Chronic Data .....	60
<b>Table III. Reproductive Effects Code .....</b>	<b>61</b>
Paternal Effects .....	61

Maternal Effects .....	61
Effects on Fertility .....	61
Effects on Embryo or Fetus .....	62
Specific Developmental Abnormalities .....	62
Tumorigenic Effects .....	62
Effects on Newborn .....	63
<b>Table IV. Routes of Administration to, or Exposure of, Animal Species to Toxic Substances ...</b>	<b>64</b>
<b>Table V. Species .....</b>	<b>66</b>
<b>Table VI. Master File Data Types (Position 10) .....</b>	<b>69</b>
<b>Table VII. Line Numbers for "V", "W", "X", and "Y" Data .....</b>	<b>70</b>
<b>Table VIII*. Letter Codes for Species, System Organ Classes, and Cells, Tissue or Organ in Specific System Organ Class for In Vitro Studies .....</b>	<b>71</b>
Species .....	71
System Organs .....	71
Cells, Tissue, or Organ in Specific Organs .....	72

## Introduction

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This Comprehensive Guide to the Registry of Toxic Effects of Chemical Substances (RTECS®) describes the types of data and their format.

### RTECS Data Selection, Evaluation, and Use

The toxicity information appearing in the Registry is derived from reports of the toxic effects of chemical substances. The absence of a substance from the Registry does not imply that the substance is non-toxic. A substance may not appear for a variety of reasons. Four reasons include the following: (1) the test results could not be cited because the protocol of the study did not meet the RTECS selection criteria; (2) the substance has not yet been tested; (3) the substance has been tested, but the RTECS literature search has not yet uncovered the data; or (4) the data are not publicly available.

RTECS consists of tabulations of the lowest dose reported to have caused the listed toxic effect in the designated species by the designated route of administration. The Registry includes substances that have been selected primarily for the toxic effect produced by single doses. However, when the toxic effect has been described by the author as mutagenic, tumorigenic, or as a reproductive toxicant, the toxic dose data are reported for both single and multiple dose studies. [Other Multiple Dose Toxicity Data and References](#) includes any other effects from multiple dose studies.

For human data, any reported adverse effect is included.

The report of the lowest total dose administered to produce the toxic effect is given preference although some editorial license is taken so that additional references might be cited. No restrictions are placed on the amount of a substance producing death in an experimental animal nor on the time period over which the dose was given. The inclusion of data with the notation LD50 > \_\_\_mg/kg or LC50 > \_\_\_ppm is intended to indicate that the substance cited has been tested up to the indicated level without reaching that level of toxicity.

The [Detailed File Description](#) of RTECS provides details of the format and content of the various toxicity data lines. Studies reporting primary irritation to the skin and eyes are described in Section 10; Section 11 describes the mutagenic test systems and the organisms and cell types used in mutagenic testing; elements of the reproductive effects toxicity lines are described in Section 12; reports of positive or equivocal tumorigenic effects included in the Registry are described in Section 13. (Other tumorigenic data may be found on the [International Agency for Research on Cancer \[IARC\] review lines](#) [described in Section 17b] and the [NTP carcinogenesis bioassay status lines](#) [Section 20d]). Section 14 describes [acute toxicity data](#), including the system of [Toxic Effects Codes](#) (TEC). [Other Multiple Dose Data](#) is described in Section 15.

Toxicity data reported in the literature are transformed into Registry format using the criteria presented in the [Detailed File Description](#). The quality of the data on which the report is based has not been evaluated. In most cases no attempt is made to resolve any questions about the data.

It is not the purpose of the Registry to quantitate a hazard through the use of the toxic concentration or dose data that are presented with each substance.

**IMPORTANT! UNDER NO CIRCUMSTANCES CAN THE TOXIC DOSE VALUES PRESENTED WITH THESE CHEMICAL SUBSTANCES BE CONSIDERED DEFINITIVE VALUES FOR DESCRIBING SAFE VERSUS TOXIC DOSES FOR HUMAN EXPOSURE.**

### General Comments

The Editor will appreciate assistance from representatives of the industrial, academic, and governmental communities in supplying data for this Registry. Such assistance may be offered in the form of reprints of scientific publications, technical data sheets, sales or promotional material, other publicly available reference material, and data presented on unpublished studies. All material received will be considered to be in the public domain and as such may be made available to any person or organization. Data cited and published in the Registry will be selected according to the criteria presented herein. Information on errors in the file is also solicited as are general comments or recommendations. All correspondence should be addressed to:

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## Detailed File Description

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### Substance Selection

**Substances Included:** For the purpose of this publication, the phrase “all known toxic substances” is interpreted by the Editor to mean all mined, manufactured, processed, synthesized, and naturally occurring inorganic and organic compounds. The list of substances includes drugs, food additives, preservatives, ores, pesticides, dyes, detergents, lubricants, soaps, plastics, extracts from plant and animal sources, plants and animals which are toxic by contact or consumption, and industrial intermediates and waste products from production processes. Some of the information in the file thus refers to materials whose composition is not perfectly known. The chemical substances included in this list are assumed to exhibit the reported toxic effect in their pure state unless otherwise noted. However, even in the case of a supposedly “pure” substance, there is usually some degree of uncertainty as to its exact composition and the impurities which may be present. This possibility must be considered in attempting to interpret the data presented since the toxic effects observed could in some cases be caused by a contaminant.

**Substances Excluded:** Excluded from the Registry are trade name products representing compounded or formulated proprietary mixtures available as commercial products. These exclusions are necessary because of difficulties in assessing the contribution of each component of a mixture to the toxicity of that substance and because the formulation of a product is often changed by varying the components, their concentration, or the purity of the ingredients. Commercial product trade names are included, however, when they represent a single active chemical entity or a well-defined mixture of relatively consistent composition. Radioactive substances are included, but the effect reported is the chemically produced effect rather than the radiation effect.

### Format

All substance prime names and synonyms in the file are listed in alphabetical order, ignoring special characters, such as numerals, Greek letters, and prefixes indicating substituent locations, and stereochemical or other structural features. These components are taken into account for secondary ordering in ascending alphabetical and numerical order.

Each substance prime name is identified by a nine-position sequence number (two letters and seven numbers) which varies directly with the alphabetic sequence of the name, so that toluene, for example, has a higher number than benzene. Each synonym is cross-referenced to its appropriate prime name sequence number. The sequence number is simply an identifier assigned alphabetically and numerically to each substance in the Registry. It is not intentionally related to the toxicity or structure of the compound although compounds with alphabetically similar names and, in some cases, therefore, similar structures are grouped together.

For each prime name sequence number the following data are provided when available: the substance prime name and synonyms; a description of the substance (where necessary); date when the RTECS data records last updated; CAS Number; Beilstein Reference Number; RTECS Number; molecular formula; molecular weight; Wiswesser Line Notation (WLN); compound descriptor code(s); primary irritation; mutagenic, reproductive, and tumorigenic effects data; acute toxicity data; other multiple dose toxicity data; ACGIH Threshold Limit Values, IARC Monograph reviews; toxicological reviews; existing Federal standards; NIOSH Criteria Documents, Current Intelligence Bulletins, recommended exposure levels, surveillance data and analytical methods; the NTP Carcinogenesis Testing Program; and the EPA TSCA Inventory, GENE-TOX, TSCATS Database, Section 8(a) preliminary assessment, Section 8(b) chemical inventory, and Section 8(e) status programs. Each data line and citation is referenced by CODEN to the source from which the information was extracted. A list of CODEN abbreviations and their

respective titles is provided in the CODEN Master File. Each field in the RTECS data record is discussed below.

### Substance Prime Name (Data Type A)

The prime name of each substance in the Registry is derived from the nomenclature used by the American Chemical Society's Chemical Abstracts Service (CAS) in the Collective Index of Chemical Abstracts. The names are given in the inverted form. The complete RTECS data record for each substance follows its prime name.

Some entries, however, appear under the chemical or descriptive names used in the reference from which the toxic data were obtained. This is particularly true for those substances of questionable composition, such as plant or animal extracts. A brief description or definition ("DEF") (Data Type C) accompanies these prime names by listing the source of the substance, a general statement of constituents, or other pertinent information, and the CODEN citation of the reference that contained the definition.

[Synonym](#) cross references are tabulated as Data Type B.

### Update (Data Type E)

This field specifies when the data record of a substance was last changed.

The format is YYYYMM, e.g., 198105 = May 1981. All 33,929 substances in the file as of January 1979 were initialized with a date of 197901. When data on a new substance are first input to the file, the update field is assigned the month and year of entry. When the data record is subsequently revised, the date is changed to reflect the month and year the change was made. Any revision, for example, deletion of an invalid synonym, addition of new toxicity data, change in the NTP status, or correction of a molecular formula, will cause the update field of the substance to change.

### Chemical Registry Number (Data Type D)

There are two types of chemical registry numbers included in this field. The CAS Registry Number is a numeric designation assigned by the [Chemical Abstracts Service](#) of the [American Chemical Society](#) that uniquely identifies a specific chemical compound, regardless of the name or nomenclature system used. CAS occasionally assigns new numbers to selected chemicals without withdrawing the previously assigned numbers, causing some confusion. This situation occurs when a substance is better described or more accurately identified. RTECS lists the most recent CAS number available for a chemical and includes previous CAS numbers in a second number line. Up to ten (10) such previous CAS numbers will be listed for a substance.

An additional set of Registry Numbers for organic chemicals is also included in this data field. These are the Beilstein Registry Numbers (BRN) and Beilstein Handbook References originally created by the [Beilstein Institute of Frankfurt-am-Main](#), Germany. This database currently maintained by Elsevier is a listing of structures, properties, and reactions. Each of these numbers is assigned a specific line number within the field.

### RTECS Number (Data Type G)

The RTECS number is a unique 9-position alphanumeric designation assigned to each prime chemical name. These numbers are permanently assigned and will not change. (They are not to be confused with the alphanumeric sequence numbers by which the file is sorted.)

## Molecular Weight (MW) (Data Type H)

The molecular weight is calculated from the molecular formula using standard elemental molecular weights (carbon = 12.01).

## Molecular Formula (MF) (Data Type F)

The molecular formula designating the elemental composition of the substances is structured according to the [Hill System](#) ([Journal of the American Chemical Society, 22\(8\):478-494, 1900](#)), in which carbon and hydrogen (if present) are listed first, followed by the other elemental symbols in alphabetical order. The formulas for compounds that do not contain carbon are ordered strictly alphabetically by elemental symbol. Compounds such as salts or those containing waters of hydration have molecular formulas incorporating the CAS dot- disconnect convention, in which the components are listed individually and separated by a period.

The individual components of the formula are generally given in order of decreasing carbon atom count and component ratios. A lowercase "x" indicates that the ratio is unknown. A lower case "n" indicates a repeating polymer-like structure. The formula is obtained from one of the cited references or a chemical reference text, or is derived from the name of the substance.

## Wiswesser Line Notation (WLN) (Data Type J)

The Wiswesser Line Notation is a line-formula chemical notation that precisely and concisely describes the structural formula of a chemical compound. This linear representation for a three-dimensional structure facilitates substructure searching for special functional groups and constituents that are part of the molecule. The WLN's allow machine retrieval by chemical characteristics.

## Synonyms (Data Type L)

Synonyms for the substance prime name are listed alphabetically according to the rule described under [Format](#). Synonyms include other chemical names, trade names, common or general names, foreign language names (with the language in parentheses), or codes. Some synonyms consist wholly or in part of registered trademarks. These trademarks are not identified as such in the RTECS file because of limitations in the computer character sets used to produce the Registry. The Editor is aware of the problem of trademarks becoming generic trade names through common usage. While the Registry does not presently have a mechanism for noting trademarks, the lack of the appropriate registered trademark symbol does not imply that the trademarks contained herein are considered generic synonyms. Those trade names that are known to be obsolete, either because production and marketing of the substance has ceased or because the compound is currently manufactured under another name, are indicated with the abbreviation "(Obs. )."

The [American Conference of Governmental Industrial Hygienists](#) (ACGIH) in their listing of [Threshold Limit Values](#) (TLV<sup>®</sup>), [Department of Transportation](#) (DOT) in the [Hazardous Substances List](#), and the [Occupational Safety and Health Administration](#) (OSHA) in the listing of [Permissible Exposure Limits](#) (PELs) on occasion use other than the prime chemical name in their designations. For the convenience of the user, RTECS adds to the appropriate synonym name in parentheses the designation ACGIH, DOT, and/or OSHA. For example, the prime name chemical 2-Pentanone, 4-Hydroxy-4-Methyl includes in its synonym field the following: Diacetone Alcohol (ACGIH:OSHA).

The reader is cautioned that some synonyms, particularly common names, may be ambiguous and refer to more than one substance. The substances may or may not be chemically similar. For example, some common names are applied in the literature both to a particular compound and to various metallic salts of that compound. In addition, the Registry's list of synonyms is not exhaustive, and the file may not include an entry for every existing use of a particular common name. Therefore, when using a synonym

## Detailed File Description

to look up data in the Registry, care must be taken to ensure that the substance record retrieved is for the particular substance in question and not for one with an identical common name.

### Compound Descriptor Codes (Data Type N)

For each code found in position 10, a one-letter code appears in column 14. These codes are listed below and can be used as selection keys to extract defined subfiles of the master file. A substance entry may contain multiple descriptor codes.

CODE	COMPOUND TYPE	From Substance Record	References Cited in RTECS	DESCRIPTIONS
A	<a href="#">Agricultural Chemical</a>		X	Compounds used to improve crop yields, such as fertilizers and pesticides of all kinds.
C	<a href="#">Tumorigen</a>	X		Substances with positive or negative tumorigen citations.
D	<a href="#">Drug</a>		X	Both commercially available (approved) compounds, as well as those that have been identified as experimental.
H	<a href="#">Hormone</a>		X	Includes both those naturally found in the body and synthetic substances that act like hormones.
M	<a href="#">Mutagen</a>	X		The substance contains one or more mutagenic data lines.
N	<a href="#">Natural Product</a>		X	Organic compounds that are produced by plants, animals, and microorganisms and not commercially synthesized
O	<a href="#">Organometallic</a>		X	Includes organic compounds comprised of a metal or metalloids attached directly to carbon.
P	<a href="#">Human Data</a>	X		5 categories: Human (Hum), Man (Man), Woman (Wmn), Child (Chd), Infant (Inf)
S	<a href="#">Primary Irritant</a>	X		Substances that contain one or more skin or eye irritation data lines.
T	<a href="#">Reproductive Effector</a>	X		Substances that contain one or more reproductive effects data lines.

This compound descriptor field was developed as a search tool.

The RTECS compound descriptor codes do not represent an evaluation of the toxicity of a substance, nor are the codes all-inclusive with respect to use (that is, there may be some substances in the RTECS file that should be, but are not, coded as belonging to certain application classes). The codes must be interpreted only in conjunction with the other information found in each substance data record.

The RTECS descriptor codes fall into two categories: (1) those based on the types of toxicity data found in the substance data records and (2) those based on related information found in the references from which the data were extracted. In the first category are the following descriptor codes: tumorigen, mutagen, reproductive effector, primary irritant, and human data. As mentioned, these five classifications do not represent an evaluation of the overall toxicity of a substance. Rather, they indicate the type(s) of toxicity data line(s) found in the substance data record.

These codes do not represent an evaluation of the toxicity of a substance, nor are the codes all-inclusive with respect to use (that is, there may be some substances in the RTECS file that should be, but are not, coded as belonging to certain application classes). Interpret these codes only in conjunction with other information found in the substance data record.

## Tumorigen (C)

The descriptor code “Tumorigen” denotes a “substance with positive or negative tumorigen citation(s).” That is, any substance with the descriptor code “tumorigen” will have one or more of the following in its data record:

- One or more tumorigenic data lines (Data Type S, see [Tumorigenic Data](#)).
- One or more [U.N. International Agency for Research on Cancer](#) (IARC) review lines (Data Type V), regardless of whether the IARC review concluded that the carcinogenicity of the substance was noted as Sufficient Evidence, Limited Evidence, Inadequate Evidence, No Evidence, or Evidence Suggesting Lack of Carcinogenicity .
- One or more [National Toxicology Program](#) (NTP) carcinogenesis bioassay studies status lines (Data Type Y), regardless of whether the substance had only been selected for test or whether the NTP study showed Clear Evidence, Some Evidence, Equivocal Evidence, No Evidence, or Inadequate Study of Carcinogenicity, or that the test is still in progress.

Based on the above criteria, therefore, there may be some substances in RTECS that have only negative IARC reviews or NTP status lines, but that still appear with the descriptor code “tumorigen.” This is done to bring the significance of the results of the IARC reviews and the NTP studies to the user’s attention. Again, this points out the need to review the complete data record before drawing any conclusion about the total toxic potential of a substance. The user must not rely solely on the descriptor code.

## Reproductive Effector (T)

Any substance with the descriptor code “Reproductive Effector” contains:

- One or more [reproductive effects](#) data lines (Data Type R) or
- One or more [tumorigenic](#) data lines (Data Type S) that cite either transplacental carcinogenesis (Toxic Effects Code [TEC] T65) or tumors to the reproductive system (TEC T61, T62, T63, T64, or T69). Thus, a substance reported to cause these latter two types of effects will contain both tumorigen and reproductive effector compound descriptor codes.

## Mutagen (M)

Any substance with the descriptor code “Mutagen” will contain one or more mutagenic data lines (Data Type Q).

See [Mutation Data](#) for more information.

## Primary Irritant (S)

Any substance described as a “Primary Irritant” will contain one or more skin or eye irritation data lines (Data Type P) in its RTECS data record.

### Human Data

The descriptor code “Human Data” will access all 5 categories:

Hum	Human
Man	Man
Wmn	Woman
Chd	Child
Inf	Infant

### Other Descriptors

The remaining five descriptor codes (Agricultural Chemical, Drug, Organometallic, Hormone, and Natural Product) are use or application codes included in the file based only on information found in the references cited in RTECS. For example, if an article that reports an oral-rat LD50 value for a substance indicates the substance is used as a drug or a pesticide, that’s the record used for the entry. However, if the article makes no such indication, descriptor codes are not added to the data record. Recognize that these classifications are not all-inclusive; they are based solely on information in the references compiled by the RTECS.

Agricultural chemicals include those used to improve crop yields, such as fertilizers and pesticides of all kinds. Drugs include both commercially available (approved) compounds, as well as those that have been identified as experimental. Organometallic includes organic compounds comprised of a metal or metalloids attached directly to carbon. Hormones include both those naturally found in the body and synthetic substances that act like hormones. Natural products include organic compounds that are produced by plants, animals, and microorganisms and that are not commercially synthesized.

### Skin and Eye Irritation Data (Data Type P)

Each irritation data line includes, in sequence, the tissue tested (skin or eye); the species of animal tested; the total dose and where applicable, the duration of exposure; for skin tests only, whether open or occlusive; an interpretation of the irritation response severity when noted by the author; and the reference from which the information was extracted. Only positive irritation test results are included in the Registry.

Substances applied topically to the skin or the mucous membranes can elicit either, systemic effects of an acute or chronic nature, or local effects called “primary irritation.” A primary irritant is a substance that, if present in sufficient quantity for a sufficient period of time, will produce a non-allergic, inflammatory reaction of the skin or of the mucous membrane at the site of contact. RTECS limits primary irritants to those substances that are not corrosive. Hence, RTECS does not classify concentrated sulfuric acid as a primary irritant.

### Primary Skin Irritation

In experimental animals, a primary skin irritant is defined as a chemical substance that produces an irritant response on first exposure in a majority of the test subjects. However, in some instances compounds act more subtly and require either repeated contact or special environmental conditions (humidity, temperature, occlusion, etc.) to produce a response.

One of the standard animal irritation tests is the [Draize procedure](#) ([Journal of Pharmacology and Experimental Therapeutics, 82: 377-390, 1944](#)). This procedure has been modified and adopted as a regulatory test by the [Consumer Product Safety Commission](#) (CPSC) in [16 CFR 1500.41](#). In this test a

known amount (0.5 ml of a liquid or 0.5 gm of a solid or semisolid) of the test substance is introduced under a one square inch gauze patch. The patch is applied to the skin (clipped free of hair) of twelve albino rabbits. Six rabbits are tested with intact skin and six with abraded skin. The abrasions are minor incisions made through the stratum corneum, but are not sufficiently deep to disturb the dermis or produce bleeding. The patch is secured in place with adhesive tape, and the entire trunk of the animal is wrapped with an impervious material, such as rubberized cloth, for a 24-hour period. The animal is immobilized during exposure. After 24 hours the patches are removed and the resulting reaction evaluated for erythema, eschar, and edema formation. The reaction is again scored at the end of 72 hours (48 hours after the initial reading), and the two readings are averaged. A substance producing any degree of positive reaction is cited in the Registry as an irritant.

As the modified Draize procedure described above has become the standard test specified by the U.S. Government, nearly all of the primary skin irritation data either strictly adhere to the test protocol or involve only simple modifications to it. When test procedures other than those described above are reported in the literature, appropriate codes are included in the irritation data line to indicate those deviations.

The most common modification is the lack of occlusion of the test patch, so that the treated area is left open to the atmosphere. In such cases, the notation "open" appears in the irritation data line. Another frequent modification involves whole arm or whole body immersion in the test substance or, more commonly, in a dilute aqueous solution of the test substance. This type of test is often conducted on soap or detergent solutions. Immersion data are identified by the abbreviation "imm" in the data line.

The dose reported is based first on the lowest dose producing an irritant effect and second on the latest study published. The dose is expressed as follows:

- Single application by the modified Draize procedure is indicated by only a dose amount. If no exposure time is given, then the data are for the standard 72-hour test. For test times other than 72 hours, the dose data are given in mg (or in an appropriate unit)/duration of exposure, e.g., 10mg/24H.
- Multiple applications involve administration of the dose in divided portions applied periodically. The total dose of test substance is expressed in mg (or appropriate unit)/duration of exposure, with the symbol "I" indicating intermittent exposure, e.g., 5mg/6D-I.

The method of testing substances for primary skin irritation given in the [U.S. Code of Federal Regulations](#) (CFR) does not indicate an interpretation of the response. However, some authors do include a subjective rating of the irritation observed. If such a severity rating is given, it is included in the data line as mild ("MLD"), moderate ("MOD"), or severe ("SEV"). The Draize procedure employs a rating that is included here for informational purposes only since other researchers may not categorize response in this manner.

Category Draize	Code	Skin Reaction
Mild	MLD	Well defined erythema and slight edema (edges of area well defined by definite raising)
Moderate	MOD	Moderate to severe erythema and moderate edema (area raised approximately 1 mm)
Severe	SEV	Severe erythema (beet redness) to slight eschar formation (injuries in depth) and severe edema (raised more than 1 mm and extending beyond area of exposure)

### Primary Eye Irritation

In experimental animals, a primary eye irritant is defined as a chemical substance that produces an irritant response in the test subject on first exposure. [Eye irritation study procedures developed by Draize](#) have been modified and adopted as a regulatory test by [CPSC](#) in [16 CFR 1500.42](#). In this procedure, a known amount of the test material (0.1 ml of a liquid or 100 mg of a solid or paste) is placed in one eye of each of six albino rabbits; the other eye remains untreated, serving as a control. The eyes are not washed after instillation and are examined at 24, 48, and 72 hours for ocular reaction. After the recording of ocular reaction at 24 hours, any or all eyes may be further examined, following the application of fluorescein. Any or all of eyes may also be washed with a sodium chloride solution (U.S.P. or equivalent) after the 24- hour reaction has been recorded.

A test is scored positive if any of the following effects are observed: (1) ulceration (besides fine stippling); (2) opacity of the cornea (other than slight dulling of normal luster); (3) inflammation of the iris (other than a slight deepening of the rugae or circumcorneal injection of the blood vessel); (4) swelling of the conjunctiva (excluding the cornea and iris) with eversion of the eyelid; or (5) a diffuse crimson-red color with individual vessels not clearly identifiable. A substance is an eye irritant if four of six rabbits score positive. It is considered a nonirritant if none or only one of six animals exhibits irritation. If intermediate results are obtained, the test is performed again. For the purpose of RTECS, substances producing any degree of irritation in the eye are identified in the Registry as irritants. When an author has designated a substance as either a mild, moderate, or severe eye irritant, this designation is also reported.

The dose reported is based first on the lowest dose producing an irritant effect and second on the latest study published. Single and multiple applications are indicated as described in Section 10a above. Test times other than 72 hours are noted in the dose. All eye irritant test exposures are assumed to be continuous, unless the reference states that the eyes were washed after instillation. In this case, the notation "rns"(rinsed) is included in the data line.

### Species Exposed

Since [Draize procedures](#) for determining both skin and eye irritation specify rabbits as the test species, most of the animal irritation data in the Registry are for rabbits, although any of the species listed in Table V may be used. The Editor endeavors to include as much human data as possible since this information is directly applicable to occupational exposure. Much of this data comes from studies conducted on volunteers (such as the cosmetic or soap ingredients) or from persons accidentally exposed. When an accidental exposure, such as a spill, is cited, the data line includes the abbreviation "nse" (non-standard exposure). In these cases it is often very difficult to determine the precise amount of the substance to which the individual was exposed. Therefore, for accidental exposures an estimate of the concentration or the strength of the substance, rather than a total dose amount, is generally provided.

### Mutation Data (Data Type Q)

Mutation data include both whole animal and in vitro studies. Each mutation data line includes, in sequence, the mutation test system utilized, the species of tested organism (and, where applicable, the route of administration or cell type), the exposure concentration or dose, and the reference from which the information was extracted. Only positive mutation test results are cited in the Registry.

A mutation is defined as any heritable change in genetic material. Unlike irritation, reproductive effects, tumorigenic, acute, and other multiple dose toxicity data (see Sections 10, 12, 13, 14, and 15, respectively), which report the results of whole animal studies, mutation data also include studies on lower organisms such as bacteria, yeasts, molds, and insects, as well as in vitro mammalian cell cultures. Studies of plant mutagenesis are not now included in the Registry. No attempt is made to evaluate the significance of the data or to rate the relative potency of the compound as a mutagenic risk to man.



## Mutation Test System

A number of test systems are used to detect genetic alterations caused by chemical substances. Those systems currently cited in the Registry are listed below. Others found in the literature have been grouped together under the general term "other mutation test system" (oms). Each test system is identified by the 3-letter code shown in parentheses. For additional information about mutation tests, the reader may wish to consult the [Handbook of Mutagenicity Test Procedures](#), edited by B.J. Kilbey, M. Legator, W. Nichols, and C. Ramel (Amsterdam: Elsevier, Second Edition, 1984).

Mutation in Microorganisms (mmo) - System is based on the detection of heritable genetic alterations in microorganisms exposed directly to the chemical substance. An enzymatic activation step is automatically included in the test procedure. To differentiate between early tests in which the activation step was not an automatic inclusion, the notation "with S9" or "without S9" will appear on the dataline.

- **Micronucleus Test (mnt)** - System utilizes the fact that chromosomes or chromosome fragments may not be incorporated into one or the other of the daughter nuclei during cell division.
- **Specific Locus Test (slt)** - System utilizes a method for detecting and measuring rates of mutation at any or all of several recessive loci.
- **DNA Damage (dnd)** - System detects the damage to DNA strands, including strand breaks, crosslinks, and other abnormalities.
- **DNA Repair (dnr)** - System utilizes methods of monitoring DNA repair as a function of induced genetic damage.
- **Unscheduled DNA Synthesis (dns)** - System detects the synthesis of DNA during usually non-synthetic phases.
- **DNA Inhibition (dni)** - System detects inhibition of DNA synthesis.
- **Gene Conversion and Mitotic Recombination (mrc)** - System utilizes unequal recovery of genetic markers in the region of the exchange during genetic recombination.
- **Cytogenetic Analysis (cyt)** - System utilizes cultured cells or cell lines to assay for chromosomal aberrations following the administration of chemical substances.
- **Sister Chromatid Exchange (sce)** - System detects the interchange of DNA in cytological preparations of metaphase chromosomes between replication products at apparently homologous loci.
- **Sex Chromosome Loss and Nondisjunction (sln)** - System measures the non-separation of homologous chromosomes at meiosis and mitosis.
- **Dominant Lethal Test (dlt)** - A dominant lethal is a genetic change in a gamete that kills the zygote produced by that gamete. In mammals, the dominant lethal test measures the reduction of litter size by examining the uterus and noting the number of surviving and dead implants.
- **Mutation in Mammalian Somatic Cells (msc)** - System utilizes the induction and isolation of mutants in cultured mammalian cells by identification of the gene change.
- **Host-Mediated Assay (hma)** - System uses two separate species, generally mammalian and bacterial, to detect heritable genetic alteration caused by metabolic conversion of chemical substances administered to host mammalian species in the bacterial indicator species.
- **Sperm Morphology (spm)** - System measures the departure from normal in the appearance of sperm.
- **Heritable Translocation Test (trn)** - Test measures the transmissibility of induced translocations to subsequent generations. In mammals, the test uses sterility and reduced fertility in the progeny of the treated parent. In addition, cytological analysis of the F1 progeny or subsequent progeny of the treated parent is carried out to prove the existence of the induced translocation. In *Drosophila*,

## Detailed File Description

heritable translocations are detected genetically using easily distinguishable phenotypic markers, and these translocations can be verified with cytogenetic techniques.

- **Morphological Transformation (mtr)** - System utilizes morphological criteria to detect cytological differences between normal and transformed tumorigenic cells.
- **Phage Inhibition Capacity (pic)** - System utilizes a lysogenic virus to detect a change in the genetic characteristics by the transformation of the virus from noninfectious to infectious.
- **Body Fluid Assay (bfa)** - System uses two separate species, usually mammalian and bacterial. Test substance is first administered to host, from whom body fluid (e.g., blood or urine) is subsequently taken. This body fluid is then tested in vitro, and mutations are measured in the bacterial species.
- **DNA Adduct (dna)** - System detects the covalent bonding of chemical substances to DNA through the identification of modified nucleotides.

## Test Species

Those test species that are peculiar to mutation data cited in the Registry are designated by the 3-letter codes shown in the following table. Other species are listed in Table I.

	Code	Species
<b>Bacteria:</b>	bcs	Bacillus subtilis
	esc	Escherichia coli
	hmi	Haemophilus influenzae
	klp	Klebsiella pneumoniae
	sat	Salmonella typhimurium
	srm	Serratia marcescens
<b>Molds:</b>	asn	Aspergillus nidulans
	nsc	Neurospora crassa
<b>Yeasts:</b>	smc	Saccharomyces cerevisiae
	ssp	Schizosaccharomyces pombe
<b>Protozoa:</b>	clr	Chlamydomonas reinhardi
	eug	Euglena gracilis
	omi	Other microorganisms
<b>Insects:</b>	dmg	Drosophila melanogaster
	dpo	Drosophila pseudo-obscura
	grh	Grasshopper
	slw	Silkworm
	oin	Other insect
<b>Fish:</b>	sal	Salmon
	ofs	Other fish

If the test organism is a cell type from a particular species (generally mammalian), the parent species is reported, followed by a colon and the cell type designation. For example, human leukocytes are coded “hmn:leu.” The various cell types currently cited in the Registry are listed in the following table:

Designation	Cell Type
Ast	Ascites tumor
Bmr	Bone marrow
Emb	Embryo
Fbr	Fibroblast
Hla	HeLa cell
Kdy	Kidney
Leu	Leukocyte
Lng	Lung
Lvr	Liver
Lym	Lymphocyte
Mmr	Mammary gland
Ovr	Ovary
Spr	Sperm
Tes	Testis
Oth	Other cell types not listed above

In the case of host-mediated and body fluid assays, the host and indicator organisms are given as follows: host organism/indicator organism, e.g., “ham/sat” for a test in which hamsters were exposed to the test chemical and *S. Typhimurium* was used as the indicator organism.

For in vivo mutagenic studies, the route of administration is specified following the species designation, e.g., “mus-ori” for oral administration to mice. See Table IV for a complete list of routes cited in the Registry. The route of administration is not specified for in vitro data.

### Units of Exposure

The lowest dose producing a positive effect is cited. The author’s calculations are used to determine the lowest dose at which a positive effect was observed. If the author fails to state the lowest effective dose, two times the control dose will be used. Ideally, the dose should be reported in universally accepted toxicological units such as milligrams of test chemical per kilogram of test animal body weight. While this is possible when the actual intake of a chemical by an organism of known weight is reported, it is not possible in many systems using insect and bacterial species. When a dose is reported or where the amount can be converted to a dose unit, it is normally listed as milligrams per kilogram (mg/kg). However, grams (gm), micrograms (ug), nanograms (ng), or picograms (pg) per kilogram may also be used for convenience of presentation. Concentrations of gaseous substances in air are listed as parts per hundred (pph), million (ppm), billion (ppb), or trillion (ppt).

Test systems using microbial organisms usually report exposure data as an amount of chemical per liter (L), or amount per plate, well, or disc. The amount may be on a weight (gm, mg, ug, ng, or pg) or molar (millimole [mmol], micromole [umole], nanomole [nmole], or picomole [pmole]) basis. These units describe the exposure concentration rather than the dose actually taken up by the test species. Insufficient data currently exists to permit the development of dose amounts from this information. In such cases, therefore, the substance concentration units used by the author are reported.

Since the exposure values reported in host-mediated assays are the doses delivered to the host organism, no attempt is made to estimate the exposure concentration to the indicator organism. The exposure values cited for host-mediated assay data are in units of milligrams (or other appropriate unit of weight) of substance administered per kilogram of host body weight or in parts of vapor or gas per million (ppm) parts of air (or other appropriate concentration) by volume.

### Reproductive Effects Data (Data Type R)

Each reproductive effects data line includes, in sequence, the reproductive effects code(s), the route of exposure, the species of animal tested, the type of dose, the total dose amount administered, the time and duration of administration, and the reference from which the information was extracted. Only positive reproductive effects data for mammalian species are cited in the Registry. Because of differences in the reproductive systems among species and the systems' varying responses to chemical exposures, no attempt is made to extrapolate animal data or to evaluate the significance of a substance as a reproductive risk to humans. Each element of the reproductive effects data line is discussed below:

#### Reproductive Effects Code

For purposes of the Registry, the reproductive effects for which dose data are cited have been grouped into seven categories (see [Table III](#)): paternal effects, maternal effects, effects on fertility, effects on the embryo or fetus, specific developmental abnormalities, tumorigenic effects, and effects on the newborn. Within these seven categories, specific effects have been defined. The effects cited on a given data line were reported to occur in the species and at the dose level given on that line. Up to three reproductive effects are cited on a single data line. If more than three reproductive effects are reported for the same route-species- dose level-duration combination, duplicate lines will appear in this section of the file to allow complete coding of the reproductive effects.

#### Route of Exposure or Administration

See [Table IV](#) for a complete list of abbreviations and definitions of the various routes of exposure reported in the Registry. For reproductive effects data, the specific route is listed in RTECS either when the substance was administered to only one of the parents or when the substance was administered to both parents by the same route. However, if the substance was administered to each parent by a different route, the route is indicated as "mul" (multiple).

#### Species Exposed

Reproductive effects data are cited in the Registry for mammalian species only. Species abbreviations are the same as those used for acute toxicity data and are shown in [Table V](#). Also shown in Table V are approximate gestation periods.

#### Type of Exposure

Only two types of exposure, TDLo and TCLo, are used to describe the dose amounts reported for reproductive effects data. These two terms, which are also used to describe toxic dose data, are defined in Section 14d.

## Dose Amounts and Units

The total dose amount that was administered to the exposed parent is given. If the substance was administered to both parents, the individual amounts to each parent are added together and the total amount shown. Where necessary, appropriate conversion of dose units is made. The dose amounts listed are those for which the reported effects are statistically significant. The statistical test is that used by the author. If no statistic is reported, a Fisher's Exact Test is applied with significance at the 0.05 level, unless the author makes a strong case for significance at some other level.

Dose units are usually given as an amount administered per unit body weight or as parts of vapor or gas per million parts of air by volume. A complete description of dose units is given in Section 14e. There is no limitation on either the quantity or concentration of the dose or the duration of exposure reported to have caused the reproductive effect.

## Time and Duration of Treatment

The time when a substance is administered to either or both parents may significantly affect the results of a reproductive study, because there are differing critical periods during the reproductive cycles of each species. Therefore, to provide some indication of when the substance was administered, which should facilitate selection of specific data for analysis by the reader, a series of up to four terms follows the dose amount. These terms indicate to which parent(s) and at what time the substance was administered. The terms take the general form:

(uD male/vD pre/w-xD preg/yD post)

where

u = total number of days of administration to male prior to mating

v = total number of days of administration to female prior to mating

w = first day of administration to pregnant female during gestation

x = last day of administration to pregnant female during gestation

y = total number of days of administration to lactating mother after birth of offspring

If administration is to the male only, then only the first of the above four terms is shown following the total dose to the male, e.g., 10 mg/kg (5D male). If administration is to the female only, then only the second, third, or fourth term, or any combination thereof, is shown following the total dose to the female. For example:

10 mg/kg (3D pre)

10 mg/kg (3D pre/4-7D preg)

10 mg/kg (3D pr/4-7D per/5D post)

10 mg/kg (3D pre/5D post)10 mg/kg (4-7D preg)

10 mg/kg (4-7D preg/5D post)

10 mg/kg (5D post)

**Note:** This example indicates administration to the lactating mother only after birth of the offspring.)

If the administration is to both parents, then the first term and any combination of the last three terms are listed, e.g., 10 mg/kg (5D male/3D preg/4-7D post). If administration is continuous through two or more of the above periods, the above format is abbreviated by replacing the slash (/) with a dash (-). For example, 10 mg/kg (3D pre-5D post) means a total of 10 mg/kg administered to the female for three days prior to mating, on each day during gestation, and for five days following birth. Approximate gestation period for various species are shown in [Table V](#).

### Multigenerational Studies

Some reproductive studies entail administration of a substance to several consecutive generations, with the reproductive effects measured in the final generation. The protocols for such studies vary widely. Therefore, because of the inherent complexity and variability of these studies, they are cited in RTECS® in a simplified format as follows:

The specific route of administration is reported if it was the same for all parents of all generations; otherwise, the abbreviation “mul” is used. The total dose amount shown is that administered to the F0 generation only (as described in Section 12e above); doses to the Fn (where n = 1,2,3, etc.) generations are not reported. The time and duration of treatment for multi-generation studies are not included in the data line. Instead, the dose amount is followed by multi-generation, e.g., 10 mg/kg multi-generation. The reader must consult the cited reference for complete details of the study protocol.

### Tumorigenic Data

Tumorigenic dose data also appears under ‘Data Type R’. The format of these data types are identical to that of the acute toxicity data line, which is described in detail in Section 14. Briefly, each tumorigenic data line sequentially includes toxic effects code(s), the route of exposure, the species of animal studied, the type of dose (either TDLo or TCLo), the total dose amount administered, the duration of exposure, and the reference from which the information was extracted. Only positive or equivocal tumorigenic reports are cited in this section. For other information about tumorigenicity, the reader should see the IARC monograph review lines (Section 17b), the ACGIH review lines (Section 17a), and the NTP status lines (Section 20d).

The importance attached to reports of the carcinogenic activity of substances necessitates a more detailed discussion of the criteria used to include this type of data in the Registry. Tumorigenic citations are classified according to the reported results of the study only to aid the reader in selecting appropriate references for in-depth review and evaluation. Two classifications used are V01, indicating a positive carcinogenic finding, and V02, indicating a study producing benign tumors. A third classification, V03, denotes those studies reporting uncertain, but seemingly positive, results. The criteria for these three classifications are listed below. These criteria are used to abstract the data in individual reports on a consistent basis and do not represent a comprehensive evaluation of the tumorigenic potential of a substance to humans.

The Registry cites multiple studies in which tumorigenic responses were reported. That is, for a given substance, a particular route-species combination may be cited more than once if the results of the multiple studies are coded V01, V02, or V03. These multiple tumorigenic entries have been cited simply with a toxicity measure of TD (toxic dose) or TC (toxic concentration).

The following nine technical criteria are used by RTECS to abstract the toxicological literature and classify studies that report positive tumorigenic responses.

**IMPORTANT! NO ATTEMPTS ARE MADE EITHER TO EVALUATE THE VARIOUS TEST PROCEDURES OR TO CORRELATE RESULTS FROM DIFFERENT EXPERIMENTS.**

- a. A citation is coded with the TEC “V01” (Carcinogenic by RTECS criteria) when review of a study reveals that all of the following criteria are satisfied:
  - A statistically significant increase in the incidence of tumors in the test animals. The statistical test used is that used by the author. If no statistic is reported, a [Fisher’s Exact Test](#) is applied with significance at the 0.05 level, unless the author makes a strong case for significance at some other level.
  - A control group of animals is used and the treated and control animals are maintained under identical conditions.

- The sole experimental variable between the groups is the administration or non-administration of the test substance (see i below).
  - The tumors consist of autonomous populations of cells of abnormal cytology capable of invading and destroying normal tissues, or the tumors metastasize as confirmed by histopathology.
- b. A citation is coded with the TEC “V02” (Neoplastic by RTECS criteria) when review of a study reveals that all of the following criteria are satisfied:
- A statistically significant increase in the incidence of tumors in the test animals. The statistical test used is that used by the author. If no statistic is reported, a Fisher’s Exact Test is applied with significance at the 0.05 level, unless the author makes a strong case for significance at some other level.
  - A control group of animals is used, and the treated and control animals are maintained under identical conditions.
  - The sole experimental variable between the groups is the administration or non-administration of the test substance (see i below).
  - The tumors consist of cells that closely resemble the tissue of origin, that are not grossly abnormal cytologically, that may compress surrounding tissues, but that neither invade tissues nor metastasize; or
  - The tumors produced cannot definitely be classified as either benign or malignant.
- c. A citation is coded with the TEC “V03” (Equivocal tumorigenic agent by RTECS criteria) when some evidence of tumorigenic activity is presented, but one or more of the criteria listed in (a) or (b) above is lacking. Thus, a report with positive pathological findings, but with no mention of control animals, is coded V03. Reports in which the results are not interpretable are not cited in the Registry.
- d. Since an author may make statements or conclusions based on a larger context than that of the particular data reported, papers in which the author’s conclusions differ substantially from the evidence presented in the paper are subject to review by the RTECS Editorial Review Board.
- e. All doses except for those for transplacental carcinogenesis are reported in RTECS in one of the following formats.
- For all routes of administration other than inhalation: Cumulative dose in mg (or other appropriate unit)/kg/duration of administration.  
Whenever the dose reported in the reference is not in the above units, conversion to this format is made based on the information given in Section 14e. The total cumulative dose is derived from the lowest dose level that produces tumors in the test group.
  - For inhalation experiments: Concentrations in ppm (or mg/m<sup>3</sup>)/total duration of exposure.  
The concentration refers to the lowest concentration that produces tumors.
- f. Transplacental carcinogenic doses are reported in RTECS in one of the following formats:
- For all routes of administration other than inhalation: Cumulative dose in mg/kg/(time of administration during pregnancy). The cumulative dose is derived from the lowest single dose that produces tumors in the offspring. The chemical is administered to the mother.
  - For inhalation experiments: Concentration in ppm (or mg/m<sup>3</sup>)/(time of exposure during pregnancy). The concentration refers to the lowest concentration that produces tumors in the offspring. The mother is exposed to the chemical either during pregnancy or lactation.

- g. For the purposes of RTECS, all test chemicals are reported as pure, unless otherwise stated by the author. This does not rule out the possibility that unknown impurities may have been present.
- h. A mixture of compounds whose test results satisfy the criteria in (a), (b), or (c) above is included if the composition of the mixture can be clearly defined.
- i. For tests involving promoters or initiators, a study is included if the following conditions are satisfied (in addition to the criteria in (a), (b), or (c) above):
  - The test chemical is applied first followed by an application of a standard promoter. A positive control group in which the test animals are subjected to the same standard promoter under identical conditions is maintained throughout the duration of the experiment. The data are not used if no mention of positive and negative control groups is made in the reference.
  - A known carcinogen is first applied as an initiator, followed by application of the test chemical as a promoter. A positive control group in which the test animals are subjected to the same initiator under identical conditions is maintained throughout the duration of the experiment. The data are not used if no mention of positive and negative control groups is made in the reference.

### Acute Toxicity Data (Data Type T)

Each dose data line sequentially includes toxic effects; the route of exposure; the species of animal studied; the type of dose; the amount of substance per body weight or concentration per unit of air volume and, where applicable, the duration of exposure; and the reference from which the information was extracted. Each element of the acute toxicity line is discussed below.

### Toxic Effects

The toxic effects listed in the Registry should not be viewed as an exhaustive representation of all the potential toxic effects of a compound. These effects are noted in the Registry by means of an alphanumeric Toxic Effects Code (TEC). The TEC permits a detailed coding of the toxic effects reported in the literature and is included for human and animal data.

In the database, the TEC is the first entry on the toxicity data line; it appears to the left of the route of administration. Each TEC is made up of one or more code segments, each of which contains three characters. Each TEC, which may contain as many as three code segments, is preceded by a single digit (1, 2, or 3) that indicates the number of segments. For example, the entry "2J18K13" indicates two code segments: J18 and K13. An explanation of the individual code segments is given below.

The first position of each segment is alphabetic and describes an organ, tissue or functional system, or other major physiological or behavioral grouping. Positions two and three are numeric damage codes that specify individual toxic effects within each system. A complete list of TECs, including all major system groupings and individual damage codes, appears in Table II. Using Table II to decode the preceding example (2J18K13), the reader finds that for the "J18" TEC segment, the "J" represents the lung as the affected organ and the "18" indicates pleural thickening. For "K13," "K" represents the gastrointestinal system and "13" means nausea or vomiting.

In using the TEC, the reader should be aware of the following restrictions:

- TECs listed in each line describe effects reported only for the route and species specified on that line.
- The TECs listed in the Registry should not be viewed as an exhaustive representation of all the potential toxic effects of a compound. This caution results from two considerations. The first is that a maximum of three code segments is reported for each RTECS data line. For studies in which more than three effects were reported, only those deemed most significant will be listed. Second, the effects are limited to those that meet the basic selection criteria for inclusion in the Registry, i.e.,



lowest dose for a given route-species combination. Studies done to determine acute LD50 values often report little other information besides the LD50 itself.

## Route of Exposure or Administration

Although many exposures to substances in the industrial community occur via the respiratory tract or skin, most studies in the published literature report exposures of experimental animals in which the test substances were introduced primarily through the mouth by pills, in food, in drinking water, or by intubation directly into the stomach.

In an Aquatic toxicity study, a chemical is usually added to the tank with water (dissolved in water). In Vitro route of administration is used for in vitro toxicity studies. A new code “vit” was added for in vitro administration. The abbreviations and definitions of the various routes of exposure reported in the Registry are found in [Table IV](#).

## Species Exposed

Since the effects of exposure of humans are of primary concern, we have indicated, when available, whether the results were observed in man, woman, child, or infant. If no such distinction was made in the reference, the abbreviation “hmn” (human) is used. (NOTE: it is also possible to search out all human data by using the Compound Descriptor Code “P” for human data). However, the results of studies on rats or mice are the most frequently reported and hence provide the most useful data for comparative purposes. A description of the test system for in vitro studies is composed from the Species and Cells (tissue) that were used. Three letter codes for Test system are composed according to following rule:

- The first letter – letter code for species ([Table VIII, part 1](#))
- The second letter – letter code for system organ class corresponding to letters used in RTECS TECs ([Table VIII, part 2](#))
- The third letter – letter code for specific cells, tissue or organ in specific system organ class ([Table VIII, part 3](#))

If the three letter code is not found in the rule above, the species and abbreviations used in reporting toxic dose data are listed alphabetically in [Table I](#).

## Description of Exposure

Six abbreviations are used to describe the administered dose reported in the literature. These abbreviations indicate whether the dose caused death (LD) or other toxic non-lethal effect (TD), or whether it was administered as a lethal concentration (LC) or toxic concentration (TC) in the inhaled air. In general, the term “Lo” is used where the number of subjects studied was not a significant number from the population or the calculated percentage of subjects showing an effect was 100. For “in tank” route of exposure abbreviations are used to indicate whether chemical was administered as a lethal concentration (LC) or toxic concentration (TC).

The doses and concentrations are defined as follows:

**TDLo - Toxic Dose Low** - The lowest dose of a substance introduced by any route, other than inhalation, over any given period of time and reported to produce any toxic effect in humans or animals, or to produce tumorigenic, reproductive, or multiple dose effects in animals.

**TCLo - Toxic Concentration Low**- The lowest concentration of a substance in air to which humans or animals have been exposed for any given period of time that has produced any toxic effect in humans or animals, or produced tumorigenic, reproductive, or multiple dose effects in animals.

**LDLo- Lethal Dose Low**- The lowest dose (other than LD50) of a substance introduced by any route, other than inhalation, over any given period of time in one or more divided portions and reported to have caused death in humans or animals.

**LD50- Lethal Dose Fifty**- A calculated dose of a substance which is expected to cause the death of 50% of an entire defined experimental animal population. It is determined from the exposure to the substance by any route other than inhalation of a significant number from that population. Other lethal dose percentages, such as LD1, LD10, LD30, and LD99, may be published in the scientific literature for the specific purposes of the author. Such data would be published in the Registry if these figures, in the absence of a calculated lethal dose (LD50), were the lowest found in the literature.

**LClo - Lethal Concentration Low** - The lowest concentration of a substance in air, other than LC50, which has been reported to have caused death in humans or animals. The reported concentrations may be entered for periods of exposure that are less than 24 hours (acute) or greater than 24 hours (subacute and chronic).

**LC50 - Lethal Concentration Fifty** - A calculated concentration of substance in air, exposure to which for a specified length of time is expected to cause the death of 50% of an entire defined experimental animal population. It is determined from the exposure to the substance of a significant number from that population.

**In vitro** - New abbreviations are used to describe the administered dose reported in the literature for in vitro studies to distinguish in vivo and vitro data. These abbreviations indicate inhibitory concentration (IC). Inhibitory concentration is a lethal or toxic concentration caused calculated percentage of cells showing an effect (IC50, IC75 etc.). The term “Lo” is used where the percentage of affected cells was not a significant number.

The concentrations are defined as follows:

**ICLo - Inhibitor Concentration Low** - The lowest concentration of a substance introduced by in vitro route over any given period of time and reported to produce any toxic effect in cells in tissues.

**IC50 - Inhibitor Concentration Fifty** - a calculated concentration of a substance which is expected to cause the effect of 50% or in 50% of tested cells.

Other inhibitory concentration percentages, such as IC10, IC30, and IC99, may be published in the scientific literature for the specific purposes of the author.

### Units of Dose Measurement

As in almost all experimental toxicology, the doses given are expressed in terms of the quantity administered per unit body weight, quantity per skin surface area, or quantity per unit volume of the respired air. The duration of time over which the dose was administered is also listed, as needed.

Dose amounts are generally expressed as milligrams (one-thousandth of a gram) per kilogram (mg/kg). In some cases, because of dose size and its practical presentation in the file, micrograms (one millionth of a gram) per kilogram (ug/kg), or nanograms (one billionth of a gram) per kilogram (ng/kg) are used. Volume measurements of dose were converted to weight units by appropriate calculations. Densities were obtained from standard reference texts. Where densities were not readily available, doses were reported as milliliters per kilogram (ml/kg).

All body weights are converted to kilograms (kg) for uniformity. For those references in which the dose was reported to have been administered to an animal of unspecified weight or a given number of animals in a group (e.g., feeding studies) without weight data, the weights of the respective animal species are assumed to be those listed in Table V and the dose listed on a per kilogram body weight basis. Assumptions for daily food and water intake are found in Table V to allow approximating dosages for humans and experimental animals where the dose was originally reported as a concentration in food or water. The values presented are selections which are reasonable for the species and convenient for dose calculations.

Concentrations of a gaseous substance in air are generally listed as parts of vapor or gas per million parts of air by volume (ppm). However, parts per hundred (pph or percent), parts per billion (ppb), or

parts per trillion (ppt) may be used for convenience of presentation. If the substance is a solid or a liquid, the concentrations are listed preferably as milligrams per cubic meter ( $\text{mg}/\text{m}^3$ ), but may, as applicable, be listed as micrograms per cubic meter ( $\text{ug}/\text{m}^3$ ), nanograms per cubic meter ( $\text{ng}/\text{m}^3$ ), or picograms per cubic meter ( $\text{pg}/\text{m}^3$ ) of air. For those cases in which other measurements of contaminants are used, such as the number of fibers or particles, the measurement is spelled out.

In aquatic toxicity studies with in tank exposure usually report exposure data as an amount of chemical per liter (L). The amount may be on a weight (gm, mg,  $\mu\text{g}$ , ng, or pg). These units describe the exposure concentration rather than the dose actually taken up by the test species.

In aquatic toxicity studies with standard RTECS routes of administration (oral etc) dose amounts are generally expressed as milligrams (one thousandth of a gram) per kilogram ( $\text{mg}/\text{kg}$ ). In some cases, because of dose size and its practical presentation in the file, micrograms (one millionth of a gram) per kilogram ( $\text{ug}/\text{kg}$ ), or nanograms (one billionth of a gram) per kilogram ( $\text{ng}/\text{kg}$ ) are used. Volume measurements of dose were converted to weight units by appropriate calculations. Densities were obtained from standard reference texts. Where densities were not readily available, doses were reported as milliliters per kilogram ( $\text{ml}/\text{kg}$ ).

In Vitro studies usually report exposure data as an amount of chemical per liter (L), or amount per plate, well, or disc. The amount may be on a weight (gm, mg,  $\mu\text{g}$ , ng, or pg) or molar (millimole [ $\text{mmol}$ ], micromole [ $\mu\text{mole}$ ], nanomole [ $\text{nmole}$ ], or picomole [ $\text{pmole}$ ]) basis. These units describe the exposure concentration rather than the dose actually taken up by the test species.

A data format with metals or other elements in parentheses indicates that the dose is calculated for the metal or other element only rather than for the whole substance. This type of dose is used if a substance's toxicity is related to a specific element and the rest of the substance does not contribute to the toxicity. For example, for arsenious acid as its monosodium salt ( $\text{AsO}_2\text{Na}$ ), a dose unit of  $\text{mg}(\text{As})/\text{kg}$  indicates that the amount is for As (arsenic) only and does not include the weight of elements other than As.

A data format with "(base)" indicates that the non-salt form of the substance is used for the dose calculation. For example, for neomycin sulfate, a dose unit of  $\text{gm}(\text{base})/\text{kg}$  indicates that the amount is for the weight of free neomycin only.

## Duration of Exposure

The duration of exposure is included to give an indication of the testing period during which the human or animal was exposed to the total dose.

Where the duration of exposure is available, time is presented as minutes (M), hours (H), days (D), weeks (W), or years (Y). Additionally, continuous (C) indicates that the exposure was continuous over the time administered, such as ad libitum feeding studies or 24-hour, 7-day per week inhalation exposures. Intermittent (I) indicates that the dose was administered during discrete periods, such as daily, twice weekly, etc. In all cases, the total duration of exposure appears first after the kilogram body weight and slash, followed by descriptive data; e.g.,  $10 \text{ mg}/\text{kg}/3\text{W-I}$  means ten milligrams per kilogram body weight administered over a period of three weeks, intermittently in a number of separate, discrete doses. This description is intended to provide the reader with enough information for an approximation of the experimental conditions, which can be further clarified by studying the reference cited.

## Frequency of Exposure

Frequency of exposure to the test substance varies depending on the nature of the experiment. For the purposes of the Registry, frequency of exposure is given for inhalation experiments, for human exposures (where applicable), or where reproductive, tumorigenic, or other multiple dose data are specified (see Sections 12, 13, and 15 respectively).

## Other Multiple Dose Toxicity Data (Data Type U)

Citations in this field include the results of multiple dose toxicity studies, of variable duration, which relate to other than mutagenic, reproductive, or tumorigenic effects. The format is similar to that found in the tumorigenic effects data field, where toxic rather than lethal doses are indicated, including duration of exposure. The numerical dose data is a cumulative amount over the duration of the study. The most common study designs include thirteen week, twenty-six week, fifty-two week, and two year studies.

### Toxicity Data Summary

Shown below is a summary of the several categories of toxicity data entries (Sections 12-15), where they appear in the file, and how they are used.

Toxic Data Type				
	Exposure Regime	Route of Exposure	Human	Animal
<b>LD50</b>	Single dose	All except inhalation	Not applicable	Acute lethality (data type T) statistically determined
<b>LC50</b>	Single dose	Inhalation	Not applicable	Acute lethality (data type T) statistically determined
<b>LDLo</b>	Single dose (except for human data)	All except inhalation	Data type T	Acute lethality (data type T)
<b>LCLo</b>	Single dose (except for human data)	Inhalation	Data type T	Acute lethality (data type T)
<b>LD</b>	Single dose	All except inhalation	Not applicable	Acute lethality (data type T) lethal dose > dose reported
<b>LC</b>	Single dose	Inhalation	Not applicable	Acute lethality (data type T) lethal dose > dose reported
<b>TDLo</b>	Single or multiple dose	All except inhalation	All non-lethal (data types R, S, T, U)	Non-lethal (data types R, S, T, U)
<b>TCLo</b>	Single or multiple dose	Inhalation	All non-lethal (data types R, S, T, U)	Non-lethal (data types R, S, T, U)
<b>TD</b>	Single or multiple dose	All except inhalation	Not applicable	Tumorigenic (data type S)
<b>TC</b>	Single or multiple dose	Inhalation	Not applicable	Tumorigenic (data type S)

## Cited References

All references cited are publicly available. No government classified documents have been used for source information. All references have been given a unique six-letter CODEN character code (derived from the American Society for Testing and Materials "CODEN for Periodical Titles," which identifies periodicals, serial publications, and individual published works). For example, "CNREA8" is the CODEN for Cancer Research, and "PCBPBS" for Pesticide Biochemistry and Physiology. For those references for which no CODEN was found, the corresponding six-letter codes includes asterisks (\*) in the last one or two positions, following the first four or five letters of the acronym for the publication title. Following the CODEN designation (for most entries) is the number of the volume, followed by a comma; the page number of the first page of the article, followed by a comma; and a four-digit number, indicating the year of publication. When the cited reference is a report, the report number is listed. Where contributors have provided information on their unpublished studies, the CODEN consists of the first three letters of the last name, the initials of the first and middle names, and a number sign (#). The date of the letter supplying the information is listed. All CODEN acronyms are listed in alphabetical order and defined in the CODEN Master File, (coden.del). The format of this file is as follows:

Field Number	Field Name	Position	Description
1	CODEN	1 – 6	Alphanumeric
2	Line Number	7 – 8	Numeric
3	Bibliographic Data	12 – 105	Alphanumeric

## Reviews (Data Type V)

Three types of reviews are listed: (1) [Threshold Limit Values](#) (TLVs®), which are limits proposed by the [American Conference of Governmental Industrial Hygienists](#) (ACGIH®); (2) [International Agency for Research on Cancer](#) (IARC) monograph reviews, which are published by the [United Nations, World Health Organization](#) (WHO); and (3) general toxicology review articles.

### Threshold Limit Value (TLVs)

The TLV is an ACGIH guideline and refers to the airborne concentration of a substance to which nearly all workers may be repeatedly exposed, day after day, over a working lifetime, without adverse health effects. The TLVs® may be expressed as a time-weighted average (TWA), as a short-term exposure limit (STEL), or as a ceiling value (CL). The TWA is for a normal 8-hour workday or 40-hour work week. The STEL is the maximum concentration to which workers can be exposed for up to 15 minutes, provided no more than four excursions per day are permitted with at least 60 minutes between exposure periods and provided the daily TWA is not also exceeded. The CL is the concentration that should not be exceeded during any part of the working exposure. The notation "(skin)" refers to a potential significant contribution to the overall exposure by cutaneous routes, even though the airborne exposures are at or below the TLV.

A separate TLV review line is included for those substances that ACGIH has developed a carcinogen classification;

Confirmed Human Carcinogen (A1)

Suspected Human Carcinogen (A2)

Confirmed Animal Carcinogen with Unknown Relevance to Humans (A3)

Not Classifiable as a Human Carcinogen (A4) Not Suspected as a Human Carcinogen (A5).

The TLVs can be found in the "The Documentation of the Threshold Limit Values and Biological Exposure Indices". Copies of the complete TLVs Documentation may be ordered from:

ACGIH  
1330 Kemper Meadow Drive  
Cincinnati, Ohio 45240  
Telephone (513) 742-2020, FAX (513) 742-3355.  
email: [mail@acgih.org](mailto:mail@acgih.org)

The reader is cautioned that the TLVs are revised periodically. A [Notice of Intended Changes](#) for substances for which either a TLV is proposed for the first time or for which a change to an existing TLV is proposed is published annually by ACGIH. Proposed changes are considered trial limits for two years, after which they are considered for inclusion as adopted TLVs. Only substances for which TLVs have been adopted and final documentation prepared are cited in the Registry.

In addition, some TLVs are recommended for classes of substances rather than for individual compounds. These classes may be based on certain chemical or physical properties, such as solubility, that have not been determined for all potential members of the class. This makes it difficult to cite individual substances belonging to the class. Any questions about the TLV citations in the Registry should be directed to ACGIH. Any errors should be brought to the attention of the RTECSEditor at the address given in the [Introduction](#).

### IARC Cancer Reviews

In the [United Nations International Agency for Research on Cancer](#) (IARC) monographs, information on suspected environmental carcinogens are examined, and summaries of available data with appropriate references are presented. Included in these reviews are synonyms, physical and chemical properties, uses and occurrence, and biological data relevant to the evaluation of carcinogenic risk to humans.

The RTECS entry IARC CANCER REVIEW indicates that some carcinogenicity data pertaining to a compound has been reviewed by an IARC Working Group. The Registry summarizes the Working Group's conclusion.

The IARC program of evaluation of carcinogenic risks to humans has evolved over the years since it began in 1969. The IARC classification entered into the Registry is applicable for the volume reviewed.

Monographs 1-42 published between 1971-1987, and Supplement 7: [Overall Evaluations of Carcinogenicity: An updating of the IARC Monographs Volumes 1 to 42](#), published in 1987, are described below.

The evidence of carcinogenicity in experimental animals was assessed by the Working Group and judged to fall into one of four groups defined as follows:

- SUFFICIENT EVIDENCE of carcinogenicity is provided when there is an increased incidence of malignant tumors: (a) in multiple species or strains; or (b) in multiple experiments (preferably with different routes of administration or using different dose levels); or (c) to an unusual degree with regard to the incidence, site or type of tumor, or age at onset. Additional evidence may be provided by data on dose-response effects.
- LIMITED EVIDENCE of carcinogenicity is available when the data suggest a carcinogenic effect but are limited because (a) the studies involve a single species, strain, or experiment; (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or (c) the neoplasms produced often occur spontaneously, and in the past, have been difficult to classify as malignant by histological criteria alone (e.g., lung adenomas and adenocarcinomas, and liver tumors in certain strains of mice).
- INADEQUATE EVIDENCE is available when, because of major qualitative or quantitative limitations, the studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect.

- **NO EVIDENCE** applies when several adequate studies are available which show that within the limitations of the tests used, the chemical is not carcinogenic.

It should be noted that the categories **SUFFICIENT EVIDENCE** and **LIMITED EVIDENCE** refer only to the strength of the experimental evidence that these chemicals are carcinogenic and not to the extent of their carcinogenic activity, nor to the mechanism involved. The classification of any chemical may change as new information becomes available.

The evidence for carcinogenicity from studies in humans was assessed by the Working Group and judged to fall into one of four groups defined as follows:

- **SUFFICIENT EVIDENCE** of carcinogenicity indicates that there is a causal relationship between the exposure and human cancer.
- **LIMITED EVIDENCE** of carcinogenicity indicates that a causal relationship is credible, but that alternative explanations, such as chance, bias, or confounding, could not adequately be excluded.
- **INADEQUATE EVIDENCE**, which applies to both positive and negative evidence, indicated that one of two conditions prevailed: (a) there are few pertinent data; or (b) the available studies, while showing evidence of association, do not exclude chance, bias, or confounding.
- **NO EVIDENCE** applies when several adequate studies are available which do not show evidence of carcinogenicity.

Monographs beginning with Volume 43 and beyond are classified as below.

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

- **SUFFICIENT EVIDENCE** of carcinogenicity: The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) in two or more independent studies in one species carried out at different times or in different laboratories or under different protocols.

Exceptionally, a single study in one species might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumor or age at onset.

- **LIMITED EVIDENCE** of carcinogenicity: The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; or (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the study; or (c) the agent increased the incidence only of benign neoplasms or lesions of uncertain neoplastic potential, or of certain neoplasms which may occur spontaneously in high incidences in certain strains.
- **INADEQUATE EVIDENCE** of carcinogenicity: The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.
- **EVIDENCE SUGGESTING LACK OF CARCINOGENICITY**: Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic. A conclusion of evidence suggesting lack of carcinogenicity is inevitably limited to the species, tumor sites and levels of exposure studied.

The evidence relevant to carcinogenicity from studies in humans is classified into one of the following categories:

- **SUFFICIENT EVIDENCE** of carcinogenicity: The Working Group considers that a causal relationship has been established between the agent and human cancer. That is, a positive relationship has been

observed between the exposure and cancer in studies in which change, bias and confounding could be ruled out with reasonable confidence.

- **LIMITED EVIDENCE of carcinogenicity:** A positive association has been observed between the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.
- **INADEQUATE EVIDENCE of carcinogenicity:** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.
- **EVIDENCE SUGGESTING LACK OF CARCINOGENICITY:** There are several adequate studies covering the full range of levels of exposure that human beings are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. A conclusion of 'evidence suggesting lack of carcinogenicity' is inevitably limited to the cancer sites, conditions and levels of exposure and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

'Human No Adequate Data' or 'Animal No Adequate Data' have been added to the status when the Working Group found no data available for review.

IARC also began publishing in Supplement 7, an 'overall evaluation' taking into consideration the total body of evidence. In Supplement 7, and in monographs 43 onward, chemicals have been classified in the following groups:

Group 1	The Working Group concluded that the listed agents are carcinogenic to humans.
Group 2	The Working Group concluded that the listed agents are probably carcinogenic to humans.
Group 2B	The Working Group concluded that the listed agents are possibly carcinogenic to humans.
Group 3	The Working Group concluded that the listed agents are not classifiable as to their carcinogenicity to humans.
Group 4	The Working Group concluded that the listed agent is probably not carcinogenic to humans.

For any chemical listed in RTECS which appears in one of these groups, its group designation is noted in the Review field, immediately following the IARC Monograph lines.

These cancer reviews reflect only the conclusions of the IARC committees based on the data available for the committee's evaluation. Hence, for some substances there may be disagreement between the IARC determination and the information on the tumorigenic data lines (see Section 13). Also, some substances previously reviewed by IARC may be reexamined as additional data become available. These substances will contain multiple IARC review lines, each of which is referenced to the appropriate IARC volume.

### Toxicology Reviews

The entry TOXICOLOGY REVIEWS indicates that the cited review article has been located in the literature. Each review is identified by its CODEN citation. These articles discuss one or more facets of the toxicology of the substance or the general class to which the substance belongs. Most of these references do not contain specific dose values that can be cited in the Registry. However, the reviews do provide useful



information about the toxicity of the substance or group of related substances. The reader is cautioned that the scope of discussion varies greatly among the reviews. Some articles may contain a complete, detailed description of the toxicity of a substance; others may address only a particular aspect of the toxicity (e.g., effect of a substance on fetal development, or body fluid and tissue levels of a substance found under conditions of poisoning); and others may only list the substance in a general discussion of the toxicity of a class of compounds.

## Standards and Regulations (Data Type W)

This section contains notations indicating the substance is regulated by an agency of the United States Government, either by EPA, MSHA, or OSHA, or as Occupational Exposure Limits (OEL) by other nations around the world. EPA refers to substances regulated by the Federal Insecticide Fungicide, and Rodenticide Act (FIFRA) of the U.S. Environmental Protection Agency. MSHA refers to standards promulgated by the Mine Safety and Health Administration, under Subpart D, Section 56 of the Federal Mine Safety and Health Act of 1977. These have been codified in Code of Federal Regulations (CFR) Title 30. OSHA refers to standards promulgated under Section 6 of the Occupational Safety and Health Act of 1970. These have been codified in 29 CFR, and are referred to as Permissible Exposure Limits (PELs). OEL refers to the Occupational Exposure Limits published by several nations around the world.

All United States standards and regulations are listed in the appropriate Federal Register (FR) or Code of Federal Regulations (CFR). Because of frequent changes to and litigation of federal regulations, it is recommended that the reader contact the applicable agency for information about the current standards for a particular substance. Omission of a substance or regulatory notation from the Registry does not imply any relief from regulatory responsibility.

- a. EPA FIFRA standards indicate pesticides that are subject to registration or re-registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended. The amendments were issued in four parts, representing four lists of pesticides: (a) Federal Register 54(35), page 7740, Feb 22, 1989; (b) Federal Register 54(100), page 22706, March 25, 1989; (c) Federal Register 54(140), page 30848, July 24, 1989; and (d) Federal Register 54(204), page 4388, October 24, 1989.
- b. MSHA air contaminants standards are noted with the entry "air," preceded by "MSHA STANDARD." See 30 CFR Parts 56 and 57 for additional information.
- c. OSHA air contaminant standards are noted by the entry "OSHA PEL" (Permissible Exposure Limit). The four cited sections are:

General Industry Standards	29 CFR 1910.1000
Constructions Standards	29 CFR 1926.55
Shipyards Standards	29 CFR 1915.1000
Standards for Federal Contractors	41 CFR 50-204.50.

The PEL can be further described by one or more of the following terms: "8-hour TWA" (time-weighted average); "STEL" (short term exposure limit); or "CL" (ceiling). The TWA is the employee's airborne exposure in any 8-hour work shift of a 40-hour work week which shall not be exceeded. The STEL is the employee's 15-minute time-weighted average, which shall not be exceeded at any time during the work day. A time period other than 15 minutes may be specified in parentheses behind the notation "STEL." The CL is the employee's exposure, which shall not be exceeded at any time during the work shift. The notation "(skin)," following the PEL for a substance indicates that even though the air contaminant concentration may be below the PEL, significant additional exposure to the skin may be dangerous. The use of personal protective equipment, engineering controls, or

## Detailed File Description

work practices is required. (Another designation is applied to substances listed on the Z-2 table: "PK," which refers to the acceptable maximum peak concentration above the ceiling concentration.)

Some workplace exposures consist of more than one contaminant. OSHA regulations provide for the reduction of PELs based on additive or synergistic health effects.

OSHA Cancer Hazard and OSHA Suspect Cancer Agent designations may appear on a subsequent data line for selected substances regulated by OSHA as carcinogens.

The reader is cautioned that some OSHA PELs are promulgated for classes of compounds rather than for individual substances. These classes may be based on certain chemical or physical properties that have not been well defined for every member of the class. Any questions about specific OSHA PELs should be directed to:

OSHA  
Office of Public Affairs  
Room N-3647  
Department of Labor  
200 Constitution Avenue, NW Washington, D.C. 20210  
Telephone (202) 219-8151.

- d. International Occupational Exposure Limits (OELs). The nations whose standards are listed, and the source from which RTECS obtained the OELs, are as follows:

Nation	Source
Arab Republic of Egypt	Letter from: National Institute of Occupational Safety and Health, Heliopolis, A.R.E. Mrs. Laila El Hariry, General Director of the International Relations Department
Argentina	Letter from Dr. Carlos Anibal Rodrigues, Ministerio de Trabajo y Seguridad Social de la Nacion Buenos Aires, Argentina
Australia	Occupational Safety and Health Series, No. 37 Occupational Exposure Limits for Airborne Toxic Substances International Labour Office, Geneva
Austria	Maximale Arbeitsplatz-Konzentrationen Gesundheitsschädlicher Arbeitsstoffe MAK-Werte-Liste
Belgium	Occupational Safety and Health Series, No. 37 Occupational Exposure Limits for Airborne Toxic Substances International Labour Office, Geneva
Colombia	Letter from: Consejo Colombiano de Seguridad Renan Alfonso Rojas Gutierrez, Executive Director
Denmark	Grænseværdier for stoffer og materialer Copenhagen
France	Valeurs limites d'exposition professionnelle Aux agents chimiques en France

Nation	Source
Germany	Deutsche Forschungsgemeinschaft List of MAK and BAT Values, 1974 Commission for the Investigation of Health Hazards of Chemical Compounds In the Work Area Report No. 30
Hungary	Letter from: ORSZAGOS Munkavedelmi Tudomanyos Kutató Intézet Dr. Jenó Molnar, Director
India	Directorate General Factory Advice Service and Labour Institute Government of Industry, Ministry of Labour H. N. Gupta, Director General
Japan	Occupational Exposure Limits for Airborne Toxic Substances Occupational Safety and Health Series, No.37 International Labour Office, Geneva
Jordan	Letter from: The Hashemite Kingdom of Jordan Vocational Training Corporation Occupational Safety and Health Institute A. Abdel-Jaber, Director
Korea	Korea Industrial Safety Corporation (KISCO) Industrial Safety and Health Research Institute Seoul, Korea Park Pil - Soo, December 21, 1996
The Netherlands	De Nationale MAC-lijst - 1995 - P 145
New Zealand	Letter and booklet (Workplace Exposure Standards) from: Occupational Safety and Health General Manager's Office Wellington, New Zealand Phillip Marshal, Information Manager
Norway	Letter and list from: Direktortet for Arbeidstilysnet Oslo, Norway Nils-Petter Wedege, Deputy Director-General
The Philippines	Letter from: Republic of the Philippines Occupational Safety and Health Center Department of Labor and Employment Evelyn F. Tablang, Officer-in-Charge

Nation	Source
Poland	Interdepartmental Commission for Updating the Register of Maximum Allowable Concentrations and Intensities for Harmful Agents in the Working Environment Ministry of Labour and Social Policy Poland
Portugal	Letter from Instituto de Desenvolvimento e Inspeção das Condições de Trabalho Álvaro Durão O Vice-presidente Lisboa, Portugal
Russia	Occupational Exposure Limits for Airborne Toxic Substances International Labour Office, Geneve
Singapore	Letter from: Republic of Singapore Department of Industrial Health Ministry of Labour Tan Kia Tang, Director
Sweden	Statute Book of the Swedish National Board Of Occupational Safety and Health: Occupational Exposure Limit Values
Switzerland	Valeurs limites d'exposition and postes de travail SUVA-CNA-INSAI
Thailand	Letter and table of values from: National Institute for the Improvement of Working Conditions and Environment (NICE) Department of Labour Bangkok, Thailand Dr. Chaiyuth Chavalitnitikul, Director
Turkey	Letter from: Occupational Health and Safety Institute P.K. 393 06443 YeniSehir Ankara, Turkey Dr. Handan Uysal Sabir, Director
United Kingdom	Occupational Exposure Limits Guidance Note EH 40/95 Health and Safety Executive

### NIOSH Standards Development and Surveillance Data (Data Type X)

This section contains information generated by NIOSH in two areas of endeavor. The Standards Development Programs produces Recommended Exposure Levels (RELs). The Surveillance Program has conducted two nationwide surveys of work sites and some of its findings are noted in this field.

- a. NIOSH Recommended Exposure Level (REL). This section indicates that a NIOSH recommendation for occupational exposure has been published. The RELs may appear in any of several document forms: Criteria Documents, Current Intelligence Bulletins, Special Hazard Reviews, Occupational Hazard Assessments, and Technical Guidelines. NIOSH also periodically presents testimony before various Congressional committees and at regulatory hearings convened by OSHA and MSHA. The testimony presented always includes the current NIOSH policy concerning the particular hazard in question. A compendium of NIOSH recommendations is contained in DHHS (NIOSH) Publication 92-100 and further revisions can be found in DHHS (NIOSH) Publication 95-121).
- b. NIOSH Occupational Exposure Survey data. NIOSH Survey Data (NOHS, 1974, or NOES, 1983) lines indicate that data on potential occupational exposure to the substance exist in one or both of the databases assembled as a result of national surveys of industry in the United States. The first survey, the National Occupational Hazard Survey (NOHS) was conducted from February 1972 to June 1974; the second, the National Occupational Exposure Survey (NOES) from November 1980 to May 1983. The intent of both surveys was to associate potential exposure agents (chemical, physical, and biological) with industry types, occupations, and specific surveyed facilities.

In both surveys, the sample of surveyed facilities was designed to permit projections to the national level based, on survey results. It is possible, for example, to estimate the total number of people potentially exposed to a particular agent. Among other data reporting capabilities of each survey are the actual number of industries, occupations, or facilities in which an agent was observed.

There are several limitations, dictating the need for caution, and some reservations that must be observed in the interpretation and any subsequent use of the occupational exposure data presented in this field.

- The occupational exposure data presented for each survey were representative of the workplace at the respective times each survey was conducted. The data are becoming progressively more dated, and as a consequence, less representative of the current situation.
- Data in both surveys were collected using observational techniques. No environmental levels of chemical or biological contaminants or degrees of physical hazards were actually measured.
- Neither survey covered industries in mining or agriculture. The sample universe of the NOHS did not include rural areas. The NOES did not include Federal, State, or local governments, financial, real estate, or retail trade industries.
- Exposure data reported for both surveys are provisional. In both cases, the majority of exposure data (approximately 70%) recorded during both surveys was by trade name product. Subsequent detailed component information for these trade name products was sought from the manufacturers and incorporated into the respective survey databases.

Basic Parameters of both surveys are as follows:

Parameter	Survey	
	NOHS	NOES
Start date of field survey	February 1972	November 1980
End date for field survey	June 1974	May 1983
Estimated number of plants in the survey universe	739,244	508,697
Estimated number of employees in the survey universe	38,262,627	33,409,031

## Detailed File Description

Parameter	Survey	
	NOHS	NOES
Number of plants surveyed	4,636	4,490
Number of employees surveyed	893,725	1,830,330
Number of different occupations surveyed	453	410
Number of agents seen	8,000+	9,000+
Number of unique trade name products	80,000	100,000

Types of data appearing on the survey data lines for each substance and the abbreviations used in the text are as follows:

HAZARD CODE (HZD) - a five-position identifier used exclusively for search and retrieval of data from either survey database.

NUMBER OF INDUSTRIES (NIS) - number of industries, as defined by standard 4-digit industrial classification (SIC) codes, in which the agent was observed.

TOTAL NUMBER OF FACILITIES (TNF) - estimated (nationwide) total number of facilities in which the agent is thought to be present.

NUMBER OF OCCUPATIONS (NOS) - number of occupations, as defined by the Bureau of Census Occupational codes, in which the agent was observed.

TOTAL NUMBER OF EMPLOYEES (TNE) - estimated (nationwide) total number of employees thought to be exposed to the agent.

TOTAL NUMBER OF FEMALE EMPLOYEES (TFE)\* - estimated (nationwide) total number of female employees thought to be exposed to the agent.

**Note:** \*Data is available for the NOES only.

Questions specific to the occupational survey data reported in the Registry should be directed to:

NIOSH  
DSHEFS  
Mail Stop R-12  
4676 Columbia Parkway  
Cincinnati, Ohio 45226

Detailed descriptions of the surveys and their resulting databases are available in the following NIOSH technical reports:

Survey Manual (NOHS)  
DHEW (NIOSH) Publication No. 74-127 (1974)

Data Editing and Database Development (NOHS)  
DHEW (NIOSH) Publication No. 77-213 (1977)

Survey Analysis and Supplemental Tables (NOHS)  
DHEW (NIOSH) Publication No. 78-114 (1977)

Survey Manual (NOES)  
DHHS (NIOSH) Publication No. 88-106 (1987)

Sampling Methodology (NOES)  
DHHS (NIOSH) Publication No. 89-102 (1989)

Analysis of Management Interview Responses (NOES)  
DHHS (NIOSH) Publication No. 89-103 (1989)

## ATSDR, EPA, NIOSH, NTP and OSHA Status (Data Type Y)

This section provides information on the activities of various governmental agencies regarding the substance. Status lines are currently listed for ATSDR, EPA, NIOSH, NTP, and OSHA.

### The Agency for Toxic Substances and Disease Registry (ATSDR)

[The Agency for Toxic Substances and Disease Registry](#) (ATSDR) has been directed by the [Superfund Amendments and Reauthorization Act of 1986](#) (SARA) to prepare toxicological

profiles for hazardous substances that pose the most significant potential threat to human health, as determined by ATSDR and the [Environmental Protection Agency](#) (EPA). Each profile is intended to characterize the toxicological and adverse health effects information for the hazardous substance being described. The currently available profiles are noted in the Status field of the appropriate chemical records. Also noted is the [National Technical Information Service](#) (NTIS) Stock Number of each profile.

### Environmental Protection Agency (EPA)

The [Environmental Protection Agency](#) (EPA) status entries are included for five portions of the [Toxic Substances Control Act](#) (TSCA), Public Law 94-469: Section 8(a) preliminary assessment information, Section 8(b) chemical inventory, Section 8(d) health and safety studies, Section 8(e) substantial risk information, and TSCA Test Submissions Database (TSCATS). Additional status lines are listed for two other EPA programs: A genetic toxicology online data base (GENE-TOX) and the Integrated Risk Information System (IRIS).

A TSCA inventory citation indicates that the substance appears on the Chemical Inventory prepared in 1986 by the EPA in accordance with provisions of Section 8(b) of TSCA. Substances reported in the inventory include those that are produced commercially in or imported into this country. The reader should note, however, that substances already regulated by EPA under FIFRA and by the Food and Drug Administration (FDA) under the Food, Drug, and Cosmetic Act, as amended, are not included in the TSCA inventory. Similarly, alcohol, tobacco, and explosive substances are not regulated under TSCA. TSCA regulations should be consulted for an exact definition of reporting requirements.

A preliminary assessment information status line indicates that EPA has promulgated both a final and a proposed rule under Section 8(a) of TSCA, reporting and retention of information. The final rule requires chemical manufacturers and, in some cases, processors and importers to report production and exposure-related data to EPA. Included in this status line is a citation to the Federal Register issue (volume 47, page 26992, June 22, 1982) in which the rule appeared. This reference should be consulted for a complete explanation of the rule. The proposed rule (Federal Register, volume 47, page 27009, June 22, 1982) covers an additional 350 chemicals for which similar reporting would be required.

Under TSCA Section 8(d), manufacturers, importers, and/or processors of a substance specified by the EPA Administrator must submit lists and copies of unpublished health and safety studies on that substance. Specified substances include chemical substances that are selected for consideration for testing rules under TSCA section 4, as well as other chemicals that EPA had identified as of concern under TSCA. A "health and safety" study is interpreted broadly and may include not only formal studies but also other types of information relating to health and environmental effects, including relevant monitoring and exposure data.

A substantial risk status line indicates that EPA has received and reviewed information submitted under Section 8(e) of TSCA, which requires that persons who obtain information which reasonably supports the conclusion that a substance presents substantial risk of injury to human health or the environment must notify EPA within 15 days. These notices are reviewed by EPA and an initial evaluation is prepared containing, if appropriate, follow-up questions to the submitter, referrals to other agencies, and decisions to list the chemical for a Section 8 reporting rule or to undertake a formal risk assessment. The reader should note that many 8(e) notices represent a company's first review of a situation or datum and a judgment in compliance with the statute to submit a notice within 15 days of obtaining the information. EPA published its evaluations of these notices in order to make widely available this Section 8(e) information in a form understandable to the general public.

The TSCATS was developed to make unpublished test data submitted to EPA available to the public. Test is broadly defined to include case reports, episodic incidents (such as spills), and formal test study presentations. The database allows searching of test submissions according to specific chemical identity or type of study. Studies are indexed under three broad subject areas: health effects, environmental effects, and environmental fate. Additional controlled vocabulary index terms are assigned that describe the experimental protocol and test observations. Records identify reference information needed to locate the source document, as well as the submitting organization and reason for submission of the test data.

GENE-TOX: A Genetic Toxicology program status line indicates that the substance has been reported in the literature for potential genetic effects. The test protocol in the literature is evaluated by an EPA Expert Panel on Mutations and a positive or negative effect of the substance is evaluated and reported. To obtain additional information about this program, contact GENE-TOX Program, EPA, 401 M Street SW, TS796, Washington, D.C. 20460, telephone (202) 260-1513.

IRIS: The Integrated Risk Information System is the EPA electronic on-line database of summary health risk assessment and regulatory information on chemical substances. The primary purpose of IRIS is to provide guidance risk values to EPA risk assessors and decision makers for use in EPA risk management decisions. EPA staff and EPA contractors are expected to use the risk information in IRIS for those chemicals in the database. The information contained in IRIS, except as specifically noted, has been reviewed and agreed upon by intra-agency review groups comprised of EPA scientists, having extensive experience in risk assessment. Thus, the information in IRIS represents an expert Agency consensus.

### **The National Institute for Occupational Safety and Health (NIOSH)**

NIOSH status lines are included for those substances for which an analytical method(s) has been developed by NIOSH or for substances for which [NIOSH Current Intelligence Bulletins \(CIBs\)](#) have been issued. The chemicals listed in the Fourth Edition of the [NIOSH Manual of Analytical Methods \(NMAM\)](#) are also cited in the RTECS. The sampling and measurement methods in the NMAM Fourth Edition are revisions and additions to those contained in the previous editions

### **National Toxicology Program (NTP)**

There are two types of status lines listed in the RTECS file. The first indicates that the substance has been or is being tested by the [NTP](#) under its Carcinogenesis Testing Program. These entries were identified as [National Cancer Institute \(NCI\)](#) status lines in issues of the Registry prior to July 1980. However, the NCI Carcinogenesis Testing Program has been absorbed by NTP, and subsequent status lines have been reformatted accordingly. The following different citations are used to reflect the current test status of the compound: nominated for test; selected for test; currently undergoing test; or test completed.

These citations are updated as each bioassay progresses. Selection of a chemical for bioassay does not necessarily imply that it is a carcinogen. Also, a compound originally selected and even scheduled for bioassay may be withdrawn from the program anytime during testing or before testing actually begins. This initial selection is cited in the Registry but is deleted when the compound is removed from the test.



The bioassay itself normally takes about two and one half years to conduct, and another year is required to prepare the final report. When this report is released, the report number and test results are listed, and, where applicable, specific tumorigenic dose lines (see Section 13) are generated.

In June 1983, then revised in 1986, NTP adopted five categories of interpretive conclusions for use in their technical reports. The Registry citations make use of these same five categories in the NTP Status Lines. As defined by NTP, the categories (which refer to the strength of the experimental evidence) are as follows:

- CLEAR EVIDENCE of Carcinogenicity Activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- SOME EVIDENCE of Carcinogenicity Activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined), in which the strength of the response is less than that required for clear evidence.
- EQUIVOCAL EVIDENCE of Carcinogenicity Activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemically related.
- NO EVIDENCE of Carcinogenicity Activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- INADEQUATE STUDY of Carcinogenicity Activity is demonstrated by studies that because of major qualitative or quantitative limitations cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

Final reports for some bioassays may not be published because the data are insufficient, and this is noted in the Registry where applicable. Also, some substances may be selected by NTP for retest after the first bioassay is completed and the final report issued. These duplicate studies are noted on a separate NTP status line. Some of the early NCI testing was not done in accordance with the strict experimental protocols now used. The results of these studies were not published as NCI bioassay reports, but instead appeared in the literature as journal articles. These are noted on the NTP status lines as "studies" rather than "bioassays," and reference to the journals are given. To obtain additional information about the Carcinogenesis Testing Program or the status of a particular substance under test, or to obtain copies of the final bioassay reports, contact:

Central Data Management  
Mail Drop E1-02, NIEHS,  
P.O. Box 12233  
Research Triangle Park  
North Carolina 27709  
telephone (919) 541-3991

The second type of NTP status line indicates that the substance is listed in the NTP, Report on Carcinogens (RoC). This cumulative list is published in accordance with Public Law 95-622, which requires that the Secretary of Health and Human Services publish a biennial report containing ". . . a list of all substances (1) which either are known to be human carcinogens or which may reasonable be anticipated to be human carcinogens and (2) to which a significant number of persons residing in the United States are exposed . . ." Included for each of the chemicals in the report is a description of the substance, including a brief synopsis of the scientific evidence that led to its inclusion in the report. This is immediately followed by information about the regulatory activities of the NTP-participating federal agencies.

The criteria for listing a substance are as follows:

Known To Be Human Carcinogen:

## Detailed File Description

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There is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.

### Reasonably Anticipated To Be Human Carcinogen:

There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded,

or

there is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset,

or

there is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

For additional information about the report, contact:

National Toxicology Program  
P.O. Box  
12233, Research Triangle Park  
North Carolina 27709  
telephone (919) 541-4096

### **Occupational Safety & Health Administration (OSHA)**

The [OSHA](#) status line reports that a validated analytical method(s) has been developed for the chemical by OSHA and appears in its [Manual of Analytical Methods](#).

**Table I. RTECS Abbreviations**

Abbreviation	Description
alg	alga
asn	Aspergillus nidulans
ast	Ascites tumor
bcs	Bacillus subtilis
bfa	body fluid assay
BHR	Beilstein Handbook Reference
bmr	bone marrow
brd	bird (domestic)
BRN	Beilstein Reference Number
bwd	wild bird species
C	continuous
car	carp
cat	cat
cc	cubic centimeter
cfi	catfish
chd	child
ckn	chicken
CL	ceiling concentration
clr	Chyamydomonas reinhardi
cra	crab
crf	crayfish
ctl	cattle
cyt	Cytogenetic Analysis
D	day
daf	daphnia
dck	duck
dog	dog
DEF	definition
dlt	Dominant Lethal Strain

**Table I. RTECS Abbreviations**

<b>Abbreviation</b>	<b>Description</b>
dmg	Drosophila melanogaster
dna	DNA Adduct
dnd	DNA Damage
dni	DNA Inhibition
dnr	DNA Repair
dns	Unscheduled DNA Synthesis
dom	domestic
DOT	Department of Transportation
dpo	Drosophila pseudo-obscura
emb	embryo
EPA	Environmental Protection Agency
esc	Escherichia coli
eug	Euglena gracilis
eye	administration into the eye (irritant)
fb	fiber
fbr	fibroblast
frg	frog
gm	gram
gpg	guinea pig
grb	gerbil
grh	grasshopper
gup	guppie
H	hour
ham	hamster
hla	HeLa cell
hma	Host-mediated Assay
hmi	Haemophilus influenza
hmn	human
hor	horse, donkey
I	intermittent

Table I. RTECS Abbreviations

Abbreviation	Description
ial	intra-aural
IARC	International Agency for Research on Cancer
iat	intra-arterial
ice	intracerebral
icv	intracervical
idr	intradermal
idu	intraduodenal
ihl	inhalation
imm	immersion
imp	implant
ims	intramuscular
inf	infant
ipc	intraplacental
ipl	intrapleural
ipr	intraperitoneal
irn	intrarenal
isp	intraspinal
itr	intratracheal
itt	intratesticular
iu	international unit
iut	intra-uterine
ivg	intravaginal
ivn	intravenous
kdy	kidney
kfi	killifish
kg	kilogram (one thousand grams)
klp	Klebsiella pneumoniae
L	liter
LC50	lethal concentration, 50 percent kill
LCLo	lowest published lethal concentration

**Table I. RTECS Abbreviations**

<b>Abbreviation</b>	<b>Description</b>
LD50	lethal dose, 50 percent kill
LDLo	lowest published lethal dose
leu	leukocyte
lim	limanda
liq	liquid
lng	lung
lob	lobster
lvr	liver
lwm	lugworm
lym	lymphocyte
M	minute
m <sup>3</sup>	cubic meter
man	man
mam	mammal (species unspecified)
mg	milligram (one thousandth of a gram, 10 <sup>-3</sup> gram)
min	minnow
mky	monkey
mL	milliliter
MLD	mild irritant effect
mmo	Mutation in Micro-organism
mmol	millimole
mmr	mammary gland
mnt	Micronucleus test
MOD	moderate irritation effect
mol	mole
mppcf	million particles per cubic foot
mrc	Gene Conversion and Mitotic Recombination
msc	Mutation in Mammalian Somatic Cells
MSHA	Mine Safety and Health Administration

Table I. RTECS Abbreviations

Abbreviation	Description
mtr	Morphological Transform
mul	multiple routes
mus	mouse
ng	nanogram (one billionth of a gram, 10 <sup>-9</sup> gram)
nml	non-mammalian species
nmol	nanomole
NOES	National Occupational Exposure Survey
NOHS	National Occupational Hazard Survey
nsc	Neurospora crassa
NTP	National Toxicology Program
OBS	obsolete (trade name)
ocr	other crustaceans
ocu	ocular
OEL	Occupational Exposure Limit
ofs	other fish
oiv	other Invertebrate
omi	other micro-organisms
oms	other mutation test systems
oin	other insects
open	open irritation test
orl	oral
ORM	Other Regulated Materials (DOT)
OSHA	Occupational Safety and Health Administration
oth	other cell types
ovr	ovary
par	parenteral
PEL	Permissible Exposure Limit (OSHA)
pg	picogram (one trillionth of a gram, 10 <sup>-12</sup> gram)
pgn	pigeon
pic	Phage Inhibition Capacity

**Table I. RTECS Abbreviations**

Abbreviation	Description
pig	pig
pph	parts per hundred (v/v) (percent)
ppm	parts per million (v/v)
ppt	parts per trillion (v/v)
pre	prior to copulation
preg	pregnant
qal	quail
rat	rat
rbt	rabbit
rec	rectal
REGS	Standards and Regulations
REL	Recommended Exposure Level
rns	rinsed with water
RTECS	Registry of Toxic Effects of Chemical Substances
S	second
sal	salmon
sat	Salmonella typhimurium
sce	Sister Chromatid Exchange
SCP	Standards Completion Program
scu	subcutaneous
SEV	severe irritation effect
shr	shrimp
skn	administration onto the skin
sln	Sex Chromosome Loss and Nondisjunction
slw	silkworm
smc	Saccharomyces cerevisiae
spm	Sperm Morphology
sql	squirrel
srm	Serratia marcescens
ssd	silverside



Table I. RTECS Abbreviations

Abbreviation	Description
ssp	Schizosaccharomyces pombe
stb	stickleback
STEL	Short-Term Exposure Limit
sun	sunfish
TC	toxic concentration (other than lowest)
TDLo	lowest published toxic dose
tes	testis
TLV	Threshold Limit Value
tod	toad
trk	turkey
trn	Heritable Translocation Test
tro	trout
TWA	time-weighted average
unr	unreported
urc	urchin
W	week
wmn	woman
Y	year
µg	microgram (one millionth of a gram, 10 <sup>-6</sup> gram)
µmole	micromole
zfi	zebrafish
zpn	zooplankton

## Table II. Toxic Effects Codes (TEC)

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### Position 1 - Organ, Tissue, or Functional System

A	Brain and Coverings
B	Spinal Cord
C	Peripheral Nerves and Sensation
D	Sense Organs and Special Senses (Nose, Eye, Ear, and Taste)
E	Autonomic Nervous System
F	Behavioral
G	Cardiac
H	Vascular
I	Aquatic Organism Effects
J	Lung, Thorax, or Respiration
K	Gastrointestinal
L	Liver
M	Kidney, Ureter, and Bladder
N	Endocrine
P	Blood
Q	Musculoskeletal
R	Skin and Appendages
T	Reproductive
U	Nutritional and Gross Metabolic
X	In Vitro Toxicity Studies
V	Tumorigenic
Y	Biochemical
Z	Related to Chronic Data

## Positions 2 and 3 - Damage Codes, Two Digits

Each of the major headings below corresponds to one of the organs, tissues, or functional systems listed in [Position 1](#).

### A. Brain and Coverings

01	Meningeal changes
02	Changes in cerebral spinal fluid
03	Increased intracranial pressure
04	Changes in circulation (Hemorrhage, thrombosis, etc.)
05	Encephalitis
06	Demyelination
10	Changes in surface EEG
11	Recordings from specific areas of CNS
30	Other degenerative changes
60	Tumors
70	Changes in brain weight

### B. Spinal Cord

01	Meningeal changes
02	Changes in circulation
03	Inflammatory changes
04	Demyelination
30	Other degenerative changes
60	Tumors

### C. Peripheral Nerve and Sensation

01	Associated connective tissue
02	Sensory syndrome diagnostic of central lesion
03	Sensory change involving trigeminal nerve
04	Sensory change involving peripheral nerve
05	Sensory change involving segmental distribution
06	Spastic paralysis with or without sensory change
07	Flaccid paralysis with appropriate anesthesia

**Table II. Toxic Effects Codes (TEC)**

08	Flaccid paralysis without anesthesia (usually neuromuscular blockage)
09	Fasciculations
10	Paresthesia
15	Recording from afferent nerve
16	Recording from peripheral motor nerve
17	Local anesthetic
18	Structural change in nerve or sheath
60	Peripheral nerve tumors

## D. Sense Organs and Special Senses

### Olfaction

01	Deviated nasal septum
02	Ulcerated nasal septum
03	Change in olfactory nerve
04	Change in sensation of smell
07	Other changes
09	Tumors

### Eye

10	Optic nerve neuropathy
11	Cycloplegia
12	Changes in refraction
13	Ciliary spasm
14	Visual field changes
15	Miosis (pupillary constriction)
16	Mydriasis (pupillary dilation)
17	Lacrimation
18	Chromodacryorrhea
19	Increased intraocular pressure
20	Retinal changes (pigmentary depositions, retinitis, other)
21	Hemorrhage
22	Changes in circulation

**Table II. Toxic Effects Codes (TEC)**

23	Diplopia
24	Changes in extra-ocular muscles
25	Conjunctive irritation
26	Corneal damage
27	Iritis
28	Ptosis
29	Tumors
35	Other
36	Primary irritation graded mild
37	Primary irritation graded moderate
38	Primary irritation graded severe

### **Ear**

40	Change in acuity
41	Tinnitus
43	Changes in vestibular functions
44	Changes in cochlear structure or function
45	Other

### **Taste**

50	Change in taste function
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### **E. Autonomic Nervous System**

01	Sympathomimetic
02	Alpha adrenergic blockage
03	Beta adrenergic blockage
04	Central sympatholytic
05	Ganglion blocker
06	Ganglion facilitant
08	Other (direct) parasymphomimetic
09	Intensity beta adrenergic effects
15	Smooth muscle relaxant (mechanism undefined, spasmolytic)
16	Parasympatholytic

**Table II. Toxic Effects Codes (TEC)****F. Behavioral**

01	General anesthetic
02	Anticonvulsant
03	Wakefulness
04	Sleep
05	Altered sleep time (including change in righting reflex)
06	Euphoria
07	Somnolence (general depressed activity)
08	Hallucinations, distorted perceptions
09	Change in REM sleep (human)
10	Toxic psychosis
11	Tremor
12	Convulsions or effect on seizure threshold
13	Excitement
14	Anorexia (human)
15	Food intake (animal)
16	Fluid intake
17	Changes in motor activity (specific assay)
18	Muscle weakness
19	Ataxia
20	Stiffness
21	Rigidity (including catalepsy)
22	Tetany
23	Muscle contraction or spasticity
24	Coma
25	Antipsychotic
26	Antianxiety
27	Headache
29	Analgesia
30	Tolerance
31	Withdrawal

**Table II. Toxic Effects Codes (TEC)**

32	Abuse
33	Irritability
34	Straub tail
40	Alteration of classical conditioning
41	Alteration of operant conditioning
42	Changes in psychophysiological tests
43	Aggression

### **G. Cardiac**

01	Cardiomyopathy, including infarction
02	Changes in coronary arteries
03	Pericarditis
04	Arrhythmias (including changes in conduction)
05	Cardiomegaly
06	EKG changes not diagnostic of above
07	Pulse rate increase without fall in BP
08	Pulse rate
09	Change in force of contraction
10	Change in rate
11	Change in conduction velocity
12	Cardiac output
13	Changes in resting or action potential
30	Other changes
60	Tumors
70	Changes in heart weight

### **H. Vascular**

01	BP elevation not characterized in autonomic section
02	BP lowering not characterized in autonomic section
03	Pulse pressure increase
04	Regional or general arteriolar constriction
05	Regional or general arteriolar or venous dilation

**Table II. Toxic Effects Codes (TEC)**

06	Measurement of regional blood flow
07	Change in plasma or blood volume
08	Shock
15	Acute arterial occlusion
16	Structural changes in vessels
17	Thrombosis distant from injection site
20	Contraction (isolated tissues)
21	Relaxation (isolated tissues)
30	Other changes
35	Effect on gills and gill functions
60	Tumors

### I. Aquatic Organism Effects

01	Maturation delay
02	Growth retardation

### J. Lungs, Thorax, or Respiration

01	Ciliary function changes
02	Structural or functional change in trachea or bronchi
03	Bronchiolar dilation
04	Bronchiolar constriction
05	Bronchiectasis
06	Emphysema
07	Changes in pulmonary vascular resistance
08	Consolidation
12	Fibrosis, focal (pneumoconiosis)
13	Fibrosis (interstitial)
14	Fibrosing alveolitis
15	Acute pulmonary edema
16	Chronic pulmonary edema
17	Pleural effusion
18	Pleural thickening



Table II. Toxic Effects Codes (TEC)

20	Respiratory obstruction
21	Cough
22	Dyspnea
23	Sputum
24	Cyanosis
25	Respiratory depression
26	Respiratory stimulation
27	Pulmonary emboli
30	Other changes
60	Tumors
61	Bronchiogenic carcinoma
70	Changes in lung weight

## K. Gastrointestinal

01	Changes in structure or function of salivary glands
02	Changes in structure or function of endocrine pancreas
03	Changes in structure or function of esophagus
04	Alteration in gastric secretion
05	Gastritis
06	Ulceration or bleeding from stomach
07	Ulceration or bleeding from duodenum
08	Ulceration or bleeding from small intestine
09	Ulceration or bleeding from large intestine
12	Hypermotility, diarrhea
13	Nausea or vomiting
14	Decreased motility or constipation
15	Malabsorption
17	Peritonitis
20	Necrotic changes
30	Other changes
31	Contraction (isolated tissue)

**Table II. Toxic Effects Codes (TEC)**

32	Relaxation (isolated tissue)
60	Tumors
61	Colon tumors
70	Changes in pancreatic weight

**L. Liver**

01	Hepatitis (hepatocellular necrosis), diffuse
02	Hepatitis (hepatocellular necrosis), zonal
03	Fatty liver degeneration
04	Hepatitis, fibrous (cirrhosis, post-necrotic scarring)
11	Jaundice, cholestatic
12	Jaundice, other or unclassified
14	Liver function tests impaired
15	Changes in gall bladder structure or function
19	Jaundice (or hyperbilirubinemia) hepatocellular
30	Other changes
50	Multiple effects
60	Tumors
61	Angiosarcoma
70	Changes in liver weight
61	Angiosarcoma
70	Changes in liver weight

**M. Kidney, Ureter, and Bladder**

01	Changes in blood vessels or in circulation of kidney
02	Changes primarily in glomeruli
03	Changes in tubules (including acute renal failure, acute tubular necrosis)
04	Changes in both tubules and glomeruli
05	Interstitial nephritis
10	Urine volume increased
11	Urine volume decreased
12	Renal function tests depressed

**Table II. Toxic Effects Codes (TEC)**

13	Proteinuria
14	Hematuria
16	Other changes in urine composition
20	Inflammation, necrosis, or scarring of bladder
21	Structural or functional changes in ureter
29	Incontinence
30	Other changes
60	Tumors
61	Kidney tumors
70	Changes in bladder weight
71	Changes in kidney weight

## **N. Endocrine**

01	Antidiuresis
02	Changes in LH
03	Changes in GH
04	Change in gonadotropins
05	Thyroid weight (goiter)
06	Toxic goiter - hypofunction
07	Evidence of thyroid hyperfunction
08	Evidence of thyroid hypofunction
10	Hyperparathyroidism
12	Adrenal cortex hyperplasia
13	Adrenal cortex hypoplasia
15	Aldosternism
16	Androgenic
17	Estrogenic
18	Differential effect of sex or castration on observed toxicity
19	Effect on menstrual cycle
20	Gynecomastia
21	Diabetes mellitus

**Table II. Toxic Effects Codes (TEC)**

22	Hypoglycemia
23	Ketosis
24	Hyperglycemia
25	Diabetes insipidus (nephrogenic or CNS)
30	Other changes
60	Tumors
61	Adrenal cortex tumors
62	Thyroid tumors
70	Changes in endocrine weight (unspecified)
71	Changes in pituitary weight
72	Changes in adrenal weight
73	Changes in spleen weight
74	Changes in thymus weight
75	Changes in thyroid weight

**P. Blood**

01	Hemorrhage
02	Change in clotting factors
05	Normocytic anemia
06	Microcytosis with or without anemia
07	Macrocytosis
08	Pigmented or nucleated red blood cells
13	Granulocytopenia
14	Leukopenia
15	Agranulocytosis
16	Eosinophilia
17	Thrombocytopenia
20	Changes in cell count (unspecified)
22	Oxidant-related (GPD-deficient) anemia
23	Other hemolysis with or without anemia
24	Methemoglobinemia-Carboxyhemoglobin

25	Aplastic anemia
26	Changes in bone marrow not included above
27	Changes in spleen
28	Changes in serum composition (e.g., TP, bilirubin, cholesterol)
30	Other changes
60	Tumors
61	Leukemia
62	Lymphoma, including Hodgkin's disease
70	Changes in other cell count (unspecified)
71	Changes in erythrocyte (RBC) count
72	Changes in leucocyte (WBC) count
73	Changes in platelet count

## Q. Musculoskeletal

See also [Behavioral](#) for muscle change secondary to CNS or metabolic changes.

01	Changes in teeth and supporting structures
02	Osteoporosis
10	Osteomalacia
15	Joints
30	Other changes
60	Tumors

## R. Skin and Appendages

### Skin

After systemic exposure:

01	Dermatitis, allergic
02	Dermatitis, irritative
03	Dermatitis, other
04	Photosensitivity

After topical exposure:

10	Primary irritation
11	Corrosive

**Table II. Toxic Effects Codes (TEC)**

12	Dermatitis, allergic
13	Cutaneous sensitization (experimental)
14	Photosensitivity
15	Primary irritation graded mild
16	Primary irritation graded moderate
17	Primary irritation graded severe

**Other**

20	Sweating
21	Hair
22	Nails
25	Breast
30	Other glands
60	Tumors

**S. Immunological, including Allergic**

01	Increase in cellular immune response
02	Decrease in cellular immune response
03	Increase in humoral immune response
04	Decrease in humoral immune response
05	Decreased immune response
06	Increased immune response

**Allergic (Multiple organ involvement)**

When single organs are involved, coded under organ.

Cholesterol jaundice - see [Liver](#).

Aplastic anemia, agranulocytoses - see [Blood](#).

Allergic dermatitis - see [Skin](#).

15	Anaphylaxis
16	Other immediate (humoral) urticaria, allergic rhinitis, serum sickness
18	Hypersensitivity delayed
20	Autoimmune
25	Uncharacterized

## U. Nutritional and Gross Metabolic

See also [Biochemical](#) (Intermediary Metabolism).

### Gross Metabolite Changes

01	Weight loss or decreased weight gain
02	Conditioned vitamin deficiency
03	Dehydration

### Changes in Chemistry or Temperature

05	Na
06	Cl
07	Ca
08	P
09	Fe
10	K
11	Other metals
20	Metabolic acidosis
21	Metabolic alkalosis
25	Body temperature increase
28	Body temperature decrease
30	Other changes

## V. Tumorigenic

01	Carcinogenic by RTECS criteria
02	Neoplastic by RTECS criteria
03	Equivocal tumorigenic agent by RTECS criteria
05	Cells (cultured) transformed
08	Increased incidence of tumors in susceptible strains
10	Tumors at site of application
15	Tumor types after systemic administration not seen spontaneously
16	Facilitates action of known carcinogen
25	Protects against induction of experimental tumors
30	Active as anti-cancer agent

**Table II. Toxic Effects Codes (TEC)****X. In Vitro Toxicity Studies**

01	Cell counting
02	Cell viability (cell death), unspecified assay
03	Cell differentiation
04	Cell growth: colony formation
05	Cell membrane integrity: cytoplasmic enzymes leakage (lactate dehydrogenase, ATP enzymes etc.)
06	Cell metabolic activity: Alamar Blue assay etc.
07	Cell morphology: overgrowth of cell appendices etc.
08	Cell proliferation: DNA incorporation, mitotic index etc.
09	Cell viability (dye exclusion): trypan blue assay etc.
10	Cell viability (lysosomal damage): neutral red assay etc.
11	Cell viability (mitochondrial reductase assays): MTT, XTT, MTS, WSTs assays etc.
12	Hemolysis in vitro
13	Cell protein synthesis
14	Apoptosis in vitro
15	Cell membrane integrity (prelabeled cells): release of radioactive isotopes ([ <sup>51</sup> Cr], [ <sup>3</sup> H]- thymidine, [ <sup>3</sup> H]-proline, [ <sup>35</sup> S]- or [ <sup>75</sup> Se]-methionine, 5-[ <sup>125</sup> I]-2-deoxy-uridine) or fluorescent dyes (bis-carboxyethyl-carboxyfluorescein (BCECF) or calcein-AM)
16	Membrane currents
17	Phototoxicity in vitro
30	Other assays

**Y. Biochemical****Enzyme inhibition, induction, or change in blood or tissue levels**

01	True cholinesterase
02	Other esterases
03	Phosphatases
04	Other hydrolases
05	Carbonic anhydrase
06	Xanthine oxidases
07	Hepatic microsomal mixed oxidase (dealkylation, hydroxylation, etc.)



**Table II. Toxic Effects Codes (TEC)**

08	Monoamine oxidase
09	Cytochrome oxidases (including oxidative phosphorylation)
10	Dehydrogenases
11	Catalases
12	Other oxidoreductases
13	Phosphokinase
14	Hexokinases
15	Transaminases
16	Other transferases
17	Peptidases
18	Proteases
19	Isomerases
20	Multiple enzyme effects
21	Other enzymes
23	Reactivates cholinesterase

**Effect on specific coenzyme**

25	B vitamins, including folate
26	CoA
27	NAD, NADP
28	Others
29	Proportion of isoenzymes
30	Disturbed regulation

**Metabolism (intermediary)**

35	Xanthine, purine, or nucleotides, including urate
36	Porphyryn, including bile pigments
37	Lipids, including transport
38	Amino acids (including renal excretion)
39	Plasma proteins not involving coagulation
40	Other proteins
41	Glycolytic

**Table II. Toxic Effects Codes (TEC)**

42	TCA cycle
43	Pentase shunt
44	Other carbohydrates
45	Histamines (including liberation not immunochemical in origin)
50	Effect on mitochondrial function
51	Effect on active transport
52	Effect on Na-K pump
53	Other
54	Effect on cyclic nucleotides
55	Effect on inflammation or mediation of inflammation

**Neurotransmitters or modulators (putative)**

60	Catecholamine levels in sympathetic nerves
61	Catecholamine levels in CNS
64	Dopamine in striatum
65	Dopamine at other sites

**Z. Related to Chronic Data**

01	Death in the Other Multiple Dose data type field
71	Changes in ovarian weight
72	Changes in prostate weight
73	Changes in testicular weight
74	Changes in uterine weight

## Table III. Reproductive Effects Code

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### Paternal Effects

T01	Spermatogenesis (including genetic material, sperm morphology, motility, and count)
T02	Testes, epididymis, sperm duct
T03	Prostate, seminal vesicle, Cowper's gland, accessory glands
T04	Impotence
T05	Breast development
T09	Other effects in male

### Maternal Effects

T11	Oogenesis
T12	Ovaries, fallopian tubes
T13	Uterus, cervix, vagina
T14	Menstrual cycle changes or disorders
T15	Breasts, lactation (prior to or during pregnancy)
T16	Parturition
T17	Postpartum
T19	Other effects

### Effects on Fertility

T21	Mating performance (e.g., number of sperm-positive females per number of females mated; number of copulations per number of estrus cycles)
T22	Female fertility index (e.g., number of females pregnant per number of sperm-positive females; number of females pregnant per number of females mated)
T23	Male fertility index (e.g., number of males impregnating females per number of males exposed to fertile non-pregnant females)
T24	Pre-implantation mortality (e.g., reduction in number of implants per female; total number of implants per corpora lutea)
T25	Post-implantation mortality (e.g., dead and/or reabsorbed implants per total number of implants)
T26	Litter size (e.g., number of fetuses per litter, measured before birth)
T27	Abortion
T29	Other measures of fertility

**Table III. Reproductive Effects Code**

## Effects on Embryo or Fetus

T31	Extra-embryonic structures (e.g., placenta, umbilical cord)
T32	Maternal-fetal exchange
T33	Cytological changes (including somatic cell genetic material)
T34	Fetotoxicity (except fetal death)
T35	Fetal death
T39	Other effects on embryo

## Specific Developmental Abnormalities

T41	Central nervous system
T42	Eye, ear
T43	Craniofacial (including nose and tongue)
T44	Skin and skin appendages
T45	Body wall
T46	Musculoskeletal system
T47	Cardiovascular (circulatory) system
T48	Blood and lymphatic system (including spleen and marrow)
T49	Respiratory system
T50	Gastrointestinal system
T51	Hepatobiliary system
T52	Endocrine system
T53	Urogenital system
T54	Immune and reticuloendothelial system
T55	Homeostasis
T59	Other developmental abnormalities

## Tumorigenic Effects

T61	Testicular tumors
T62	Prostate tumors
T63	Ovarian tumors
T64	Uterine tumors

T65	Transplacental tumorigenesis
T69	Other reproductive system tumors

### Effects on Newborn

T71	Stillbirth
T72	Live birth index (similar to T26, except measured after birth)
T73	Sex ratio
T74	Apgar score (human only)
T75	Viability index (e.g., number alive at day 4 per number born alive)
T76	Weaning or lactation index (e.g., number alive at weaning per number alive at day 4)
T77	Other neonatal measures or effects
T81	Growth statistics (e.g., reduced weight gain)
T82	Germ cell effects (in offspring)
T83	Biochemical and metabolic
T84	Drug dependence
T85	Behavioral
T86	Physical
T87	Other postnatal measures or effects
T91	Delayed effects

**Table IV. Routes of Administration to, or Exposure of, Animal Species to Toxic Substances**

Abbreviation	Route	Definition
eye	Eyes	Administration directly onto the surface of the eye. Used exclusively for primary irritation data. See Ocular.
ial	Intra-aural	Administration into the ear
iat	Intra-arterial	Administration into the artery
ice	Intracerebral	Administration into the cerebrum
icv	Intracervical	Administration into the cervix
idr	Intradermal	Administration within the dermis by hypodermic needle
idu	Intraduodenal	Administration into the duodenum
ihl	Inhalation	Inhalation in chamber, by cannulation, or through mask
imp	Implant	Placed surgically within the body location described in reference
ims	Intramuscular	Administration into the muscle by hypodermic needle
ipc	Intraplacental	Administration into the placenta
ipl	Intrapleural	Administration into the pleural cavity by hypodermic needle
ipr	Intraperitoneal	Administration into the peritoneal cavity
irn	Intrarenal	Administration into the kidney
isp	Intraspinal	Administration into the spinal canal
itr	Intratracheal	Administration into the trachea
itt	Intratesticular	Administration into the testes
iut	Intrauterine	Administration into the uterus
ivg	Intravaginal	Administration into the vagina
ivn	Intravenous	Administration directly into the vein by hypodermic needle
mul	Multiple	Administration by more than one route
ocu	Ocular	Administration directly onto the surface of the eye or into the conjunctival sac. Used exclusively for systemic toxicity data. See Eyes.
orl	Oral	Per os, intragastric feeding, or introduction with drinking water
par	Parenteral	Administration into the body through the skin. Reference is not specific concerning the route used.

**Table IV. Routes of Administration to, or Exposure of, Animal Species to Toxic Substances**

<b>Abbreviation</b>	<b>Route</b>	<b>Definition</b>
rec	Rectal	Administration into the rectum or colon in the form of enema or suppository
scu	Subcutaneous	Administration under the skin
skn	Skin	Application directly onto the skin, either intact or abraded. Used for both systemic toxicity and primary irritant effects.
tnk	Tank	Administration into the tank for Aquatic toxicity.
unr	Unreported	Dose, but not route, is specified in the reference.
vit	In Vitro	In vitro administration

## Table V. Species

With assumptions for Toxic Dose Calculation from Non-specific Data\*

Species	Age	Weight	Approximate Consumption of Food, gm/day	Approximate Consumption of Water, mL/day	1 ppm in Food equals in mg/kg/D	Approximate Gestation Period (days)
Bird, domestic or laboratory; bird, not otherwise identified		1 kg				
Bird, wild bird species		40 gm				
Cat, adult		2 kg	100	100	0.05	64 (59 – 68)
Child	1 – 13 Y	20 kg				
Chicken, adult (male or female)	8 W	800 gm	140	200	0.175	
Cattle, horse		500 kg	10,000		0.02	284 (279 – 290)
Duck, adult (domestic)	8 W	2.5 kg	250	500	0.1	
Dog, adult	52 W	10 kg	250	500	0.025	62 (56 – 68)
Domestic animals – goat, sheep		60 kg	2,400		0.04	Goat: 152 (148-156) Sheep: 146 (144-147)
Frog, adult		33 gm				
Guinea pig, adult		500 gm	30	85	0.06	68
Gerbil		100 gm	5	5	0.05	25 (24 – 26)
Hamster	14 W	125 gm	15	10	0.12	16
Human	Adult	70 kg				



Table V. Species

Species	Age	Weight	Approximate Consumption of Food, gm/day	Approximate Consumption of Water, mL/day	1 ppm in Food equals in mg/kg/D	Approximate Gestation Period (days)
Horse, donkey		500 kg	10,000			Horse: 339 (333-345) Donkey: 365
Infant, human	0 – 1 Y	5 kg				
Mammal, species unidentified		200 gm				
Man	Adult	70 kg				
Monkey	2.5 Y	5 kg	250	500	0.05	165
Mouse	8 W	25 gm	3	5	0.12	21
Non-mammalian species						
Pigeon	8 W	500 gm				
Pig		60 kg	2,400		0.041	114 (112 – 115)
Quail (laboratory)		160 gm				
Rat, adult female	14 W	200 gm	10	20	0.05	22
Rat, adult male	14 W	250 gm	15	25	0.06	
Rat, adult, gender unspecified	14 W	200 gm	15	25		
Rat, weaning	3 W	50 gm	15	25	0.3	
Rabbit, adult	12 W	2 kg	60	330	0.03	31
Squirrel		500 gm				44
Toad		100 gm				
Turkey	18 W	5 kg				
Woman	Adult	50 kg				270

## Table V. Species

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**Note:** \* Values given here are within reasonable limits usually found in the published literature and are selected to facilitate calculations for data from publications in which toxic dose information has not been presented for an individual animal of the study. Data for lifetime exposure are calculated from the assumptions for adult animals for the entire period of exposure. For definitive dose data, the reader must review the referenced publications.

**Table VI. Master File Data Types (Position 10)**

Code Number	Data Type	Detailed File Description Format Section
A	Substance Prime Name	1
B	Synonym Cross Reference	1
C	Chemical Description/Definition	1
D	Chemical Registry Number Chemical Abstracts Service Beilstein Registry	3
E	Update Field	2
F	Molecular Formula	6
G	RTECS Number	4
H	Molecular Weight	5
J	Wiswesser Line Notation	7
L	Synonym	8
N	Compound Descriptor Code	9
P	Irritation Data	10, 16
Q	Mutation Data	11, 16
R	Reproductive Effects Data	12, 16
S	Tumorigenic Data	13, 16
T	Acute Toxicity Data	14, 16
U	Other Multiple Dose Toxicity Data	15, 16
V	Reviews	17, 16
W	Standards and Regulations	18, 16
X	NIOSH REL Documentation and Surveillance Data	19, 16
Y	ATSDR, EPA, NIOSH, NTP, and OSHA Status	20, 16

**Table VII. Line Numbers for "V", "W", "X", and "Y" Data**

Line Number	Data
V010-039	ACGIH TLV Data
V100-299	IARC Cancer Reviews
V300	IARC Cancer Review, Supplement 7
V800-899	Toxicology Review References
W100-110	Inactive at this time
W200	EPA Farm Worker Field Re-entry Data
W400-410	MSHA Standard Data
W500	OSHA PEL (General Industry)
W505	OSHA PEL (Construction)
W510	OSHA PEL (Shipyards)
W515	OSHA PEL (Federal Contractors)
W550	OSHA Cancer Suspect Agent
W600-699	International Occupational Exposure Levels
X500-510	NIOSH REL Data
X600	NOHS (1974)
X610	NOES (21983)
Y010-035	EPA Genetic Toxicology Program Data
Y050	EPA TSCA Chemical Inventory Status 8(d)
Y100	EPA TSCA 8(a)
Y130	EPA TSCA 8(b)

**Table VIII\*. Letter Codes for Species, System Organ Classes, and Cells, Tissue or Organ in Specific System Organ Class for In Vitro Studies**

## Species

Species	Letter Codes
Cat	a
Chicken	b
Cattle, horse	c
Dog	e
Domestic animals - goat, sheep	f
Frog	g
Guinea pig	h
Hamster	i
Human	j
Mammal - species unspecified	k
Monkey	l
Mouse	m
Non-mammalian species	n
Pig	o
Rat	p
Rabbit	q

## System Organs

System Organ Classes	Letter Codes
BRAIN AND COVERINGS	a
SENSE ORGANS AND SPECIAL SENSES (NOSE, EYE, EAR, and TASTE)	d
CARDIAC	g
VASCULAR	h
LUNGS, THORAX, OR RESPIRATION	j
GASTROINTESTINAL	k

**Table VIII\*. Letter Codes for Species, System Organ Classes, and Cells, Tissue or Organ in Specific System Organ Class for In Vitro Studies**

System Organ Classes	Letter Codes
LIVER	l
KIDNEY, URETER, AND BLADDER	m
ENDOCRINE	n
BLOOD	p
MUSCULOSKELETAL	q
SKIN AND APPENDAGES	r
REPRODUCTIVE	t
GENERAL	u
TUMORIGENIC	v

### Cells, Tissue, or Organ in Specific Organs

Cells, Tissue, or Organ in Specific Organ Class	Letter Codes
<b>BRAIN AND COVERINGS</b>	<b>a</b>
brain (cerebrum)	aa
brain other (hippocampus etc)	ax
cerebellum	ac
meninges	ad
neurons	ae
glioma	af
neuroblastoma	ag
other brain tumors	ah
<b>SENSE ORGANS AND SPECIAL SENSES (NOSE, EYE, EAR, and TASTE)</b>	<b>d</b>
ocular	da
otic	db
nasal	dc
<b>CARDIAC</b>	<b>g</b>
myocard	ga
cardiac conduction system	gb
<b>VASCULAR</b>	<b>h</b>
endothelium	ha

**Table VIII\*. Letter Codes for Species, System Organ Classes, and Cells, Tissue or Organ in Specific System Organ Class for In Vitro Studies**

Cells, Tissue, or Organ in Specific Organ Class	Letter Codes
fibroblast	hb
<b>LUNGS, THORAX, OR RESPIRATION</b>	<b>j</b>
lung	ja
lung fibroblast	jb
lung tumor	jc
<b>GASTROINTESTINAL</b>	<b>k</b>
intestinal	ka
colon	kb
stomach	kc
tooth	ki
oral mucosa	ke
pancreas	kf
colon tumor	kg
gastrointestinal tumor	kh
<b>LIVER</b>	<b>l</b>
liver	la
liver tumor	lb
<b>KIDNEY, URETER, AND BLADDER</b>	<b>m</b>
bladder	ma
kidney	mb
kidney tumor	mc
<b>ENDOCRINE</b>	<b>n</b>
endocrine cell(tissues)	na
endocrine tumor	nb
<b>BLOOD</b>	<b>p</b>
blood (whole or unspecified cells)	pa
erythrocytes	pb
leukocyte	pc
lymphocyte	pd
monocyte	pe

**Table VIII\*. Letter Codes for Species, System Organ Classes, and Cells, Tissue or Organ in Specific System Organ Class for In Vitro Studies**

Cells, Tissue, or Organ in Specific Organ Class	Letter Codes
macrophage	pf
bone marrow	pg
leukemia cells	ph
<b>MUSCULOSKELETAL</b>	<b>q</b>
bone	qa
muscular	qb
<b>SKIN AND APPENDAGES</b>	<b>r</b>
skin	ra
skin tumor	rb
breast	rc
breast tumor	rd
<b>REPRODUCTIVE</b>	<b>t</b>
embryo	ta
embryonic cells	tb
HeLa cell	tc
ovary	td
uterus, vagina	te
female reproductive tumors	tf
testis	tg
prostate	th
male reproductive tumors	ti
spermatozoa	tj
<b>GENERAL</b>	<b>zx</b>
other normal tissue	zx
<b>TUMORIGENIC</b>	<b>v</b>
ascites tumor	va
melanoma	vb
other tumor, organ unspecified	vx

**Note:** \* If the three-letter combination is NOT found, look for the one in Test Species list on page 15. Codes for Bacteria, Molds, Yeasts, Protozoa are listed under Mutation Data (Data Type Q).