FEATURE

An overview of the Registry of Toxic Effects of Chemical Substances (RTECS): Critical information on chemical hazards

Since 1971, the National Institute for Occupational Safety and Health (NIOSH) has been building RTECS into a definitive toxicological database with supplemental information pertinent to both the chemical industry and the occupational safety and health community. RTECS provides the technical data needed to assess workers' exposures to chemicals, particularly to lesser-known-and-used chemical substances. OSHA has designated RTECS as a primary source for toxicity data for Material Safety Data Sheets in its Hazard Communications Rule. In recent years, RTECS has grown to include more than 145,000 chemical substances, 337,000 synonymous names, and 287,000 individual toxicity citations. The toxicological data are organized into six fields: primary irritation, mutagenic effects, reproductive effects, tumorigenic effects, acute toxicity, and other multiple dose toxicity. Each data line includes the citation to its bibliographic source. RTECS provides a host of reference data including, but not limited to: CAS Numbers, OSHA PELs, ACGIH TLVs, NIOSH RELs, Carcinogenic assessments, Beilstein Reference Numbers, Bioassay results from the National Toxicology Program, and status lines pointing to several programs of the EPA [Toxic Substance Control Act (TSCA), Genetic Toxicology (GENE-TOX), Toxic Substance Control Act Test Submission (TSCATS), Integrated Risk Information System (IRIS)].

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INTRODUCTION

Since the first Toxic Substances List, mandated by Section 20(a)(6) of the Occupational Safety and Health Act (OSHA) of 1970, was released in 1971, the National Institute for Occupational Safety and Health (NIOSH) has been steadily building and expanding what has come to be known as the Registry of Toxic Effects of Chemical Substances (RTECS). In early 1999, RTECS contained over 145,000 chemical substances. RTECS is widely recognized and used as a major source of toxicity data and a pointer to the world's toxicological literature.

The RTECS file is updated quarterly. Each quarterly report provides a list of the number of all types of data lines. As of April 1999, there were 146,470 individual chemical substances listed, with 340,756 synonymous names. Exactly 121,574 of these chemicals were identified by Chemical Abstract Service (CAS) numbers, with 1744 chemicals bearing more than one CAS number.

This paper describes the contents of the RTECS database, highlights certain conventions that may cause confusion, and lists possible additions to the file that are under consideration.

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RTECS RECORD CONTENTS

Each RTECS record contains certain chemical identifiers. The most significant identifier is the CAS Number assigned as a function of the American Chemical Society. NIOSH entered into a cross-reference agreement with the Beilstein Institute. As a result, Beilstein reference numbers and Beilstein handbook references are noted within appropriate records. These entries expedite the retrieval of corresponding data from the massive collection of organic chemical information offered by Beilstein. In addition, RTECS assigns its own 9-position alpha-numeric identifier for each substance entered. These RTECS numbers have been adopted for use in numerous private chemical listings. Certain commercial catalogues (e.g.,

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Table 1. RTECS Data Fields

Line Designation	Field
A.	Prime chemical name
B.	Cross reference
C.	Definition
D.	Chemical identifiers
E.	Update field
F.	Molecular formula
G.	RTECS number
H.	Molecular weight
J.	Wiswesser line notation
L.	Synonyms
N.	Compound descriptor code
P.	Irritation data
Q.	Mutagenic effect data
R.	Reproductive effect data
S.	Tumorigenic data
T.	Acute Toxicity data
U.	Other multiple dose toxicity data
V.	Reviews
W.	Standards and regulations
X.	NIOSH documentation and surveillance
Y.	Status

the Aldrich Chemical Company, Sigma Chemicals), the International Registry of Potentially Toxic Chemicals, and the International Chemical Safety Cards list this identifier with their records.

An individual RTECS record may include as little as a single toxicity citation in addition to the identifiers, or it may contain multiple citations, in the cases of widely studied substances. Benz(a)pyrene, for example, includes more than 300 toxicity lines.

The synonym field has been valuable to users of the RTECS database. Many chemicals are known by various names. The names originate from the use of different chemical nomenclature systems, common names, foreign names, and often trade names. A user often knows only a single name, other than the prime chemical name. Since RTECS maintains an extensive synonym field, users can access the appropriate record when searching RTECS.

Table 1 provides a list of the 21 fields which all RTECS data are organized and the alphabetic symbol used to identify each field.

RTECS POLICIES, PROCEDURES, AND SOURCES

Since RTECS is the product of NIOSH, its toxicological data have been augmented with information of special importance to the occupational safety and health community. Notable among these special values or indicators are the following:

- Permissible Exposure Limits (PELs) from OSHA
- Air exposure standards from the Mine Safety and Health Administration (MSHA)
- Recommended Exposure Levels (RELs) from NIOSH
- Threshold Limit Values (TLVs) from the American Conference of Governmental Industrial Hygienists (ACGIH)
- Selected data from the Toxic Substances Control Act (TSCA) administered by the EPA

The process of maintaining and updating RTECS requires continuous searching of the world's toxicological literature to find new substances for entry into the file and additional toxicity studies to add to or modify existing records. The RTECS policy has always been "to cite the lowest published end point (exposure value) for any route-species combination." While this policy opens RTECS to the potential danger of citing outliers, the editorial staff still believes it is prudent to err on the side of safety, and retain the practice of citing the "lowest published end point for any route-species combination."

Since RTECS does cite the lowest published end point for a substance, RTECS is unique among toxicological databases. Moreover, RTECS is especially useful because it allows searchers rapid and easy access to needed chemical information. There are numerous extensive collections of toxicity data, but most of these collections simply provide abstracts of pertinent papers, leaving the extraction of numerical data to the individual user. While the preponderance of RTECS data are extracted from a core journal list of about 150 technical journals, RTECS also cites data from abstracts, textbooks, government reports, compendia, proceedings of scientific meetings, symposia, industry reports and letters, professional society reports, reports by research institutions, personal communications, and publications from a large number of nonEnglish language publications. Most recently, domestic and foreign patent reports have been searched and are included on a regular basis.

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One fact should be emphasized in any discussion of RTECS data: the RTECS editors do not evaluate the scientific validity of any cited reference.

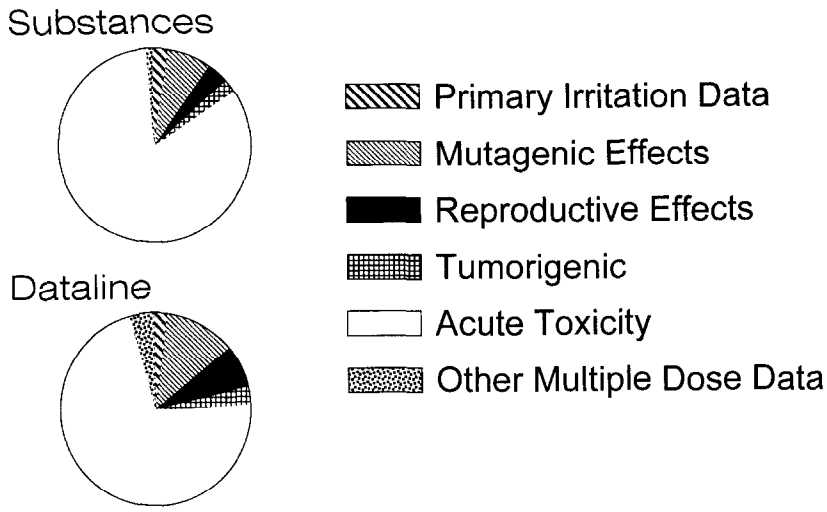

Figure 1. RTECS Toxicity Fields.

Given the quantity and scope of the database, it would be unrealistic to have a few individuals impose their judgement on the quality of the data and the studies from which they were generated. The individual user can access the original reference to evaluate the quality of the data and make his/her own judgement about its usefulness or value.

ORGANIZATION OF THE RTECS FILE

The toxicity data in RTECS are organized into six different fields: primary irritation, mutagenic effects, reproductive effects, tumorigenic effects, acute toxicity, and other multiple dose data.[1] By far, the largest group is the acute toxicity data, which is in effect the reported outcome of single dose exposure. Figure 1 shows the distribution of the types of toxicity data, first as a function of the number of chemical substances whose records contain each type of toxicity data, and second as a function of the total number of data lines cited in each field.

To use the information effectively, one needs to understand the different formats within these six fields. Four of the six fields include, where applicable, special toxic effect codes, which denote descriptive information provided by authors of cited references. These codes are structured in a three-position alphanumeric format. The first position (alphabetic) indicates the organ, tissue or functional system described, and the second and third positions (numeric) denote specific damage or aberrations produced. Table 2 lists the alphabetic coding. There are currently 460 individual damage codes in the full table.

Following is a brief description of the six toxicity fields.

First, the primary irritation data are derived from the Draize test[2] results. The Draize test provides information on skin and eye irritation. The studies are conducted on selected mammalian species, primarily the rabbit. Only positive results are cited, and the dosage noted is the level at which the positive effect occurs. If the author offers such descriptive information, the result may be further described as mild, moderate, or severe. Any deviation from the standard Draize test is noted, such as open, rinsed, or variation from standard time of test.

Table 2. RTECS Toxic Effect Codes

Organ, Tissue, or Functional System	
A.	Brain and coverings
B.	Spinal cord
C.	Peripheral nerve and sensation
D.	Sense organs and special senses (nose, eye, ear, and taste)
E.	Autonomic nervous system
F.	Behavioral
G.	Cardiac
H.	Vascular
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
V.	Tumorigenic
Y.	Biochemical
Z.	Related to chronic data

Second, the mutagenic effect data field provides only positive test result data. It includes 20 specific test systems, both in vitro and in vivo.[3] The end point in this field describes an exposure concentration rather than an administered dose, and may be expressed on a weight/volume basis or weight per plate, well, or disc. Tested organisms may include bacteria, molds, yeasts, protozoa, insects, and various cell types.

Third, the reproductive effect data include not only teratogenic data, but effects on male and female parents, effects on fertility, developmental abnormalities, effects on the embryo or fetus, tumorigenic effects, and effects on the newborn. Each data line identifies the time and duration of the study, as well as the gestation period of the test. The doses that are noted are cumulative for the total test period. There are also 65 separate reproductive effect codes used to better describe the nature of the effect noted in the reference. Only mammalian species studies are reported in this field.

Fourth, the tumorigenic effect data and the codes ascribed to them relate, in each case, only to the individual cited report. There are three major tumorigenic effect codes, namely V01, V02, V03 which denote: "carcinogenic by RTECS criteria," "neoplastic by RTECS criteria," and "equivocal tumorigenic results," in that order. The specific criteria are outlined in the RTECS detailed file description.[1] The reader is cautioned, however, that these descriptions apply only to the data lines on which they appear. As with the reproductive data, tumorigenic data end points are cumulative figures, representing the total dose administered over the designated test period.

Fifth, the acute toxicity data field is

the largest of the toxicity fields, and contains mostly single dose lethality data. Many mammalian species and a few nonmammalian species studies appear in this field. Among the nonmammalians are chickens, wild birds, quail, pigeons, frogs, and toads.

The most common measure of acute toxicity is the LD_{50} (or LC_{50} for inhalation studies). This a statistical figure denoting the dose level at which 50% of the test population is expected to expire. When insufficient data are available for a determination of LD_{50} or LC_{50}, the lowest concentration in the test protocol in which a lethality occurred is cited and labeled LDLo or LCLo.

Until recently only positive test results were reported in RTECS, whether it be lethal or toxic effect. There are substances, however, on which studies have been conducted to determine acute lethality and no deaths occurred among the test animals. Our internal researchers argued that this important information needs to be included in RTECS. After consideration, the RTECS editorial review board decided that the following notation should be added to the acute toxicity data field: LD_{50} (or $LC)_{50}$>X mg/kg. This notation signifies that the substance reported was tested at concentrations up to the level reported on the data line, and no deaths occurred among the test population. If even one lethality occurred, it would be reported as LD (or LC)Lo.

Sixth, the most recently developed data field is entitled other multiple dose toxicity data. This field is actually a collection of chronic data with toxic, but not lethal effects noted. The end points are expressed as TD or TC with route-species, dosage level, and duration of study. A sample line might read: R12Y30Z01 orl-rat TD: 100 mg/kg, 26W. The actual effects noted are described by the toxic effect codes preceding the numerical end point. These codes describe the effects that occur at the dosage level indicated. The most common study designs listed in this field are 13-week, 26-week, 52-week, and 2-year studies. The toxic effect codes are an integral part of this field.

Four of the six toxicity fields (reproductive, tumorigenic, acute and multiple dose) include, where applicable, special Toxic Effect Codes, which detail descriptive information provided by authors of cited references. RTECS is listed in the OSHA Hazard Communication Rule[4] as a reference for toxicity data for use in the preparation of MSDSs.

Table 3. RTECS Compound Descriptive Codes

Code	Compound Descriptor
A.	Agricultural chemical
C.	Tumorigen
D.	Drug
H.	Hormone
M.	Mutagen
N.	Natural product
O.	Organometallic
P.	Human data
S.	Primary irritant
T.	Reproductive effector

RTECS COMPOUND DESCRIPTOR CODES

There is one feature of the RTECS that is often misunderstood and misused. It is the field now labeled compound descriptor code. This field was designed exclusively as a search tool. It never appeared in the printed or microfiche editions. These codes are listed in Table 3 . These codes, with a single letter designation, allow the user to access blocks of data from the file for specific study. For example, all agricultural chemicals, including fertilizers and other growth enhancers, and pesticides, can be accessed by calling up compound descriptor A. All human data can be accessed with the code P. In the body of the file, human data may be more closely designated as human, man, woman, child, or infant. But ALL human data respond to the descriptor code P.

The misunderstandings arise in the series of mutagen (code M), tumorigen (code C), and reproductive effector (code R). RTECS does not arbitrarily make the decision to label a compound, but simply appends an appropriate mutagenic, tumorigenic, or reproductive effector code according to the available information cited in the data lines for the chemical. In the case of the tumorigen designation, the inclusion of any data from an IARC assessment or an NTP bioassay can also result in the use of the compound descriptor code C, whatever the nature of the cited data.

SUPPLEMENTAL INFORMATION FIELDS

The Review Field of RTECS is composed of three sections: Threshold Limit Values (TLV) from the ACGIH, carcinogenic assessments from the International Agency for Research on Cancer (IARC), and citations to articles of general toxicological interest concerning the subject chemical. TLVs are widely used in the occupational health field, even though they are consensus standards, without the force of law. In some developing countries the TLV s have been adopted as their occupational exposure limits. The IARC monographs[5] are accepted as definitive assessments of carcinogenic risk to animals and humans from exposures to chemicals and chemical processes.

The most common measure of acute toxicity is the LD_{50} (or LC_{50} for inhalation studies). This a statistical figure denoting the dose level at which 50% of the test population is expected to expire.

The NIOSH documentation and surveillance data field comprises exclusive information generated by or originating within NIOSH. It also contains the NIOSH recommend exposure levels, citations to NIOSH criteria documents, current intelligence bulletins, and documents national (U.S.) estimates of the number of

workers potentially exposed, including the number of industries and occupations in which these potential exposures were observed. These data come from the two nationwide surveys of work sites conducted by NIOSH, the National Occupational Hazard Survey (NOHS)[6] completed in 1974 and the National Occupational Exposure Survey (NOES)[7] completed in 1983. These data, unfortunately, are outdated, but it is a body of information not readily available from any other source. NIOSH is currently studying the possible design and financing of another nationwide survey.

The standards and regulations field includes regulations pertaining to chemical exposures, notably the OSHA PELs, the MSHA Air Quality Standards, and the EPA FIFRA standards. Until recently this field listed Department of Transportation (DOT) shipping and labeling regulations. Another listing is the International Occupational Exposure Levels from a number of nations around the world. (The process of updating the original entries is underway, and completion of this effort is anticipated by the October 1999 update.)

The final field in the file is titled status, and it lists the status of various governmental programs pertaining to the specific substance accessed. The EPA program status under the Toxic Substance Control Act (TSCA), entries in the TSCATS database, GENETOX, and IRIS are all noted in this field. The National Toxicology Program bioassay test status and results[7] and citations from the current issue of the *Annual Report on Carcinogens*[8] are also noted in the status field. The final entries are references to NIOSH and OSHA analytical methods.

SUMMARY AND FUTURE ADDITIONS

As can be seen from this overview of the contents of RTECS, a huge quantity of information is at the command of the user. The added advantage is that by carefully designed search strategies, highly specific subfiles can be extracted and downloaded. RTECS has been designed to offer optimum assistance to those who need information about chemical hazards. For any organization needing to produce MSDSs, the OSHA Hazards Communication Rule has designated RTECS as a prime source of toxicity data.

There are some features that are under consideration for future additions to the file, depending on the availability of funding. The addition of selected physical properties would help characterize the RTECS entries. This could be accomplished with little difficulty if the effort were confined to melting and boiling points, vapor pressure, solubility, and a measure of the tendency of a substance to accumulate in the body (oil to water partition coefficient). The listing of more than the single lowest end point for a substance is being considered. This would preserve the noting of the "worst case" toxicity level, and also reduce the risk of citing only outliers. Another addition that has been considered is the entry of chemical epidemiology studies to augment the usefulness of RTECS in profiling listed chemicals.

A primary goal is the addition of chemical structures to the master file. At present, two of the on-line vendors display chemical structures, and it would be a valuable addition to the file if all presentations of RTECS offered this display.

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