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Appendix 2: Step II Data Sources

For the purposes of the QCAT, the Step II sources identified in the Checklist (Appendix 10) will be searched for specific information, which can be used to grade chemicals undergoing the assessment process. Although considerable information is available from all of these sources, only specific information will be selected for review in support of the objectives of the QCAT to limit the level of technical expertise necessary. Information used from each database will be described in detail at the end of this appendix.

Information on how to access information within the various sites will be presented later in this appendix after the list of data sources. Step II data sources include:

Please note:
These appendices are updated frequently and may be outdated. Updated versions are available on the QCAT website at www.ecy.wa.gov/GreenChemistry/QCAT.html. Go to the website and check the dates to make sure you are using the most current version.

1. ISSCAN: InstitutoSuperiore di Sanita, 'Chemical Toxicity.'
   ISSCAN evaluates chemicals based upon structural relationships and experimental data and ranks them for level of concern for carcinogenicity and mutagenicity. These rankings can translate into an equivalent level of concern within QCAT:
   Carcinogenic ratings:
   a. Ranking = 3: Carcinogenic
   b. Ranking = 2: Undetermined or equivocal
   c. Ranking = 1: Non-carcinogenetic
   Mutagenicity in Salmonella typhimurium (Ames test) rankings (SAL):
   a. Ranking = 3: Mutagenic
   b. Ranking = 2: Undetermined or equivocal
   c. Ranking = 1: Non-mutagenic

2. European Chemicals Agency, Classification and Labeling Inventory (C&L Inventory).
   The European Chemicals Agency (ECHA) as part of its implementation of the REACH legislation has made all data submitted by manufacturers available. This data has not undergone review and

there are some concerns about its accuracy. However, it provides a valuable resource for chemical hazard assessments like QCAT and can be used until better data is available.

3. European Union Risk Assessments (EU Risk Assessments)
   The European Union conducted in the past an extensive program where risk assessments were conducted on specific chemicals of concern. These risk assessments may provide valuable information for a chemical hazard assessment tool like QCAT if one is available.

4. National Institute of Occupational Safety and Health (NIOSH), Registry of Toxic Effects of Chemical Substances (RTECS). Paid subscription. RTECS is provided by several organizations for a fee. The examples shown here are for demonstration only and are not to be taken as an endorsement of any particular RTECS provider.

   RTECS is a toxicological database that contains peer-reviewed information from international journals, textbooks, technical reports, scientific proceedings, etc. RTECS reports the results of this review. Often, RTECS will not provide specific numerical values for evaluation but evidence on whether or not the chemical of concern demonstrates specific characteristics. RTECS does provide specific values for some endpoints. For example, RTECS often includes LD50 values that can be used to determine a level of concern for Acute Mammalian Toxicity using the Technical Criteria in Appendix 8.

   The assessor should determine from this review whether RTECS provides evidence of carcinogenicity and to what degree, i.e., strong, moderate, or low. More information is provided in the following screen-capture section.

5. National Library of Medicine (NLM), Hazardous Substances Databank (HSDB).
   HSDB may contain information found in Step I sources. However, it may also report data beyond Step I sources. The assessor should select the 'full record' option and then search on portions of the term 'carcinogenicity.' More information on how to search the HSDB for this additional data are in the following screen-capture section.

6. The United Nation's Screening Information Datasets (SIDS), if available.

   SIDS may report the results of studies and other information relevant to most of the hazard endpoints used in QCAT. Typically, the results are summarized and this information can be reviewed to determine whether evidence of concern does or does not exist for the chemical of concern. The assessor reviews this information to determine the level of concern. More information is available in the following screen-capture section.

7. U.S. Department of Labor, Occupational Safety & Health Administration (OSHA) Occupational Chemical Database.
   OSHA compiles data from several sources for specific chemicals of concern including physical properties, emergency response information, NIOSH Pocket Guide, etc. If assessed, this data may be used to assign a level of concern for several endpoints used in QCAT.

8. Danish Ministry of the Environment's Environmental Protection Agency (Danish EPA) (Q)SAR Assessment of Chemical Properties of Substances.
   The Danish EPA has created a database that contains predictions on the potential toxicity of approximately 166,000 chemicals. The database predicts toxicity for mutagenicity, carcinogenicity, reproductive toxicity, acute aquatic toxicity and acute mammalian toxicity, all of which are used in QCAT.

   For the purposes of the QCAT, the full (Q)SAR database will not be used but a subset of more than 30,000 substances for which GHS classifications have been estimated. This information can be found in the Danish Advisory List for Self-classification. These GHS results are directly comparable to the GHS criteria included in QCAT's Appendix 8.

9. U.S. Environmental Protection Agency (EPA), Ecological Toxicity (ECOTOX) database.
   EPA has collected data on aquatic toxicity and published the results in ECOTOX. Unlike the HSDB and other similar databases, EPA does not conduct a technical review of the studies but solely publishes the results. For this reason, should other sources that have been reviewed conflict with ECOTOX results, the reviewed studies should be given preference. In the absence of data, ECOTOX provides an excellent resource on the latest aquatic toxicity studies. ECOTOX results are typically reported in values such as $LC_{50,}$ which can be compared against the Technical Criteria in Appendix 8 identifying a level of concern to be used in QCAT. More information is provided in the following screen capture section on how to access data in ECOTOX.

10. U.S. Environmental Protection Agency (EPA), PBT Profiler.
    The PBT Profiler is a computer model created by EPA as a screening tool to predict a chemical's potential to persist in the environment. Persistence results are reported in half-lives for various media such as water, air, soil, and sediment. Bioaccumulation results are reported in Bioconcentration Factors (BCF).These half-lives and BCF values are compared against the Technical Criteria in Appendix 8 to determine a level of concern in QCAT for persistence and bioaccumulation.

    The PBT Profiler reports results from computer modeling conducted by EPA. In the instance where other, non-modeling is available, less emphasis should be placed upon PBT Profiler results.

11. US EPA Characterization Criteria.
    As part of EPA's New Chemical Program, hazard endpoints were parsed into various levels of concern to assist EPA to better identify chemicals, which may negatively impact human health or the environment. These criteria are used by EPA's Design for the Environment Program to assign a level of concern while conducting a chemical hazard assessment and were subsequently incorporated into the GreenScreen and QCAT methodologies.

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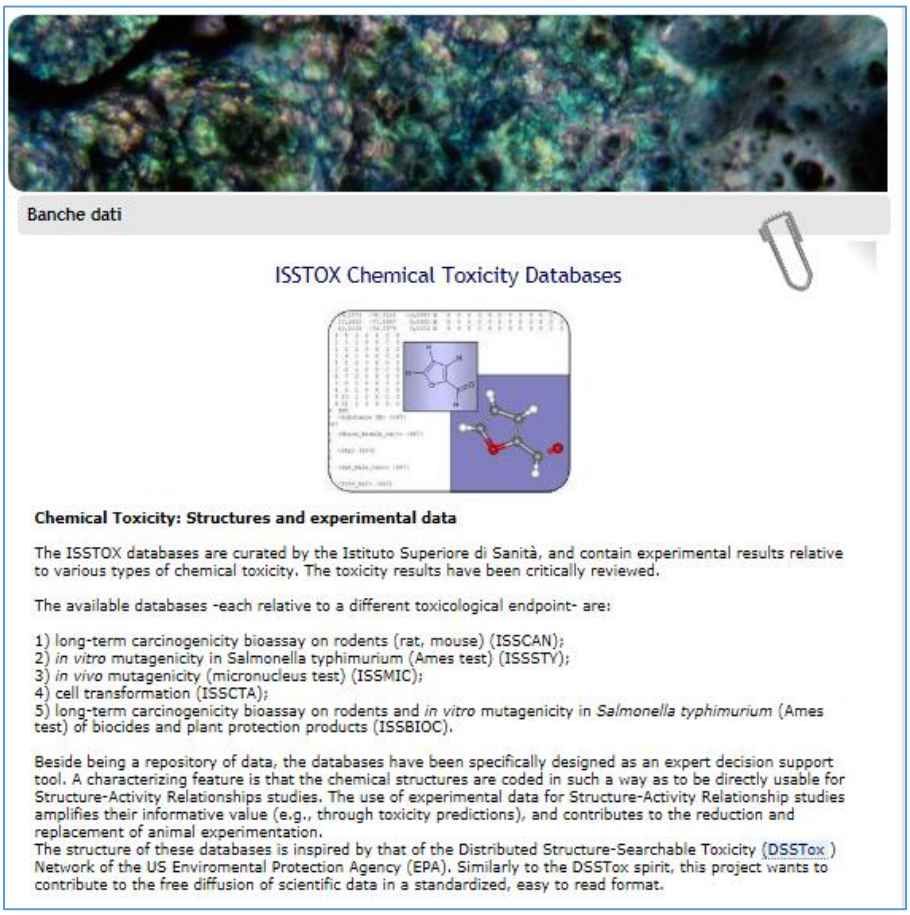
Examples of Data from Individual Databases used in Appendix 2

1. ISSCAN Chemical Carcinogens: Structures and Experimental Data

ISSCAN is an Italian database which contains information on carcinogen and mutagen potential based upon technical review of scientific studies and computer modeling input using Quality Structure Activity Relationship ((Q)SAR) processes.



Banche dati

ISSTOX Chemical Toxicity Databases

Chemical Toxicity: Structures and experimental data

The ISSTOX databases are curated by the Istituto Superiore di Sanità, and contain experimental results relative to various types of chemical toxicity. The toxicity results have been critically reviewed.

The available databases -each relative to a different toxicological endpoint- are:

1) long-term carcinogenicity bioassay on rodents (rat, mouse) (ISSCAN);
2) *in vitro* mutagenicity in Salmonella typhimurium (Ames test) (ISSSTY);
3) *in vivo* mutagenicity (micronucleus test) (ISSMIC);
4) cell transformation (ISSCTA);
5) long-term carcinogenicity bioassay on rodents and *in vitro* mutagenicity in *Salmonella typhimurium* (Ames test) of biocides and plant protection products (ISSBIOC).

Beside being a repository of data, the databases have been specifically designed as an expert decision support tool. A characterizing feature is that the chemical structures are coded in such a way as to be directly usable for Structure-Activity Relationships studies. The use of experimental data for Structure-Activity Relationship studies amplifies their informative value (e.g., through toxicity predictions), and contributes to the reduction and replacement of animal experimentation.
The structure of these databases is inspired by that of the Distributed Structure-Searchable Toxicity (DSSTox) Network of the US Enviromental Protection Agency (EPA). Similarly to the DSSTox spirit, this project wants to contribute to the free diffusion of scientific data in a standardized, easy to read format.

The information is provided in an Excel spreadsheet (red arrow below) and information on both the carcinogenic and mutagenic potential is provided.

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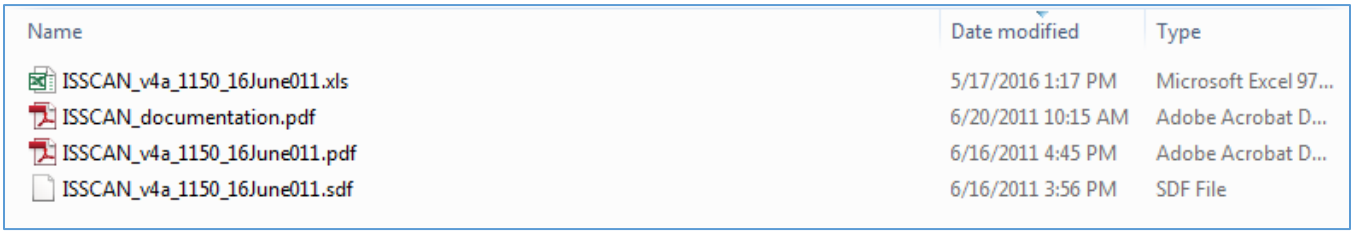
Once the ISSCAN file is downloaded and unzipped, the four files shown below are provided including background information on the process used to generate the data, abbreviations and an Excel spreadsheet with the results for each chemical.



Name	Date modified	Type
ISSCAN_v4a_1150_16June011.xls	5/17/2016 1:17 PM	Microsoft Excel 97...
ISSCAN_documentation.pdf	6/20/2011 10:15 AM	Adobe Acrobat D...
ISSCAN_v4a_1150_16June011.pdf	6/16/2011 4:45 PM	Adobe Acrobat D...
ISSCAN_v4a_1150_16June011.sdf	6/16/2011 3:56 PM	SDF File

Opening the Excel spreadsheet provides the following:

	1	2	3	4	5	13	14	15	16	17	18
1	Substance ID	FW	ChemName	Synonyms	CAS	Canc	SAL	Rat_Male_Canc	Rat_Female_Canc	Mouse_Male_Canc	Mouse_Female_Car
2	1	225.289	4-Dimethylaminoazobenzene	Solvent Yellow 2; Bu	60-11-7	3	3	3	3	3	3
3	2	223.27	4-Acetylaminofluorene	4-AAF; 4-acetamid	28322-02-3	1	3	ND	1	ND	ND
4	3	202.251	Pyrene	Benzo[def]phenant	129-00-0	1	3	ND	ND	1	1
5	4	119.377	Chloroform	Formyl trichloride; m	67-66-3	3	1	3	3	3	3
6	5	268.35	Diethylstilbestrol	3,4-bis(p-hydroxyp	56-53-1	3	1	3	3	3	3
7	6	190.156	4-Nitroquinoline-N-Oxide	4-Nitroquinoline 1-c	56-57-5	3	3	3	3	3	3
8	7	143.185	2-Naphthylamine	2-Aminonaphthaler	91-59-8	3	3	1	3	3	3
9	8	184.237	Benzidine	1,1'-Biphenyl-4,4'-D	92-87-5	3	3	3	3	3	3
10	9	223.27	2-Acetylaminofluorene	2-AAF; 2-Acetamic	53-96-3	3	3	3	3	3	3
11	10	252.309	Benzo(a)pyrene	3,4-benz[a]pyrene;	50-32-8	3	3	3	3	3	3
12	11	130.125	Hydrazine Sulphate	Diamidogen sulfate;	10034-93-2	3	3	3	3	3	3
13	12	179.201	Hexamethylphosphoramide	Hempa; Hexametap	680-31-9	3	1	3	3	ND	ND
14	13	198.221	N-Nitrosodiphenylamine	Diphenylnitrosamine	86-30-6	3	1	3	3	1	1
15	14	102.159	Ethylenethiourea	1,3-ethylene-2-thic	96-45-7	3	1	3	3	3	3
16	15	86.0892	beta-Butyrolactone	3-Hydroxybutanoic	3068-88-0	3	3	3	3	3	3
17	16	162.185	Safrole	1,2-Methylenedioxy	94-59-7	3	1	3	3	3	3
18	17	73.0938	Dimethylformamide	Dimethylformamide	68-12-2	1	1	1	1	1	1

A great deal of information is provided. The QCAT assessor, however, is primarily interested in columns 13 and 14 (red arrows above) which summarize the results for carcinogenicity (Canc) and mutagenicity (SAL). The assessor can search the spreadsheet to determine if the CAS number for the chemical being evaluated is contained within this data. If so, it may be used to assign a level of concern.

The Canc and SAL data are presented in ranges from 1 to 3 where:

1. 3 = carcinogenic or mutagenic
2. 2 = undetermined or equivocal
3. 1 = non-carcinogenic or non-mutagenic

Some chemicals were not evaluated particularly for mutagenicity due to a lack of data and are identified as ‘nd’ for ‘no data.’

For example, the ISSCAN provides the following information (additional detail excluded for the purposes of a QCAT review):

ChemName	CAS	Canc	SAL[1]
Vinyl chloride	75-01-4	3	3

Therefore for QCAT, vinyl chloride would be identified as a known carcinogen and known mutagen.

2. European Chemical Agency (ECHA) Classification and Labeling Inventory

The Classification and Labeling Database (C&L Database) is the result of the European Chemical Agency (ECHA) compiling all of the classification and labeling data submitted during chemical registration as required under REACH. ECHA made no attempt to review the submittals and there may be errors within the database. Since there is no incentive for a manufacturer to report a problem for a chemical if none exists, this database is potentially a good source for hazard data for chemicals that have been identified as containing some level of concern.

As the C&L Database has not been reviewed, there is less guarantee that chemicals in the database are correctly evaluated and there may be chemicals with hazard concerns that are not identified. QCAT users may wish to evaluate the information in this database for any data gaps remaining after evaluating other Step II sources. If a chemical is identified as a concern for any of the remaining hazard endpoints, the results can be used to define the degree of hazard involved. If there are any conflicts between this database and other Step II sources, the other sources may be given greater emphasis as this database has not been peer reviewed or audited.

[1] SAL = Mutagenicity in *Salmonella typhimurium* (Ames Test)

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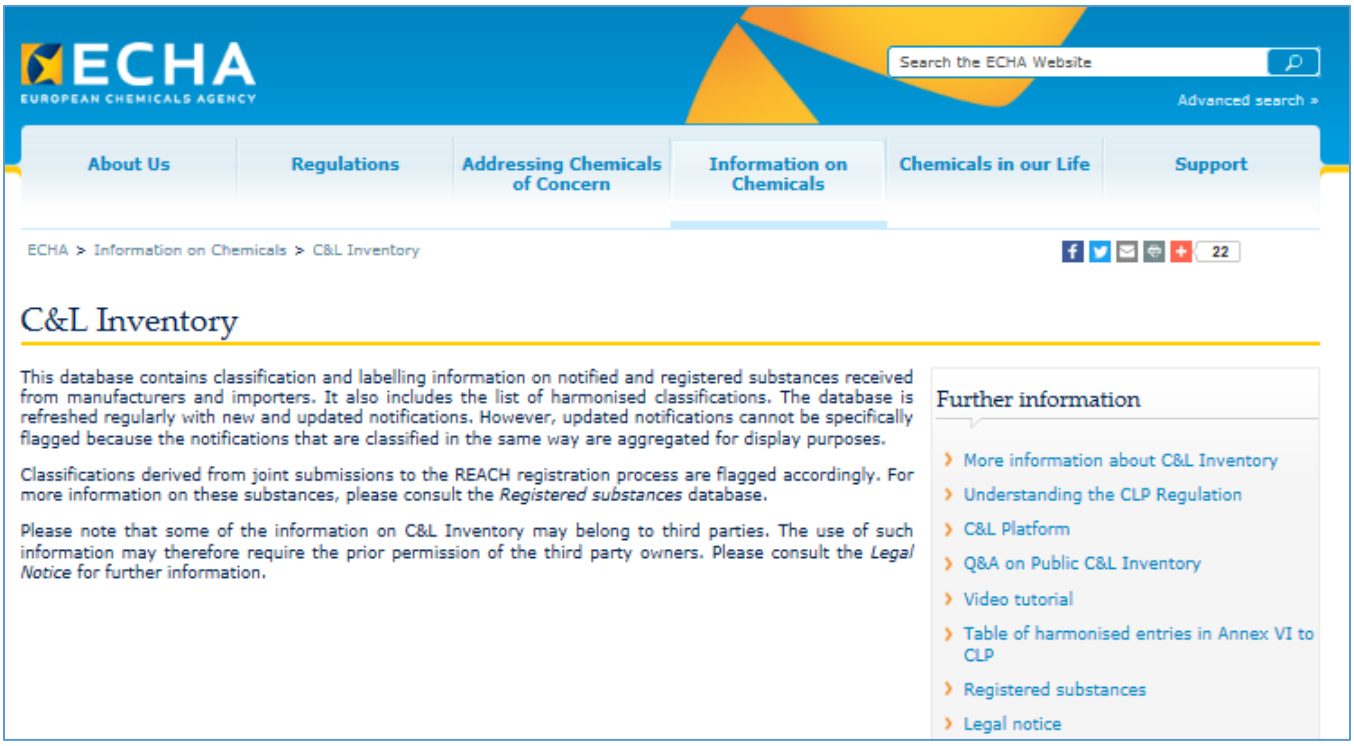
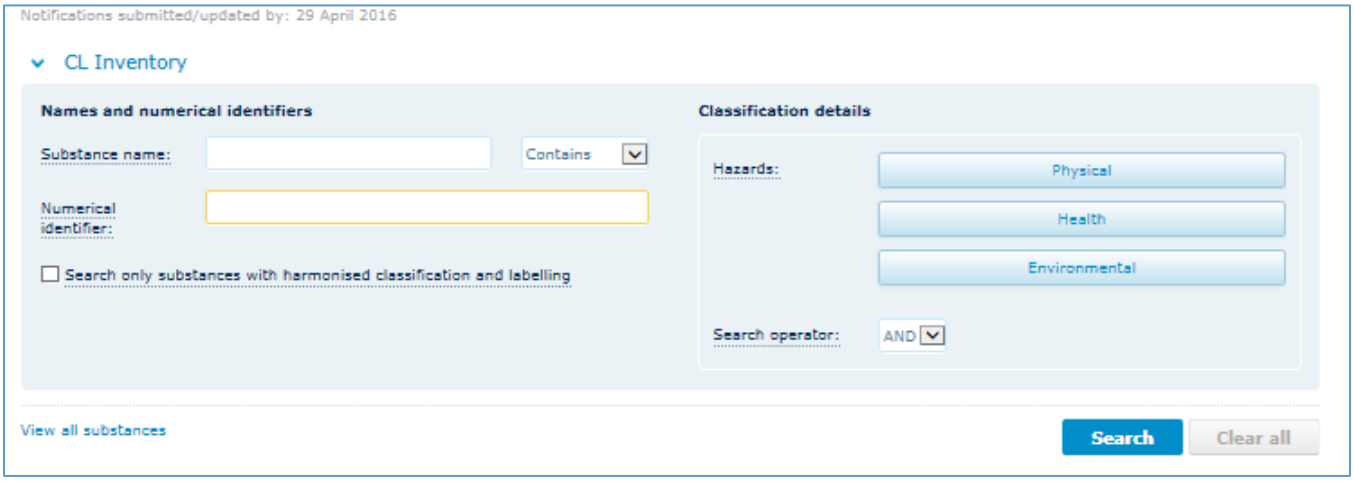
Access to the C&L database is straightforward. The opening page appears as:





The QCAT user can search for information in several ways but the recommended method is to insert the CAS number in the line called ‘Numerical Identifier.’ The CAS No. for formaldehyde ’50-00-0’, for example, is typed into the first box ‘Numerical Identifier’ and the ‘Search’ button is pressed. The following page appears:

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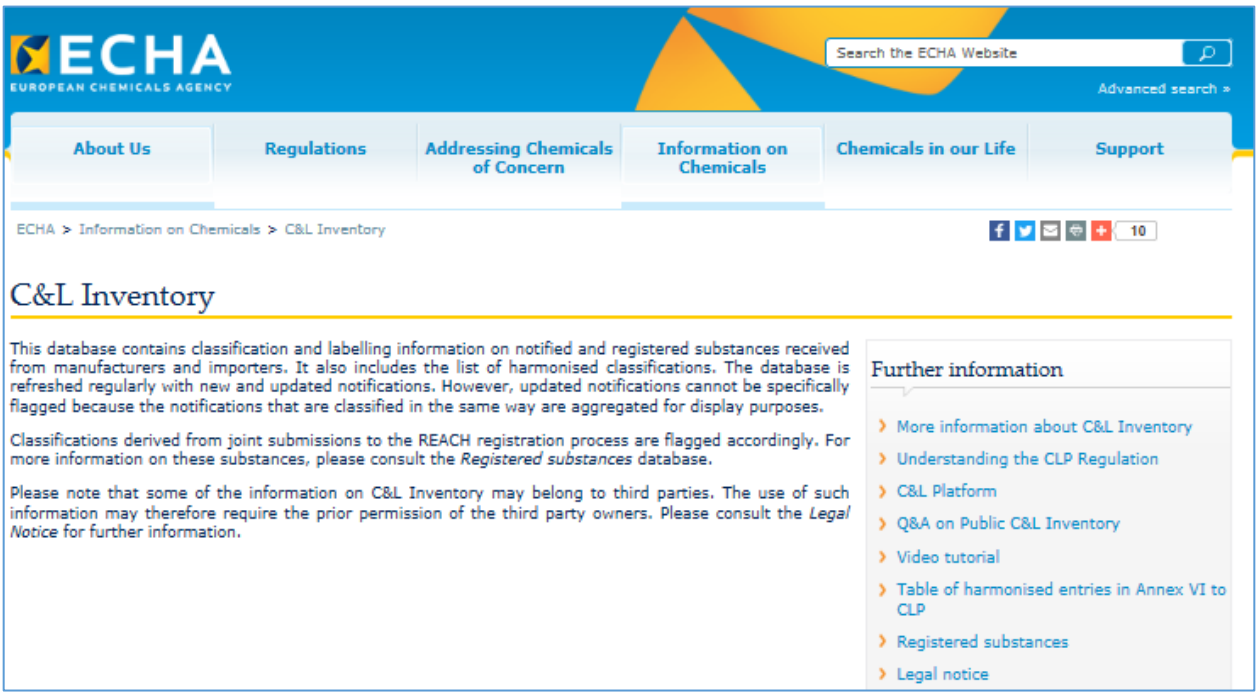
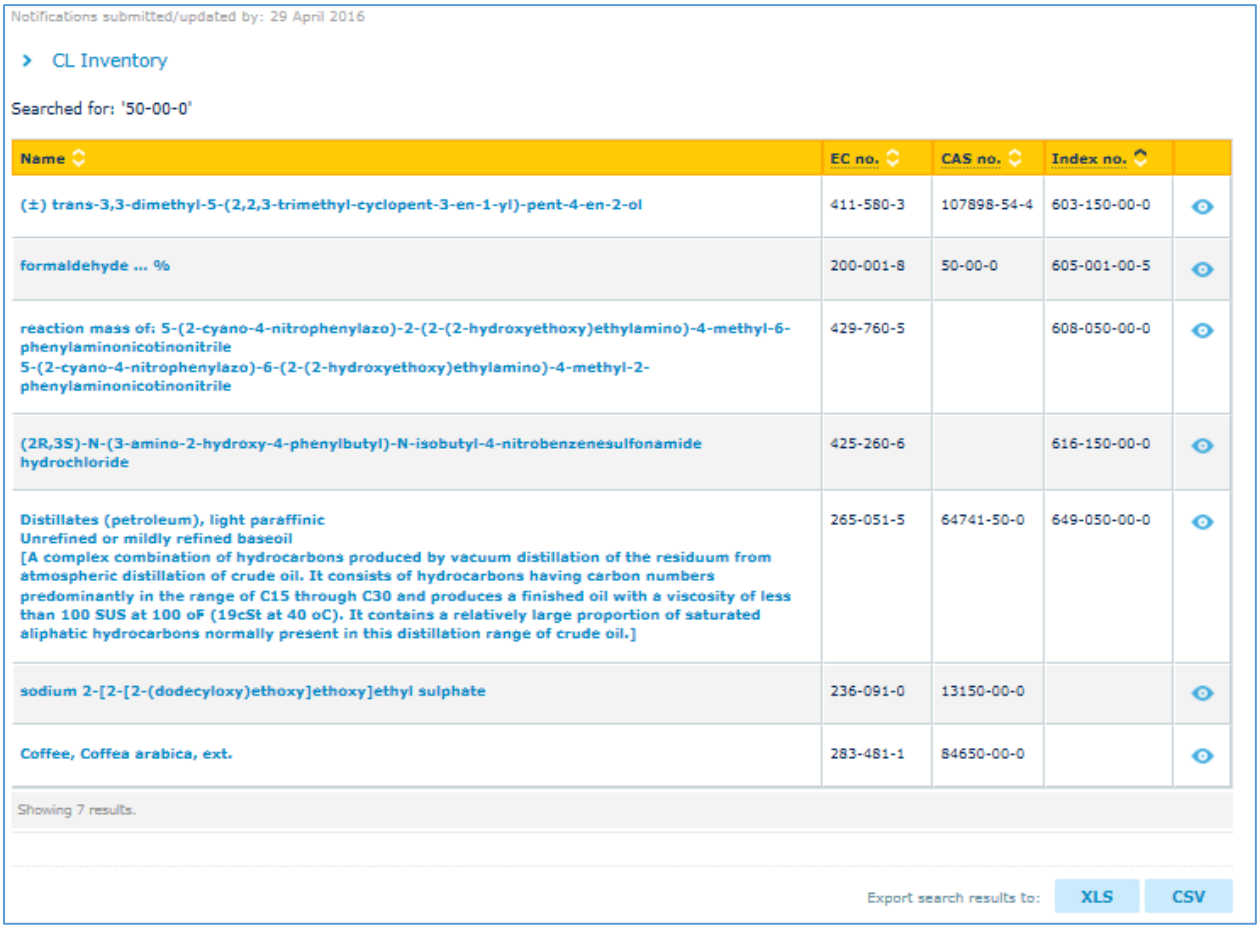
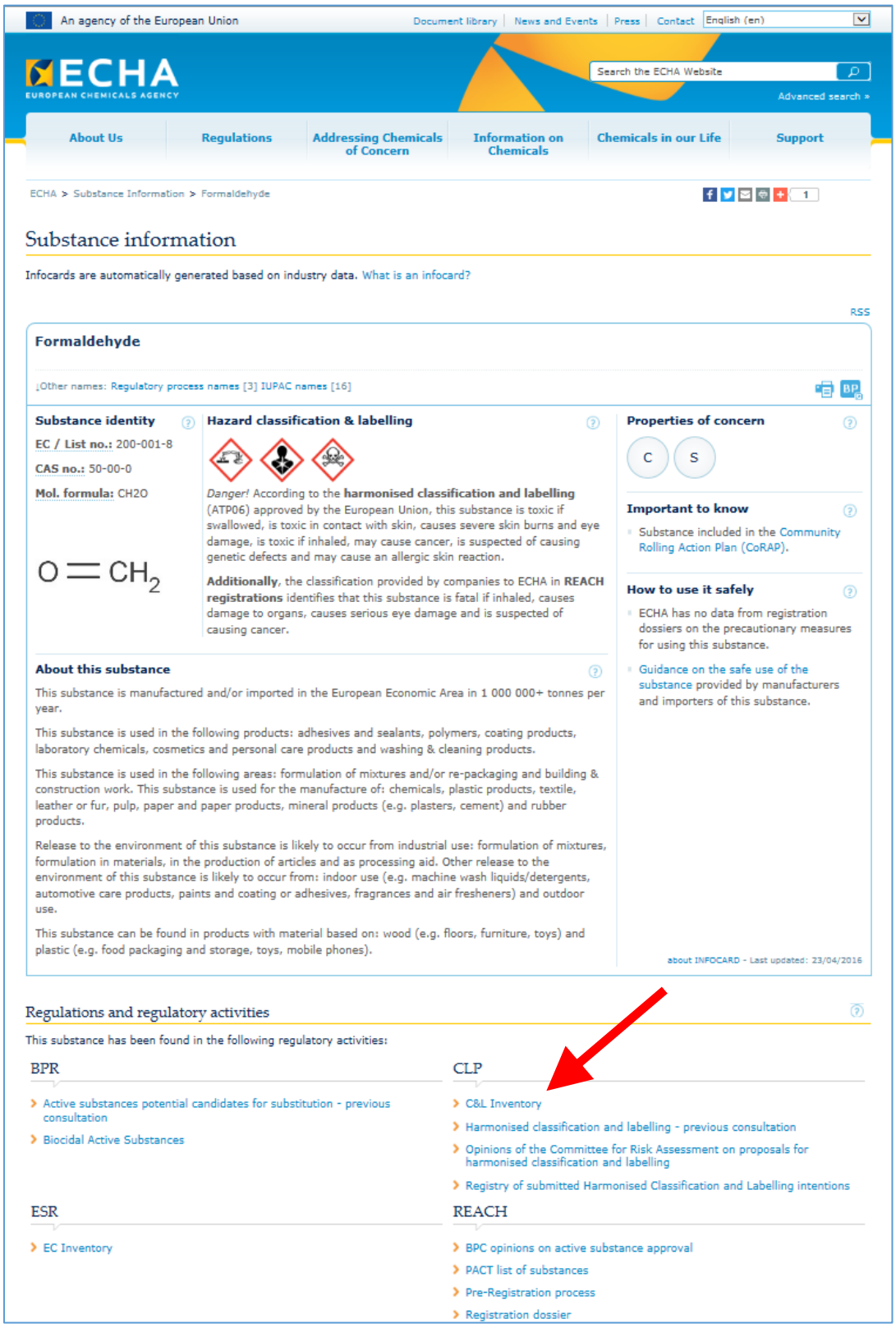




All of the entries that contain ’50-00-0’ are displayed. Clicking on the blue ‘formaldehyde….%’ leads to the following:

Updated: July 20, 2016



This page summarizes all the information currently available on formaldehyde in Europe. The information that is most useful to a QCAT assessor is 'C&L Inventory' (red arrow). Clicking on this link causes the following to appear:

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Summary of Classification and Labelling

Harmonised classification - Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation)

General Information

Index Number	EC Number	CAS Number	International Chemical Identification
605-001-00-5	200-001-8	50-00-0	formaldehyde ... %

ATP Inserted / Updated: CLP00/ATP06
CLP Classification (Table 3.1)

Classification		Labelling			Specific Concentration limits, M-Factors	Notes
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code(s)	Pictograms, Signal Word Code(s)		
Acute Tox. 3 *	H301	H301		GHS06 GHS08 GHS05 Dgr	Skin Sens. 1; H317: C ≥ 0,2% Eye Irrit. 2; H319: 5% ≤ C < 25% STOT SE 3; H335: C ≥ 5% Skin Irrit. 2; H315: 5% ≤ C < 25% Skin Corr. 1B; H314: C ≥ 25% *	Note D Note B
Acute Tox. 3 *	H311	H311				
Skin Corr. 1B	H314	H314				
Skin Sens. 1	H317	H317				
Acute Tox. 3 *	H331	H331				
Muta. 2	H341	H341				
Carc. 1B	H350	H350				

Signal Words	Pictograms
Danger	Skull and crossbones Health hazard Corrosion

DSD Classification (Table 3.2)

Classification	Risk Phrases	Safety Phrases	Indication of danger	Concentration Limits	
				Concentration	Classification
Carc. Cat. 2; R45 Muta. Cat. 3; R68 T; R23/24/25 C; R34 R43	23/24/25 34 43 45 68	45 53	T	C ≥ 25 %	T; R23/24/25
				5 % ≤ C < 25 %	Xn; R20/21/22
				C ≥ 25 %	C; R34
				5 % ≤ C < 25 %	Xi; R36/37/38
				C ≥ 0,2 %	R43

Much of the information on this page can be used to help assign a level of concern. The assessor can use the "hazard Class & Category Codes' (black box), the Hazard Statement Codes (red box), the Classification (green box) or the Risk Phrases (blue box), all of which can be found in Appendix 8. As these various codes are all related, the results should agree for all.

Not all chemicals have undergone such a detailed assessment. The assessor may have to be content with specific registration dossiers provided to the European Chemicals Agency as required by REACH. For example, the perfluorinated compound, perfluorohexanoic acid, was typed into the substance name. The search yielded the following:

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The only compound to show was not the correct one but a trichloro related compound. In this instance, it would be appropriate to conduct another search using the correct CAS No. to see if the correct compound is shown. For the purposes of this example, however, the trichlorinated compound was selected and the following page appeared:

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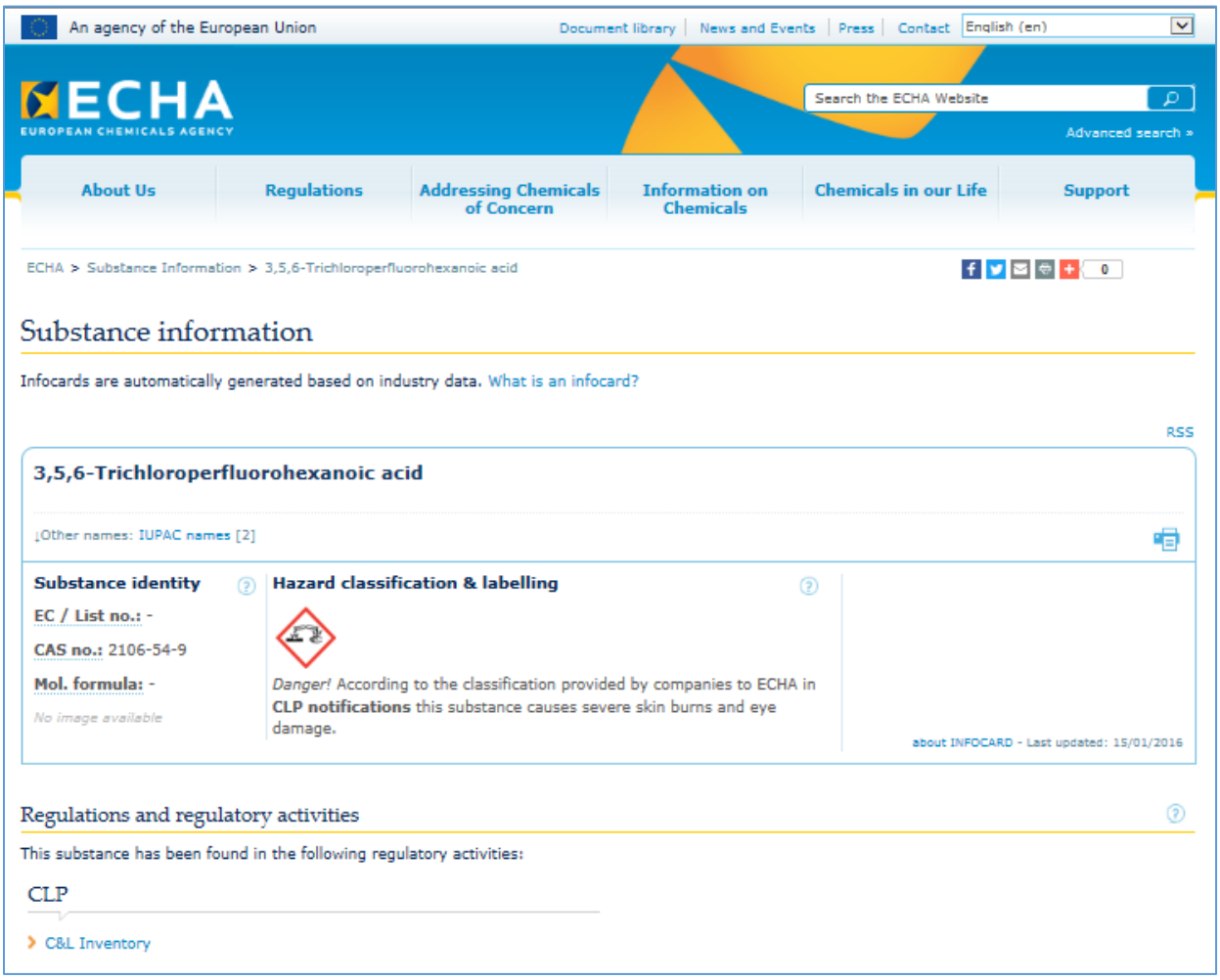

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EUROPEAN CHEMICALS AGENCY

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ECHA > Substance Information > 3,5,6-Trichloroperfluorohexanoic acid

0

Substance information

Infocards are automatically generated based on industry data. What is an infocard?

RSS

3,5,6-Trichloroperfluorohexanoic acid

↓Other names: IUPAC names [2]

Substance identity

EC / List no.: -

CAS no.: 2106-54-9

Mol. formula: -

No image available

Hazard classification & labelling

Danger! According to the classification provided by companies to ECHA in **CLP notifications** this substance causes severe skin burns and eye damage.

about INFOCARD - Last updated: 15/01/2016

Regulations and regulatory activities

This substance has been found in the following regulatory activities:

CLP

› C&L Inventory

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Less is known about this chemical compared with formaldehyde. Clicking on the 'C&L Inventory,' lead to:

Summary of Classification and Labelling

Notified classification and labelling

General Information

EC Number	EC Name	CAS Number
		2106-54-9

Notified classification and labelling according to CLP criteria

Classification		Labelling			Specific Concentration limits, M-Factors	Notes	Classification affected by Impurities / Additives	Additional Notified Information	Number of Notifiers	Joint Entries	
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code (s)	Pictograms, Signal Word Code(s)							
Skin Corr. 1B	H314	H314		GHS05 Dgr				State/Form IUPAC Names	1		

Number of Aggregated Notifications: 1

Close Window

Skin Corrosivity, not used in QCAT, is the only concern identified for this chemical. One limitation on the REACH system is that it is not clear whether the chemical was subjected to a wide battery of tests and this was the only concern identified or if the compound was not tested for the other hazard endpoints. Legislation like REACH requires only limited testing for chemicals used in small amounts. More testing is required as the amounts created or imported into the European Union increase. Regardless this source provided no data that could be used in a QCAT.

If there are any questions about the source of the information, the column at the end provides more information on the chemical. This information is unlikely to be of interest to the standard QCAT user but is available if any questions arise.

3. European Union Risk Assessments (EU RAs)

Before REACH became the primary chemical legislation in the European Union, the European Commission maintained a list of 141 chemicals that have undergone or are undergoing the risk assessment process. Many of these reports can be found in the Classification and Labeling Database. ECHA has created a separate website where these EU RAs are made available. Using the link provided in the QCAT Checklist, the following page appears:

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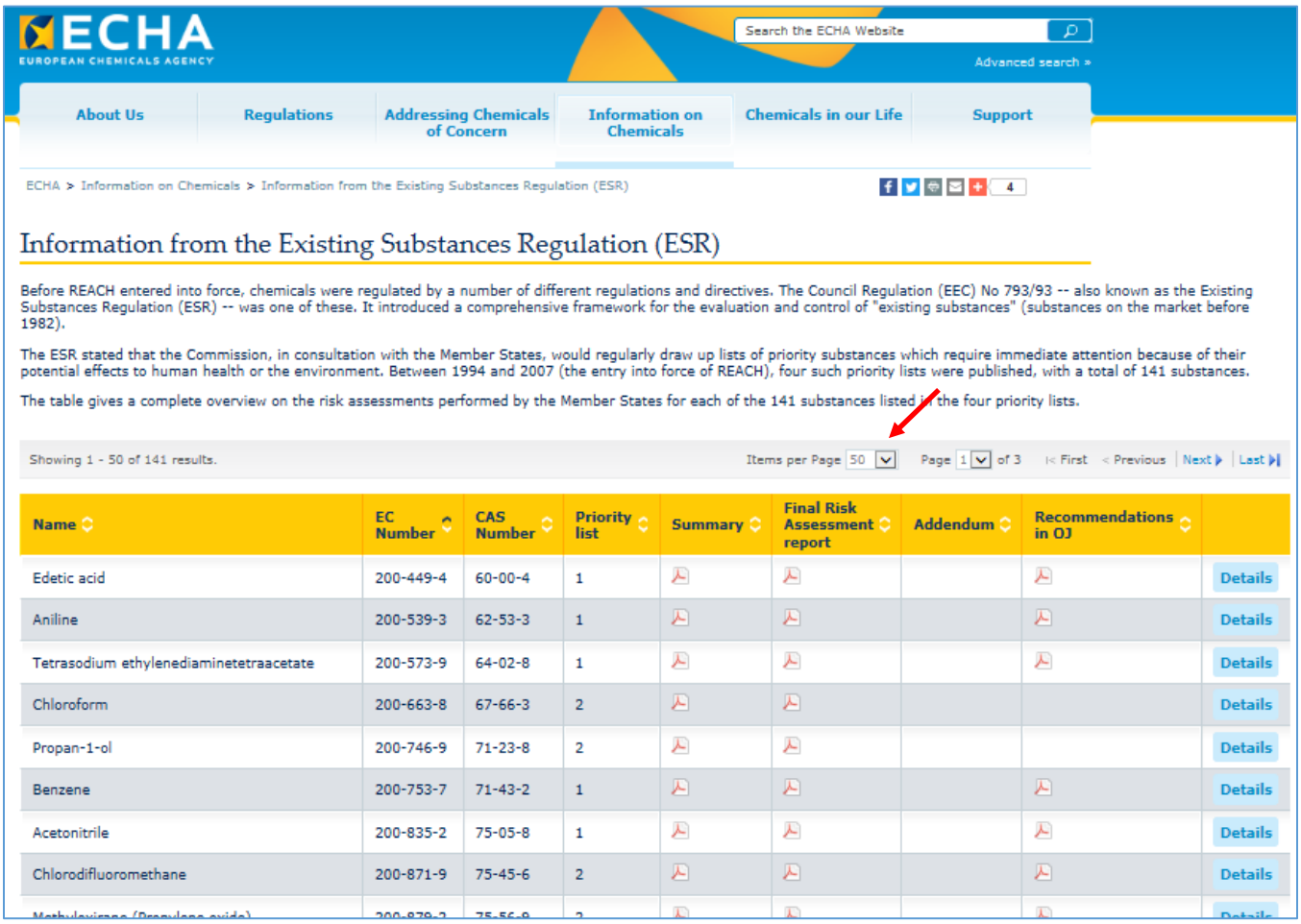

If a risk assessment has been completed for a chemical of interest, additional data reviewed during the process by experts in the various toxicity criteria and the conclusions reached may prove useful in filling any remaining data gaps. The QCAT assessor can display all 141 documents by changing the 'Items per Page' (red arrow above) from '50' shown to '200'. Once the page has refreshed, the user may search using the CAS number for the chemical under evaluation to determine if an EU RA has been done. Note: Striking the 'Ctrl' and 'F' keys simultaneously will bring up the 'Find' function into which you may enter the CAS number. If you use the 'Search the ECHA website' function shown in the figure above, you will be searching outside this area.

The EU uses a standardized format for all risk assessments, which makes access to information easier. The following is a page from the EU RA for trichloroethylene, which demonstrates the overall structure:

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4 HUMAN HEALTH 85

4.1 HUMAN HEALTH (TOXICITY) 85
4.1.1 Exposure assessment 85
4.1.1.1 General discussion 85
4.1.1.2 Occupational exposure 85
4.1.1.2.1 Manufacture of trichloroethylene 86
4.1.1.2.2 Recycling trichloroethylene 88
4.1.1.2.3 Metal cleaning 88
4.1.1.2.4 Adhesives 91
4.1.1.2.5 Use as an intermediate 92
4.1.1.2.6 Summary 93
4.1.1.3 Consumer exposure 95
4.1.1.3.1 Exposure to trichloroethylene from cloth cleaning 95
4.1.1.4 Humans exposed via the environment 96
4.1.1.5 Combined exposure 97
4.1.2 Effects assessment: hazard identification and dose (concentration) - response (effect) assessment 98
4.1.2.1 Toxicokinetics, metabolism and distribution 98
4.1.2.1.1 Studies in animals 98
4.1.2.1.2 Studies in humans 112
4.1.2.1.3 Summary of toxicokinetics 119
4.1.2.2 Acute toxicity 119
4.1.2.2.1 Studies in animals 119
4.1.2.2.2 Studies in humans 129
4.1.2.2.3 Summary of acute toxicity 139
4.1.2.3 Irritation 140
4.1.2.3.1 Studies in animals 140
4.1.2.3.2 Studies in humans 141
4.1.2.3.3 Summary of skin and eye irritation 142
4.1.2.4 Corrosivity 142
4.1.2.5 Sensitisation 142
4.1.2.5.1 Studies in animals 142
4.1.2.5.2 Studies in humans 143
4.1.2.5.3 Summary of sensitisation 144
4.1.2.6 Repeated dose toxicity 144
4.1.2.6.1 Studies in animals 144
4.1.2.6.2 Studies in humans 161
4.1.2.6.3 Summary of effects of repeated exposure 188
4.1.2.7 Mutagenicity 190
4.1.2.7.1 *In vitro* studies 190
4.1.2.7.2 Drosophila 195
4.1.2.7.3 *In vivo* tests 195
4.1.2.7.4 Human genotoxicity 200
4.1.2.7.5 Summary of genotoxicity 202
4.1.2.8 Carcinogenicity 203
4.1.2.8.1 Studies in animals 203

The Risk Assessment Report (RAR) includes an evaluation of human health and environmental toxicity including many of the QCAT criteria including:

- Biodegradation
- Bioaccumulation
- Aquatic toxicity
- Acute mammalian toxicity
- Mutagenicity
- Carcinogenicity
- Reproductive toxicity

At the end of each toxicity criteria, the RAR typically either selects a value culled from the scientific data or reaches a conclusion, which may be useful to the QCAT process.

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Chapter 4 deals with mammalian toxicity and includes a number of hazard criteria of interest. At the end of each section, the RAR summarizes what can be learned from the evaluation. Information in these summary sections may be useful when assigning a level of concern for specific hazard endpoints.

For example, Section 4.1.2.8 deals with carcinogenicity and subsection 4.1.2.8.3 '*Summary of carcinogenicity studies'* summarizes carcinogenicity conclusions that can be obtained from the previous discussions. Continuing with trichloroethylene as an example, the following information was copied from the end of the RAR section on carcinogenicity (page 231):

in support of category 1, underlined the evidence for kidney tumours in humans and the consistency with the *S*-(1,2-dichlorovinyl)-L-cysteine (DCVC) metabolic pathway and the observation of a different spectrum of somatic mutations in kidney tumours of trichloroethylene-exposed compared to unexposed patients.

A clear majority of the Specialised Experts recommended that classification of trichloroethylene as a category 2 carcinogen is warranted, based on evidence in one animal species, namely tumours in the rat kidney, supported by epidemiological data showing an association between exposure and kidney tumours and non-Hodgkin's lymphoma in humans. Some Specialised Experts stated that genotoxicity and metabolic/biochemical findings added to their concern. One expert maintained that category 1 was appropriate, one preferred category 3 but accepted the majority view.

The summary information like '*A clear majority of the Specialised Experts recommended that classification of trichloroethylene as a category 2 carcinogen is warranted…'* can be used by the assessor to identify a level of concern.

Unlike the sources in Step I, more searching is needed to determine the conclusions reached by the experts and reported in the RAR. In some instances, no distinct conclusion was reached. It is not expected that any of the details in the RAR would be used for the purposes of the QCAT if no conclusion was reached. Where such information is found, however, it may be useful in filling any data gaps which exist after a review using Step I sources. The QCAT review is limited to this level of review.

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4. Registry of Toxic Effects of Chemical Substances (RTECS)

RTECS contains data on several toxicity endpoints, which may be of interest to a GS® evaluation. However, many endpoints require technical expertise to evaluate prior to including in a safer chemical alternatives assessment. For the purposes of the QCAT, the acute mammalian toxicity (LD_{50} and LC_{50} inhalation, dermal and oral data only) and tumorigenic/carcinogenicity data may prove useful.

RTECS is available from several sources and Ecology obtains access to the data through the Canadian Centre for Occupational Health and Safety (CCOHS). Other sources contain the same information. As an example, the CCOHS search page appears as follows:

Typing in the CAS No. for formaldehyde (50-00-0), leads to the following (Note: you may be required to enter a password at this point showing you have paid for access to the data):

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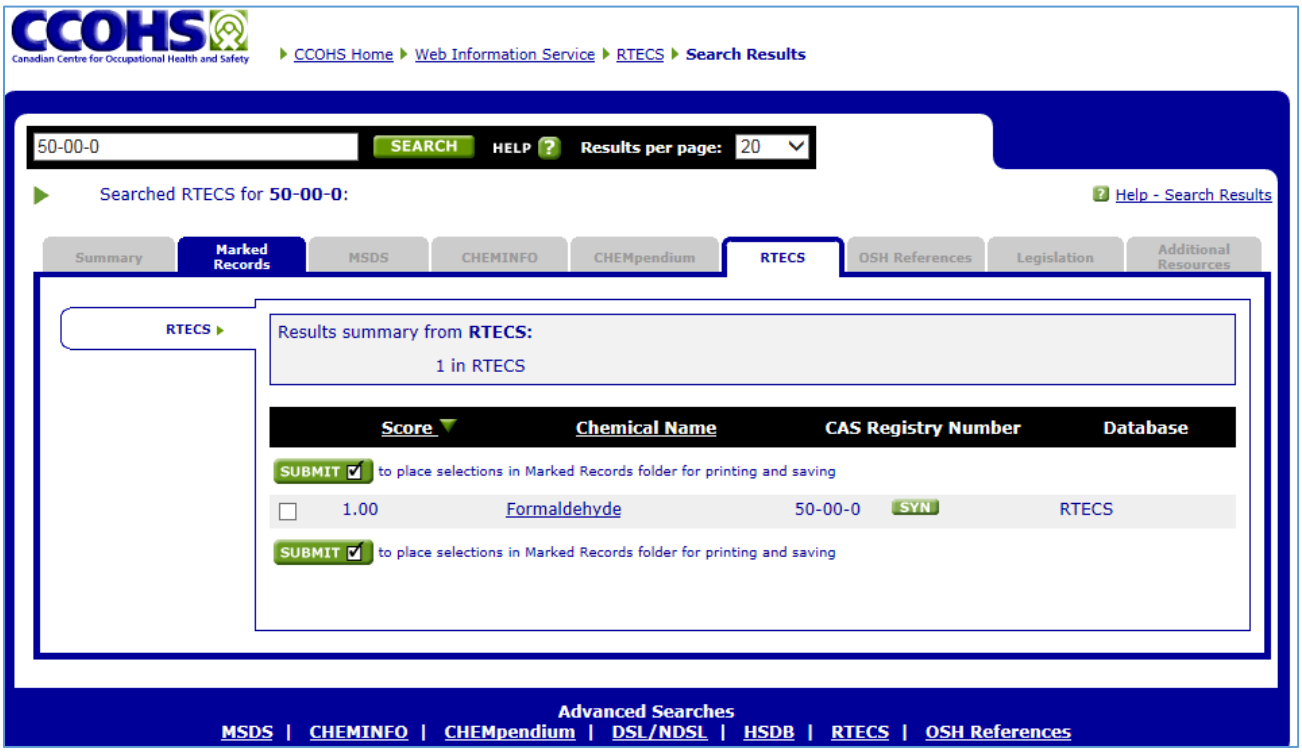
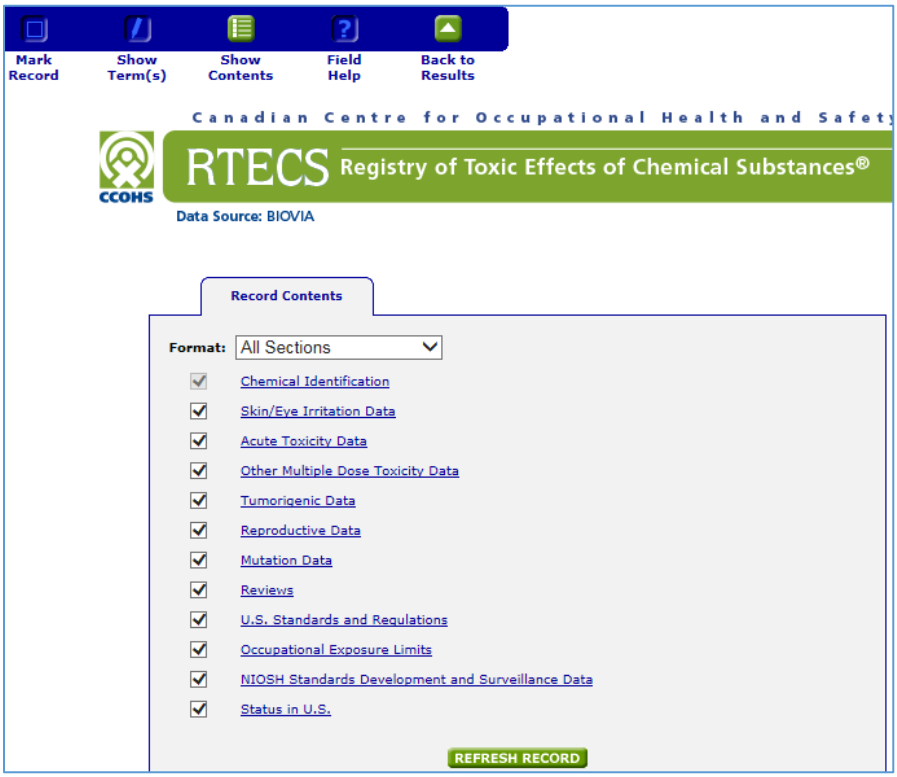


Clicking on 'Formaldehyde' leads to the actual data:



This page indicates that data for acute toxicity, tumorigenic, reproductive and mutation data are available. Not all this data may be easily interpreted and may not be applicable to a QCAT. Clicking on 'Acute Toxicity Data' directs the assessor to this actual data. Much of the available data is not useful to

the assessor as there are no criteria in Appendix 8 that can be used to interpret many of the endpoints used. Appendix 8, however, does include information on how to assess LD_{50}, the dose that will kill 50% of the population. The following are examples of LD_{50} data from RTECS:

Acute Mammalian Toxicity:

ACUTE TOXICITY DATA					
Type of Test	**Route of Exposure**	**Species Observed**	**Dose Data**	**Toxic Effects**	**Reference**
LD50 - Lethal dose, 50 percent kill	Oral	Rodent - rat	100 mg/kg	Details of toxic effects not reported other than lethal dose value	FCTOD7 Food and Chemical Toxicology. (Pergamon Press Inc., Maxwell House, Fairview Park, Elmsford, NY 10523) V.20- 1982- Volume(issue)/page/year: 26,447,1988
LC50 - Lethal concentration, 50 percent kill	Inhalation	Rodent - rat	203 mg/m3	Peripheral Nerve and Sensation - spastic paralysis with or without sensory change Behavioral - convulsions or effect on seizure threshold Behavioral - excitement	GTPZAB GigienaTruda i Professional'nyeZabolevaniya. Labor Hygiene and Occupational Diseases. (V/O MezhdunarodnayaKniga, 113095 Moscow, USSR) V.1-36, 1957-1992. For publisher information, see MTPEEI Volume(issue)/page/year: 18(2),55,1974

etc……

The RTECS acute toxicity dose data can be compared with the ranges in Appendix 8 and can be used to complete a QCAT evaluation for Acute Mammalian Toxicity.

Other data in RTECS may also be useful. For example, RTECS contains the following information for tumorigenic toxicity:

Tumorigenic/Carcinogenicity:

TUMORIGENIC DATA					
Type of Test	**Route of Exposure**	**Species Observed**	**Dose Data**	**Toxic Effects**	**Reference**
TDLo - Lowest published toxic dose	Oral	Rodent - rat	109 gm/kg/2Y (continuous)	Tumorigenic - **carcinogenic by RTECS criteria**[2] Gastrointestinal - tumors Blood - leukemia	TIHEEC Toxicology and Industrial Health. (Princeton Scientific Pub. Co., POB 2155, Princeton, NJ 08540) V.1-1985- Volume(issue)/page/year: 5,699,1989

[2] Emphasis added to show reviewer what information to use for making determination.

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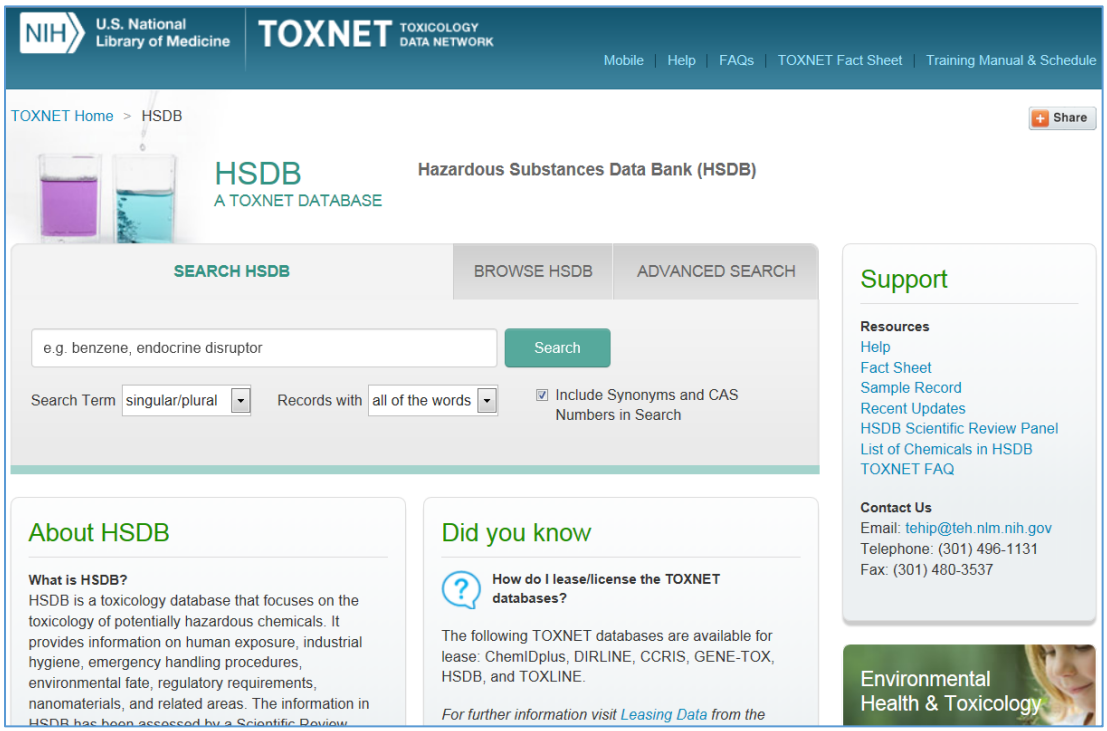
etc…..

Although 'RTECS criteria' are not specifically called out in Appendix 8, it does meet the requirement of "Strong Evidence of Carcinogencity' and could be used to classify formaldehyde if other data sources were not already available. The determination of whether or not a chemical is determined as tumorigenic/carcinogenic using the data that meets the RTECS criteria may prove useful in completing a QCAT evaluation.

5. Hazardous Substances Databank (HSDB)

The HSDB contains considerable information on the toxicity of specific chemicals. This includes excerpts from specific sources and detailed information on the specific chemical impacts. HSDB also displays specific toxicity results, which have undergone technical review and conclusions on certain toxicity criteria, which will be of use in a QCAT evaluation. The three primary toxicity criteria of interest are acute mammalian toxicity, acute aquatic toxicity, and carcinogenicity. Information may be available on other toxicity criteria included in the QCAT; however, these data vary widely from chemical to chemical and should be used with caution.

The following is HSDB's initial page:



As an example, the CAS number for formaldehyde (50-00-0) is entered into the 'Search HSDB' and the 'Search' button pressed.

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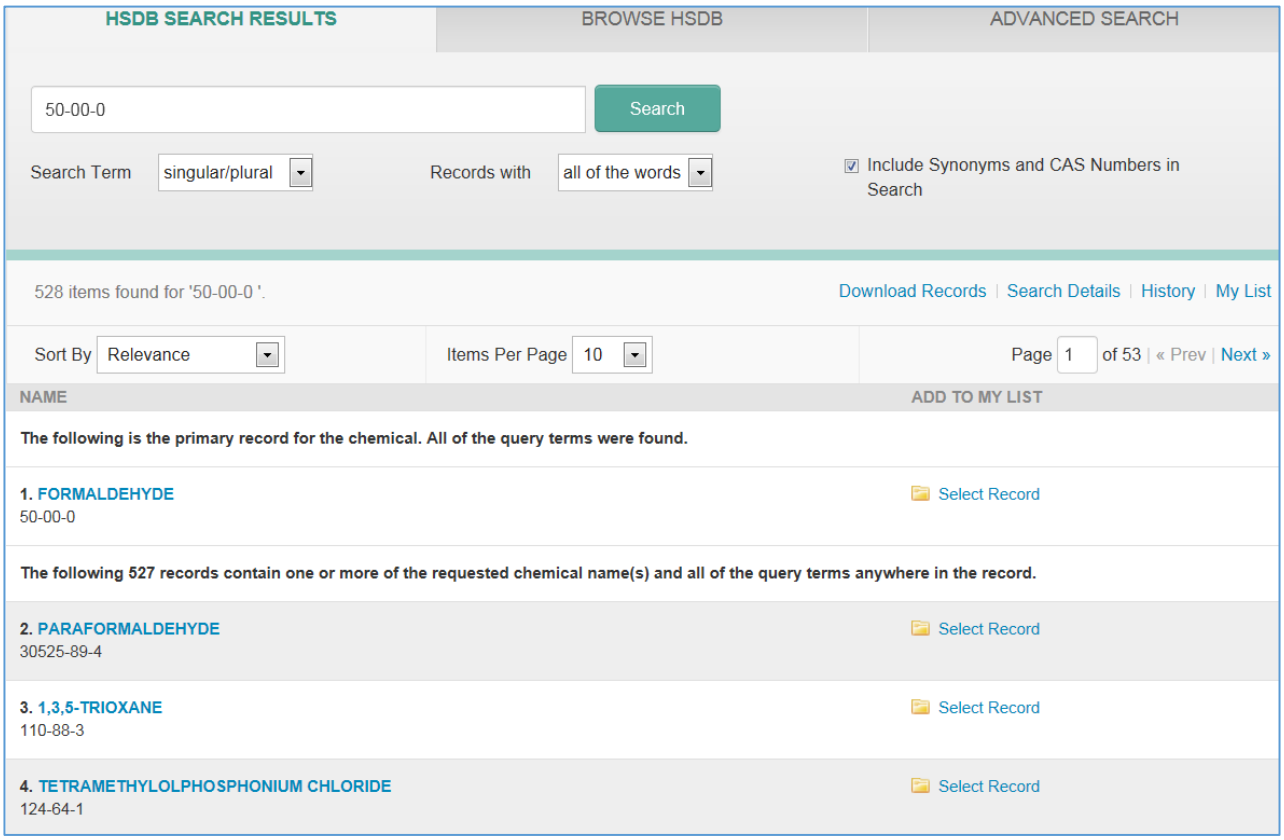
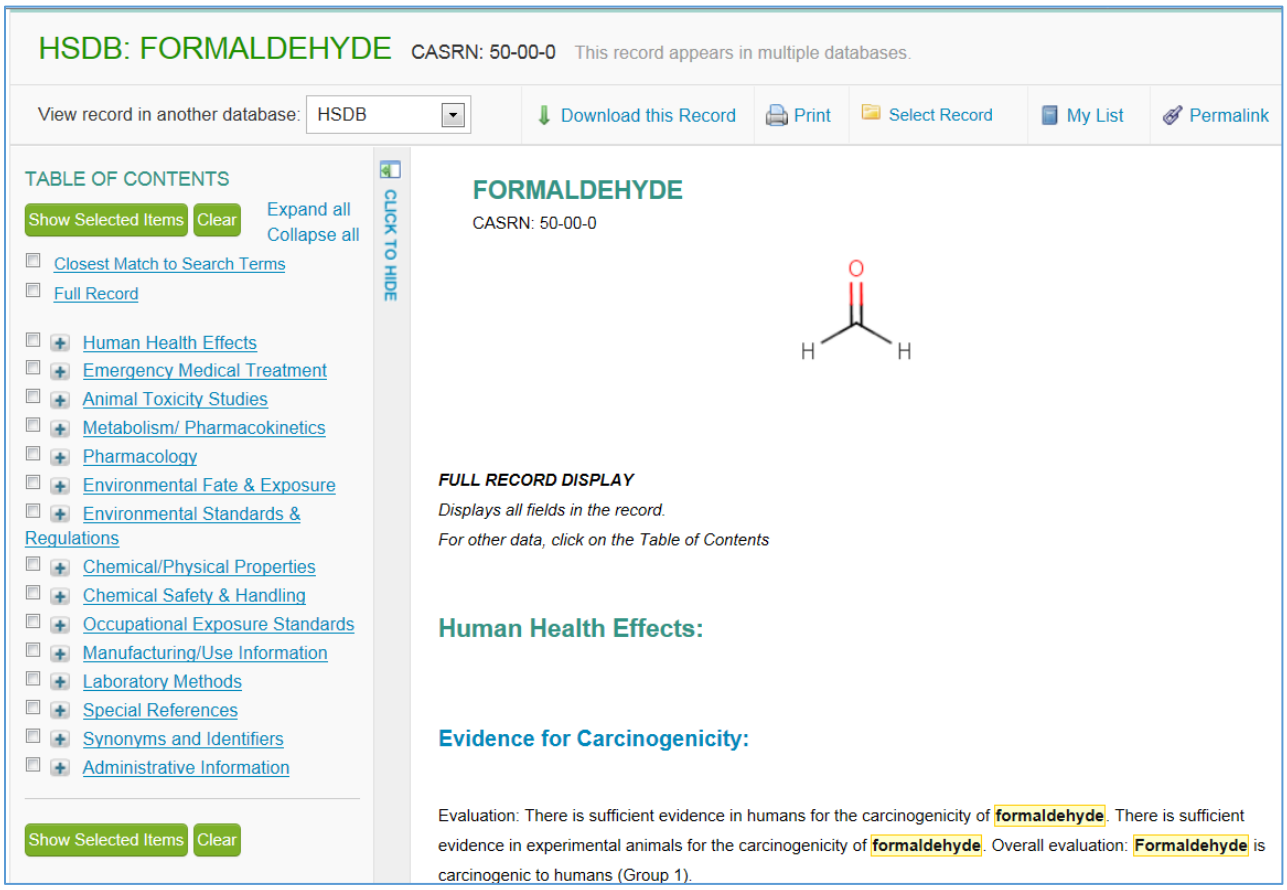


Clicking on the blue ‘Formaldehyde’ takes the assessor directly to available data in the HSDB.

Updated: July 20, 2016



Clicking on the blue 'Human Health Effects' line on the left identifies human health data, a portion of which is shown below:

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Evidence for Carcinogenicity:

Evaluation: There is sufficient evidence in humans for the carcinogenicity of **formaldehyde**. There is sufficient evidence in experimental animals for the carcinogenicity of **formaldehyde**. Overall evaluation: **Formaldehyde** is carcinogenic to humans (Group 1).

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Vol 88 Summary of Data Reported and Evaluation. (Last updated: September 7, 2004). Available from, as of June 22, 2006: http://monographs.iarc.fr/ENG/Monographs/vol88/volume88.pdf **PEER REVIEWED**

Cancer Classification: Group B1 Probable Human Carcinogen

[USEPA Office of Pesticide Programs, Health Effects Division, Science Information Management Branch: "Chemicals Evaluated for Carcinogenic Potential" (April 2006)] **QC REVIEWED**

CLASSIFICATION: B1; probable human carcinogen. BASIS FOR CLASSIFICATION: Based on limited evidence in humans, and sufficient evidence in animals. Human data include nine studies that show statistically significant associations between site-specific respiratory neoplasms and exposure to **formaldehyde** or **formaldehyde**-containing products. An increased incidence of nasal squamous cell carcinomas was observed in long-term inhalation studies in rats and in mice. The classification is supported by in vitro genotoxicity data and **formaldehyde**'s structural relationships to other carcinogenic aldehydes such as acetaldehyde. HUMAN CARCINOGENICITY DATA: Limited. ANIMAL CARCINOGENICITY DATA: Sufficient.

[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS). Summary on Formaldehyde (50-00-0). Available from, as of March 15, 2000: http://www.epa.gov/iris/ **PEER REVIEWED**

The Table of Contents on the left displays various pages of the report. Data in three specific pages will be discussed in the subsequent sections.

Acute Mammalian Toxicity: Under 'Animal Toxicity Studies', clicking on 'Non-Human Toxicity Values' provides acute mammalian toxicity values of interest for the QCAT evaluation:

Non-Human Toxicity Values:

LD50 Rat oral 100 mg/kg /SRP: percent solution not specified/

[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 1814] **PEER REVIEWED**

LD50 Rat (albino) oral 2020 mg/kg /From table/ /SRP: percent solution not specified/

[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:967] **PEER REVIEWED**

LD50 Rat oral 800 mg/kg /from table/

[Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:967] **PEER REVIEWED**

LC50 Rat inhalation 0.82 mg/L (1/2 hour)

[Tomlin, C.D.S. (ed.). The Pesticide Manual - World Compendium. 10th ed. Surrey, UK: The British Crop Protection Council, 1994., p. 525] **PEER REVIEWED**

Note: This screen capture presents only a portion of the data available and is representative of what the HSDB contains. Data may also be present in HSDB for routes of exposure not used in QCAT. The assessor should only use data for the routes identified in Appendix 8.

For the purposes of the QCAT, the LC_{50} and LD_{50} toxicity values provided are compared with the Technical Criteria in Appendix 8 to determine the level of concern.

Acute aquatic toxicity: Under 'Animal Toxicity Studies', clicking on 'Ecotoxicity values' provides acute aquatic toxicity values of interest for the QCAT evaluation:

Ecotoxicity Values:

LC50; Species: /Morone saxatilis/ (Striped bass) larvae; Conditions: static bioassay; Concentration: 10 mg/L for 48-96 hr

[Environmental Canada; Tech Info for Problem Spills: Formaldehyde p.67 (1985)] **PEER REVIEWED**

LC50; Species: Oncorhynchus mykiss (Rainbow trout) weight 0.63 g; Conditions: static; Concentration: 118 ppm for 96 hr (95% confidence limit: 99.7-140 ppm) /37% AI formulated product/

[USEPA, Office of Pesticide Programs; Pesticide Ecotoxicity Database (2000) on Formaldehyde (50-00-0). Available from, as of May 30, 2006: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

LC50; Species: Oncorhynchus mykiss (Rainbow trout) weight 0.81 g; Conditions: static; Concentration: >100 ppm for 96 hr /18.8% AI formulated product/

[USEPA, Office of Pesticide Programs; Pesticide Ecotoxicity Database (2000) on Formaldehyde (50-00-0). Available from, as of May 30, 2006: http://cfpub.epa.gov/ecotox/quick_query.htm **PEER REVIEWED**

Note: This screen capture presents only a portion of the data available and is representative of what the HSDB contains. In addition, data in HSDB may also be found in other sources such as EPA's ECOTOX database. Data in HSDB has undergone a peer review process and therefore can be assumed to be data conducted as required using best scientific practices.

For the purposes of ecotoxicity review, LC_{50} fish data will be evaluated using the process established within Washington State's Dangerous Waste Regulations (WAC 173-303):

> *'Fish LC_{50} data must be derived from an exposure period greater than or equal to twenty-four hours. A hierarchy of species LC_{50} data should be used that includes (in decreasing order of preference) salmonids, fathead minnows, and other fish species.'*

For other ecotoxicity data, the species with the most data are assumed to be indicative of the chemical's toxic effects. This information can be interpreted using the Technical Criteria for Acute Aquatic Toxicity in Appendix 8 and directly applied to the QCAT ranking criteria.

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Carcinogenicity: Where available, the HSDB also provides an assessment of whether or not a chemical is a known or suspected carcinogen. Much of the information in this assessment is pulled from other sources used in the Step I analysis and may be duplicative. However, the HSDB does include other sources that may be useful in a Step II evaluation. For example, the carcinogenicity information on formaldehyde appears under 'Human Health Effects'. Clicking on 'Evidence for carcinogenicity' provides the following:

Evidence for Carcinogenicity:

There is sufficient evidence in humans for the carcinogenicity of **formaldehyde**. **Formaldehyde** causes cancer of the nasopharynx and leukaemia. Also, a positive association has been observed between exposure to **formaldehyde** and sinonasal cancer. There is sufficient evidence in experimental animals for the carcinogenicity of **formaldehyde**. The Working Group was not in full agreement on the evaluation of **formaldehyde** causing leukaemias in humans, with a small majority viewing the evidence as sufficient of carcinogenicity and the minority viewing the evidence as limited. Particularly relevant to the discussions regarding sufficient evidence was a recent study accepted for publication which, for the first time, reported aneuploidy in blood of exposed workers characteristic of myeloid leukaemia and myelodysplastic syndromes, with supporting information suggesting a decrease in the major circulating blood-cell types and in circulating haematological precursor cells. The authors and Working Group felt that this study needed to be replicated. **Formaldehyde** is carcinogenic to humans (Group 1).

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/ENG/Classification/index.php p. V100F 430 (2012)] **PEER REVIEWED**

Cancer Classification: Group B1 Probable Human Carcinogen

[USEPA Office of Pesticide Programs, Health Effects Division, Science Information Management Branch: "Chemicals Evaluated for Carcinogenic Potential" (April 2006)] **PEER REVIEWED**

CLASSIFICATION: B1; probable human carcinogen. BASIS FOR CLASSIFICATION: Based on limited evidence in humans, and sufficient evidence in animals. Human data include nine studies that show statistically significant associations between site-specific respiratory neoplasms and exposure to **formaldehyde** or **formaldehyde**-containing products. An increased incidence of nasal squamous cell carcinomas was observed in long-term inhalation studies in rats and in mice. The classification is supported by in vitro genotoxicity data and **formaldehyde**'s structural relationships to other carcinogenic aldehydes such as acetaldehyde. HUMAN CARCINOGENICITY DATA: Limited. ANIMAL CARCINOGENICITY DATA: Sufficient.

[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS). Summary on Formaldehyde (50-00-0). Available from, as of December 15, 2014: http://www.epa.gov/iris/ **PEER REVIEWED**

A2; Suspected human carcinogen.

[American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH 2014, p. 32] **PEER REVIEWED**

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Formaldehyde: Known to be a human carcinogen.

[DHHS/National Toxicology Program; Thirteenth Report on Carcinogens: Formaldehyde (50-00-0) (2014). Available from, as of December 12, 2014: http://ntp.niehs.nih.gov/pubhealth/roc/roc13/index.html **PEER REVIEWED**

Three out of the five data points identified above are Step I sources although the conclusion from the American Conference of Governmental Industrial Hygienists TLVS and EPA's Pesticide Program are not. These sources were reviewed by experts and deemed worthy for inclusion. Additional sources like this might prove useful for other chemicals not identified in Step I sources.

Searching HSDB: An easier method for locating information in the HSDB is to click on the complete record for the chemical being evaluated. This record can then be searched (by pressing the Control key and 'F' simultaneously) to search out pertinent information for each hazard criteria. Ecology has found the following keywords (or any portion thereof) useful in evaluating data contained in the HSDB:

- Carcinogenicity
- Mutagenicity
- Genotoxicity (used to report mutagenicity results)
- Reproduction
- Developmental

Other keywords may assist in this process.

For example, the full HSDB record for formaldehyde was searched for reproductive hazards using just the fragment 'reprod' in the Control F method described above. The following information was located:

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```
 0.2.19.2 CHRONIC EXPOSURE
   A)  Allergic contact dermatitis, eczema, and other signs
       have been attributed to formaldehyde sensitivity.
0.2.20 REPRODUCTIVE HAZARDS
  A)  Formaldehyde has not been shown definitely to be
      teratogenic in animals. Formaldehyde probably presents
      little or no risk as a potential human teratogen.
  B)  Menstrual disorders have been reported in women
      occupationally exposed to formaldehyde, but these
      results are controversial. In experimental animal
      studies, some effects on spermatogenesis have been
      reported.
  C)  Occupational exposure at recommended limits is not
      thought to present a reproductive risk. Formaldehyde
      exposure among female hospital workers did not correlate
      with an increase in spontaneous abortion in one study,
      but did correlate in another.
   1)  Low-birthweight children have been reported in female
       workers exposed to urea-formaldehyde resin, but studies
       are inconclusive. Formaldehyde appears to cross the
       placental barrier in mice.
```

```
0.2.21 CARCINOGENICITY
 0.2.21.1 IARC CATEGORY
   A)  IARC Carcinogenicity Ratings for CAS50-00-0 (IARC
       Working Group on the Evaluation of Carcinogenic Risks
       to Humans, 2006; IARC Working Group on the Evaluation
       of Carcinogenic Risks to Humans, 2007; IARC Working
       Group on the Evaluation of Carcinogenic Risks to
       Humans, 2010; IARC Working Group on the Evaluation of
       Carcinogenic Risks to Humans, 2010a; IARC Working Group
       on the Evaluation of Carcinogenic Risks to Humans,
       2008; IARC, 2004):
    1)  Not Listed
 0.2.21.2 HUMAN OVERVIEW
```

Information in this area could be used to fill in the box for reproductive toxicity. Specifically:

- Reproductive toxicity: *'Menstrual disorders have been reported in women occupationally exposed…'* and *'… did not correlate with an increase in spontaneous abortion in one study, but did correlate in another.'* and *'Low-birthweight children have been reported in female workers…. but studies are inconclusive… appears to cross the placental barrier in mice.'*

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This responds to ‘indication of repro/developmental toxicity’ and would qualify as a ‘moderate’ level of concern.

The same formaldehyde record was searched for information on genotoxicity using the fragment ‘genot’. The following information resulted:

```
 0.2.21.3 ANIMAL OVERVIEW
   A)  An increased incidence of nasal squamous cell
       carcinomas was observed in long-term inhalation studies
       in rats and in mice. The classification of B1 is
       further supported by in vitro genotoxicity data and
       formaldehyde's structural relationships to other
       carcinogenic aldehydes such as acetaldehyde.
0.2.22 GENOTOXICITY
  A)   Formaldehyde appears to be mutagenic. The basis for its
       genetic activity is its ability to form cross-links in
       DNA and proteins.
  B)   Formaldehyde is a potent genotoxin and has been reported
       to be active in many short-term genetic tests, including
       the Ames Salmonella assay and other assays for mutation
       using bacteria, chromosome aberrations and sister
       chromatid exchanges in vitro and in vivo, and many
       assays detecting direct effects on DNA.
```

This information indicates that formaldehyde has a ‘high’ level of concern for mutagenicity/genotoxicity. Specifically:

- *‘Formaldehyde appears to be mutagenic.’*
- *Formaldehyde is a potent genotoxin and has been reported to be active in many short-term genetic tests….’*

By conducting searches like this, the full HSDB record can be evaluated and information pertinent to assessing specific hazard endpoints can be located. Information may be embedded in the full record and may not be obvious. It is important to remember that this data would only be necessary if mutagenicity/genotoxicity or reproductive toxicity are not covered by a Step I authoritative source.

6. United Nations Environmental Program Safety Information Datasheets (UNEP SIDS)

The UNEP SIDS are made available through the Organization for Economic Cooperation and Development (OECD) Existing Chemicals Database. Clicking on the link in the QCAT Checklist, presents the following page:

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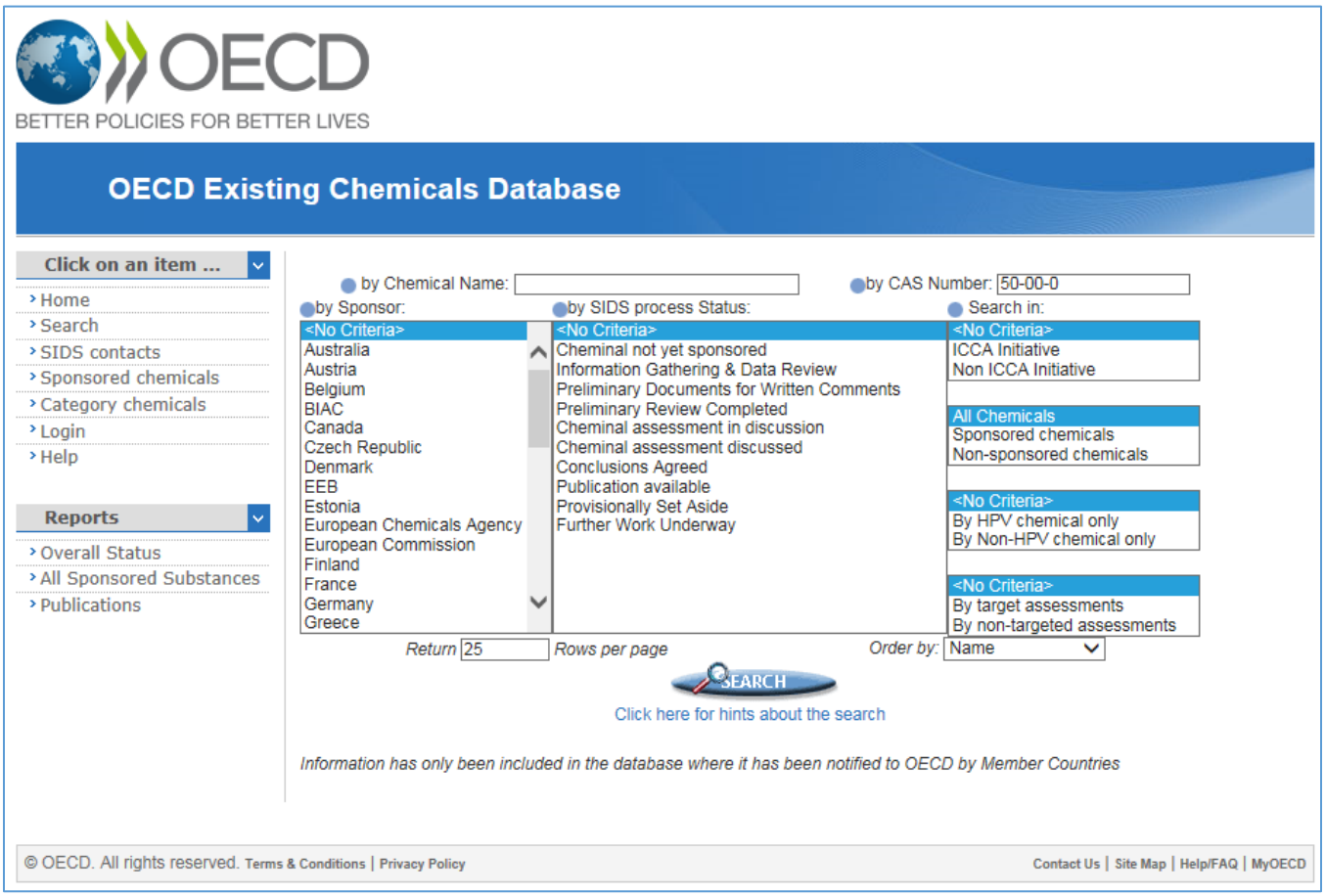

The QCAT assessor may search by name or CAS number. As a CAS number is required to use QCAT, searching by CAS is recommended. Entering the CAS number for formaldehyde (50-00-0) as an example and hitting the 'search' button leads to the following:

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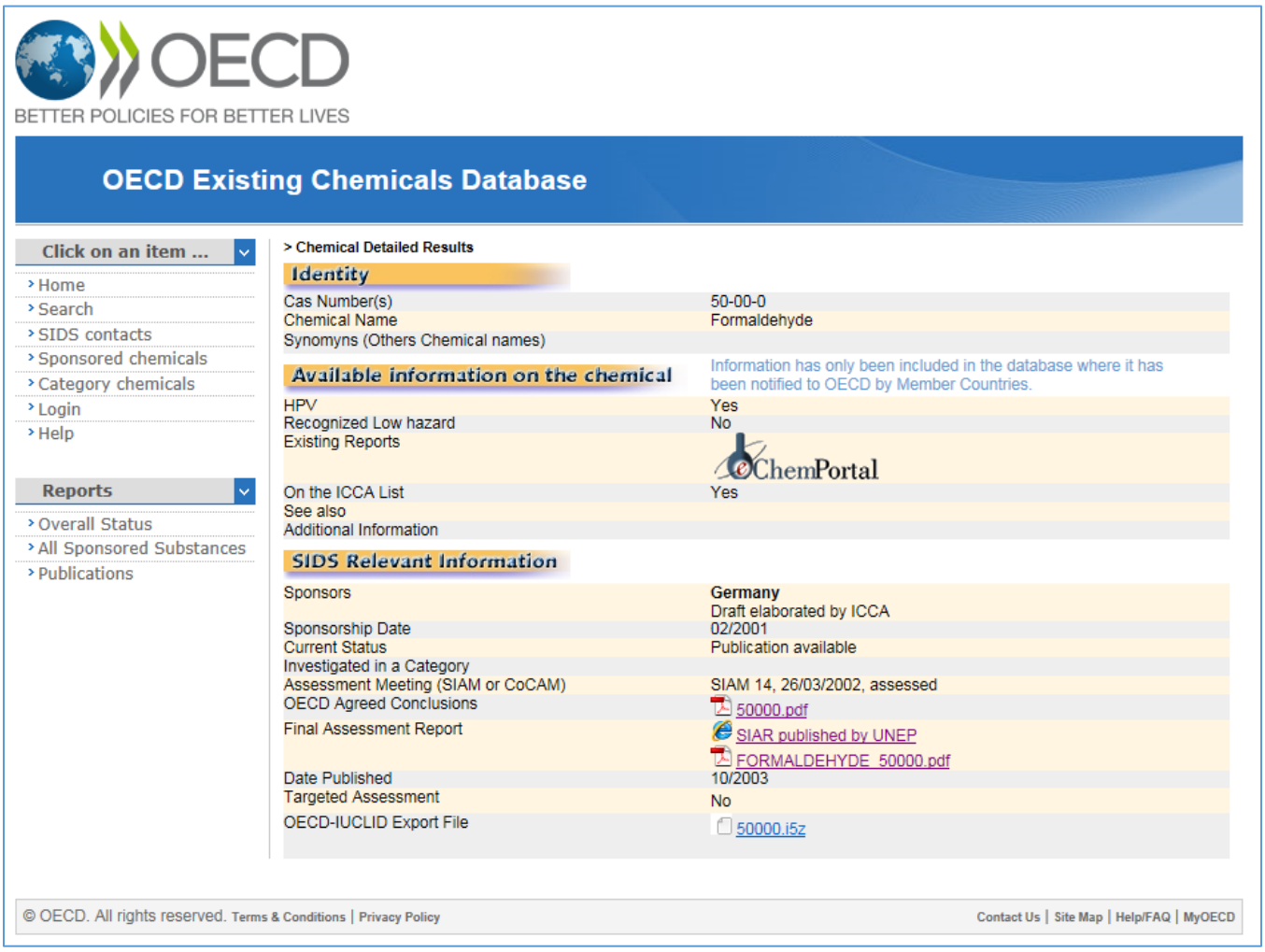

OECD
BETTER POLICIES FOR BETTER LIVES

OECD Existing Chemicals Database

Click on an item ...
- Home
- Search
- SIDS contacts
- Sponsored chemicals
- Category chemicals
- Login
- Help

Reports
- Overall Status
- All Sponsored Substances
- Publications

> Chemical Detailed Results

Identity

Cas Number(s)	50-00-0
Chemical Name	Formaldehyde
Synomyns (Others Chemical names)	

Available information on the chemical

Information has only been included in the database where it has been notified to OECD by Member Countries.

HPV	Yes
Recognized Low hazard	No
Existing Reports	eChemPortal
On the ICCA List	Yes
See also	
Additional Information	

SIDS Relevant Information

Sponsors	**Germany** Draft elaborated by ICCA
Sponsorship Date	02/2001
Current Status	Publication available
Investigated in a Category	
Assessment Meeting (SIAM or CoCAM)	SIAM 14, 26/03/2002, assessed
OECD Agreed Conclusions	50000.pdf
Final Assessment Report	SIAR published by UNEP FORMALDEHYDE_50000.pdf
Date Published	10/2003
Targeted Assessment	No
OECD-IUCLID Export File	50000.i5z

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In this example, the link for the UNEP document was broken. However, the report beneath it labeled 'FORMALDEHYDE 50000.pdf' links to the OECD SIDS, which is a publication of the UNEP.

Like the EU RAs mentioned previously, SIDS often review available data in detail and reach a conclusion. The QCAT assessor should search for the conclusions to determine if the results may be useful in conducting a QCAT assessment. For example, the formaldehyde SIDS reviews extensive data on formaldehyde's effect on aquatic toxicity. The summary at the end of the session states:

> *Conclusions on Aquatic effects*
> *Distribution modelling estimates water to be the main target compartment for formaldehyde. The most sensitive organism in an valid acute aquatic toxicity test was Daphnia pulex with an EC50 (48 h) of 5.8 mg/l……*

The EC_{50} value listed here could be compared against Technical Criteria in Appendix 8 to determine a acute aquatic toxicity concern for formaldehyde.

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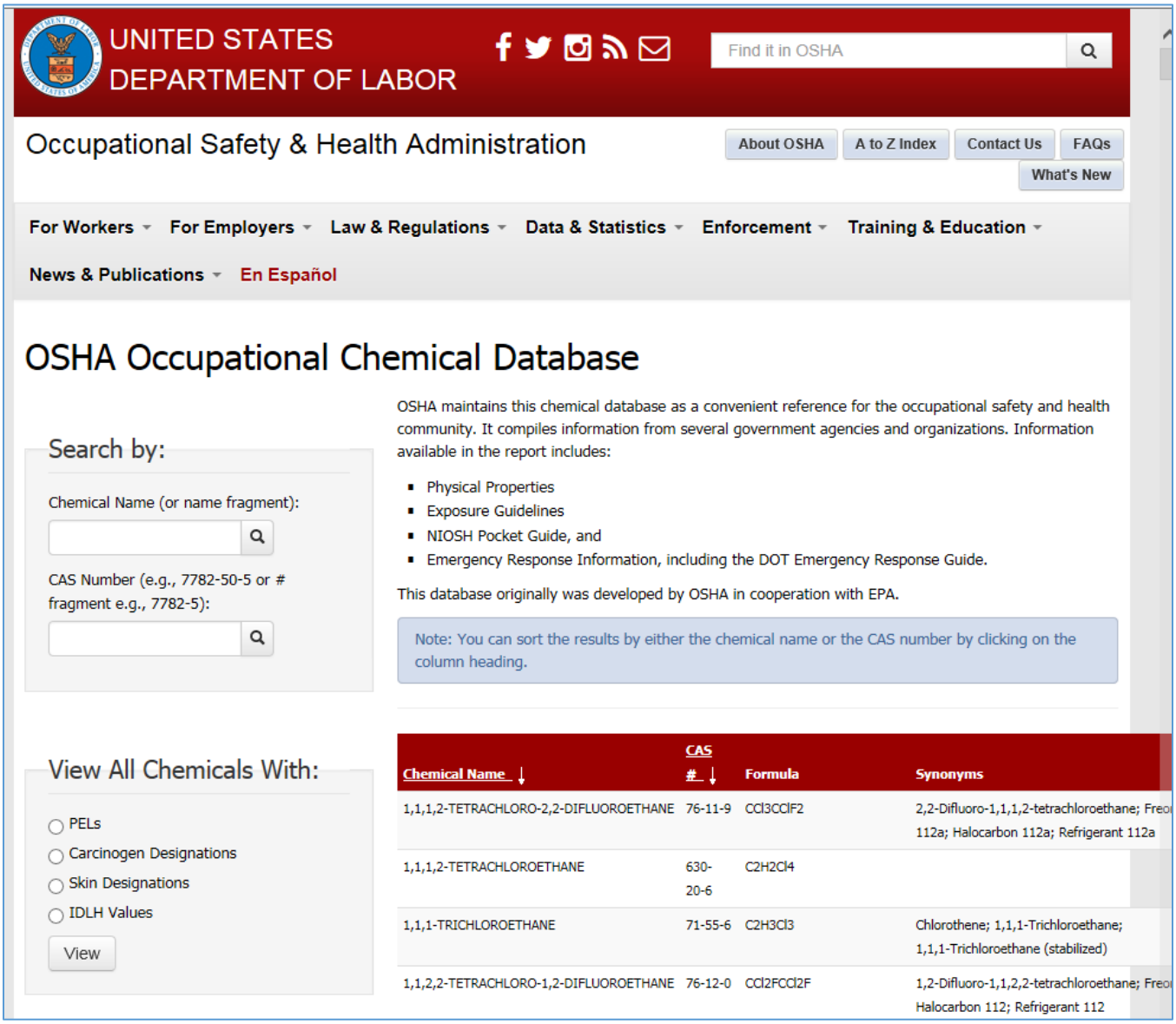
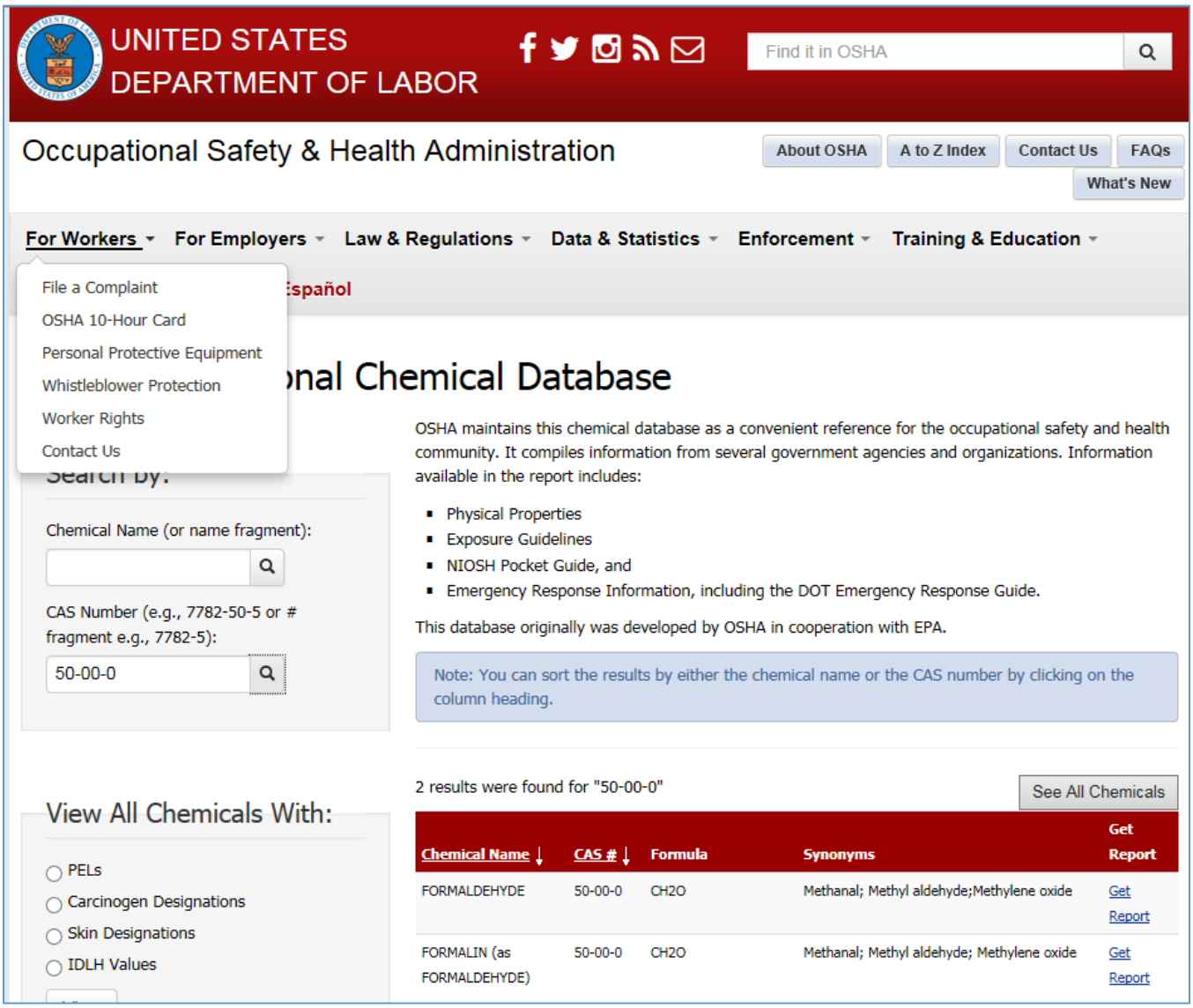
7. Occupational Safety & Health Administration (OSHA) Chemical Database (OCD)

The OCD contains information on the potential exposure concerns related to worker health and safety. Although the acute toxicity information requires considerable technical expertise, the OCD does identify chemicals as potential carcinogens. Clicking on the link provided in the QCAT Checklist, this page appears:



The QCAT assessor can search by chemical name or CAS. Entering in the CAS for formaldehyde as an example, leads to the following page:

Updated: July 20, 2016



Clicking on the 'Get Report' for formaldehyde, leads to the following results:

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UNITED STATES DEPARTMENT OF LABOR

Find it in OSHA

Occupational Safety & Health Administration

About OSHA | A to Z Index | Contact Us | FAQs | What's New

For Workers | For Employers | Law & Regulations | Data & Statistics | Enforcement | Training & Education | News & Publications | En Español

OSHA Occupational Chemical Database

Chemical Identification

Chemical Name:	**FORMALDEHYDE**
CAS#:	50-00-0
UN No:	3077
Formula:	CH2O
Synonyms:	Methanal; Methyl aldehyde;Methylene oxide

Physical Properties

Physical Description:	Nearly colorless gas with a pungent, suffocating odor.		
BP:	-6°F	**MW:**	30.0
FRZ/MLT:	FRZ: -134°F	**VP:**	>1 atm
FP:	NA (Gas)	**VD:**	1.04
Sp. GR:	NA	**IP:**	10.88 eV
LEL:	7.0%	**UEL:**	73%
NFPA Fire Rating:	NA	**NFPA Health Rating:**	NA
NFPA Reactivity Rating:	NA	**NFPA Sp. Inst.:**	NA

Exposure Limits

OSHA		NIOSH		Related Information
PEL-TWA ppm:	0.75	**REL-TWA ppm:**	0.016	**AIHA Emergency Response Planning Guidelines - ERPG-1/ERPG-2/ERPG-3:** 1 ppm/10 ppm/40 ppm
PEL-TWA mg/m3:	NA	**REL-TWA mg/m3:**	NA	
PEL-STEL ppm:	2	**REL-STEL ppm:**	NA	
PEL-STEL mg/m3:	NA	**REL-STEL mg/m3:**	NA	
PEL-C ppm:	NA	**REL-C ppm:**	0.1	
PEL-C mg/m3:	NA	**REL-C mg/m3:**	NA	**Carcinogen Classifications:** IARC-1, NIOSH-Ca, NTP-R, OSHA-Ca, TLV-A2, EPA-B1
Skin Notation:	N	**Skin Notation:**	N	
Notes: SEE 29 CFR 1910.1048		**Notes:** CARCINOGEN (Ca); 15 MINUTE CEILING		
		IDLH ppm:	20	
		IDLH mg/m3:	NA	
		IDLH Notes:	Ca	

NIOSH Pocket Guide to Chemical Hazards (Current through June 2006)

Formaldehyde	**CAS:** 50-00-0
Formula: HCHO	**RTECS:** LP8925000
Synonyms & Trade Names: Methanal, Methyl aldehyde, Methylene oxide	**DOT ID & Guide:** NA

Exposure Limits

NIOSH REL: NIOSH REL: Ca TWA 0.016 ppm C 0.1 ppm [15-minute] See Appendix A	**OSHA PEL:** OSHA PEL: [1910.1048] TWA 0.75 ppm ST 2 ppm

Note: This is an abbreviated capture of the data shown. More data is available although it is likely to be of minimal use to the QCAT assessor.

Updated: July 20, 2016

Information of interest is the information in the box labeled 'Carcinogen Classifications' (red arrow) which identifies if there are any carcinogenicity concerns associated with the chemical of interest. Although much of the information on carcinogenicity for formaldehyde is pulled from sources used in Step I, additional information on the carcinogenicity classification for chemicals not identified in Step I sources may prove useful in completing a QCAT evaluation.

8. Danish Ministry of the Environment's Environmental Protection Agency (Danish EPA) (Q)SAR Assessment of Chemical Properties of Substances

The Danish EPA has created a database that contains predictions on the potential toxicity of approximately 166,000 chemicals. The database predicts toxicity for the following criteria of importance to the QCAT:

- Mutagenicity
- Carcinogenicity
- Reproductive toxicity
- Aquatic environment
- Acute human (oral) toxicity

For the purposes of the QCAT, the full (Q)SAR database will not be used but a subset of more than 30,000 substances for which GHS classifications have been estimated and are reported in the Danish Advisory List for Self-Classification. These GHS results are directly comparable to the GHS criteria included in the Appendix 8 of QCAT.

The link available in the QCAT Checklist leads the assessor to the following page:

Updated: July 20, 2016

The advisory list for self classification of dangerous substances

Lack of data on hazardous properties of chemicals makes it difficult for companies to meet their obligations to self classify the chemicals they import or produce. To address this issue, The Danish Environmental Protection Agency (DK-EPA) publishes two lists for self classification of chemical substances" – with advisory classifications of more than 30,000 substances.

Since the new regulation for classification and labelling (the CLP-regulation) came into force, the regulation is in a transitional phase until 2015 where both regulations still are relevant in certain situations. Therefore both regulations are covered.

How to use the list

The advisory classifications are based on predictions of dangerous properties of chemicals from computer models - the so-called (Q)SARs - which has a built-in uncertainty. Statistical methods estimate that the proposals are correct in approx. 80% of the cases. Therefore, in relation to self-classification of chemicals, the Danish Environmental Agency recommends that:

- If a substance has an EU-harmonised classification, then this harmonised classification must be followed and the advisory classification should be neglected.
- All reliable information (test data and other types of information) must be considered together with the advisory classifications using a weight of evidence based approach.
- In those cases where no reliable information is available for a substance, the advisory classification can be used alone.
  It is further strongly recommended to read the additional information on self-classification and the advisory lists carefully before using the list (see below).

Search the advisory list for self classification of chemical substances.

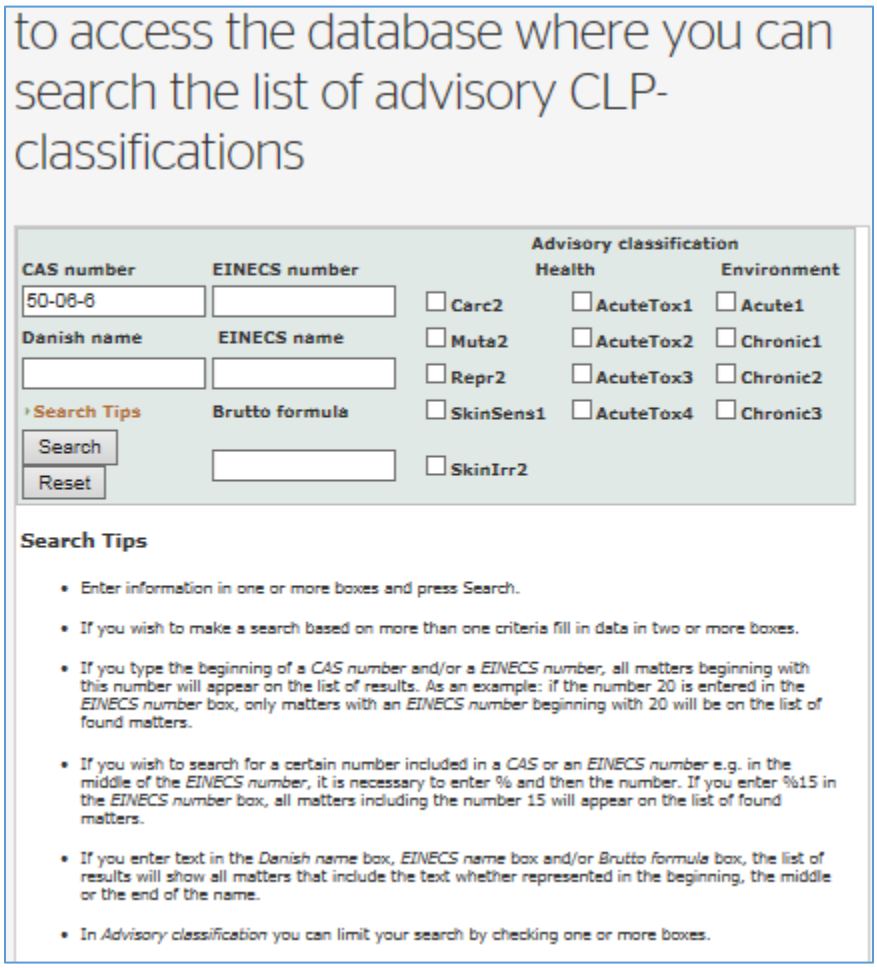
Database where you can search the list of advisory CLP-classifications.
Excel sheet with advisory CLP-classifications

Database with advisory classifications according to the old regulation
Excel-sheet with with advisory classifications according to the old regulation.

The QCAT assessor can either search the database or download an excel spreadsheet. There are two legislations for which this information was created. Both can be reviewed although the data for the CLP classifications is likely to be the most valuable.

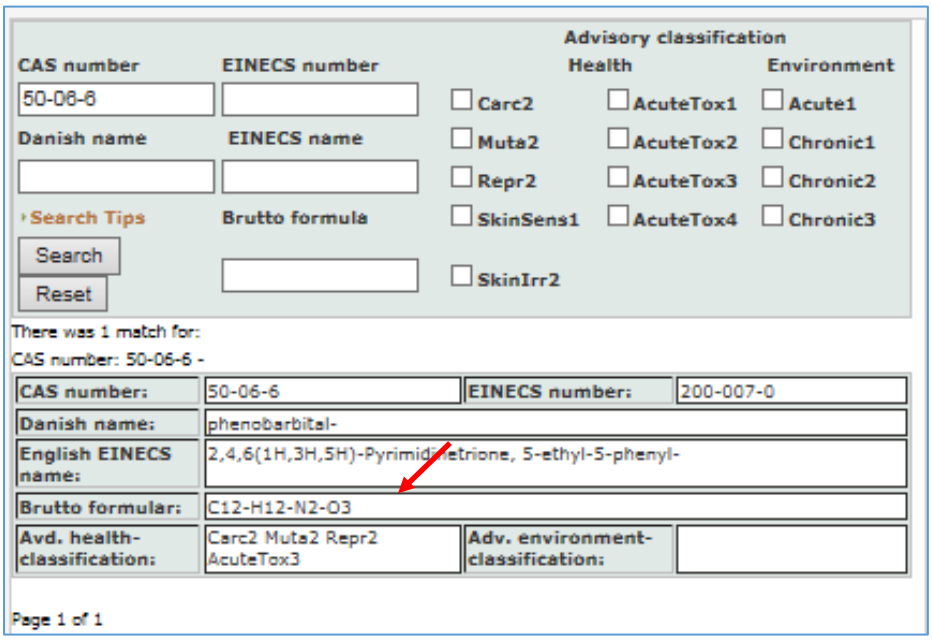
If the assessor clicks on the CLP database link (red arrow above), the following page appears:

Updated: July 20, 2016



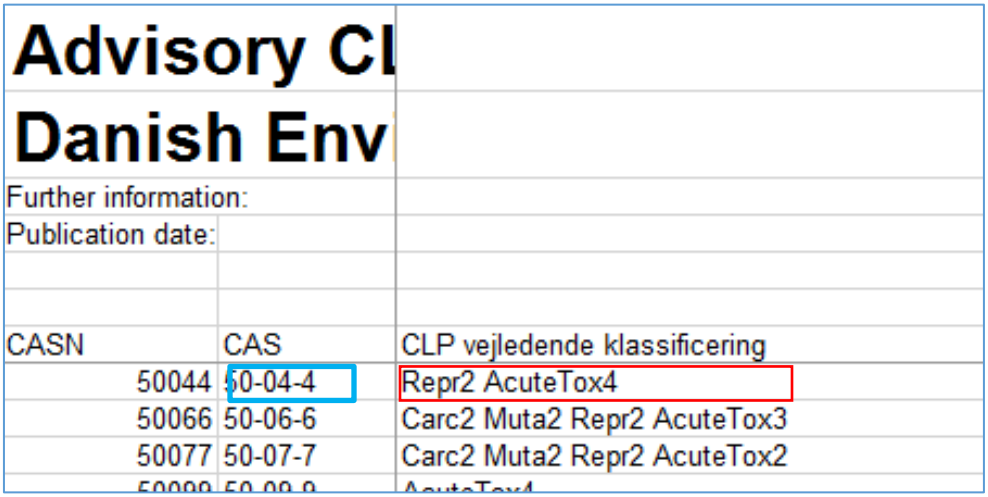
In this instance, our previous example chemical (formaldehyde) would not work since formaldehyde's impacts upon human health and the environment are well documented. However, another chemical, phenobarbital (CAS 50-06-6) is used as an example and the database searched leading to the following:

Updated: July 20, 2016



Based upon the predictive capabilities of the models used, phenobarbital is identified (red arrow) as a Category 2 carcinogen (Carc2), mutagen (Muta2) and reproductive toxicant (Repr2) and a Category 3 acute mammalian toxic (AcuteTox3). These values can be compared against the criteria in Appendix 8 and identified a level of concern for this chemical of concern.

The QCAT assessor may also download an Excel spreadsheet. Using phenobarbital again as an example, the following information is found:



Advisory Cl		
Danish Env		
Further information:		
Publication date:		
CASN	CAS	CLP vejledende klassificering
50044	50-04-4	Repr2 AcuteTox4
50066	50-06-6	Carc2 Muta2 Repr2 AcuteTox3
50077	50-07-7	Carc2 Muta2 Repr2 AcuteTox2
50099	50-09-9	AcuteTox4

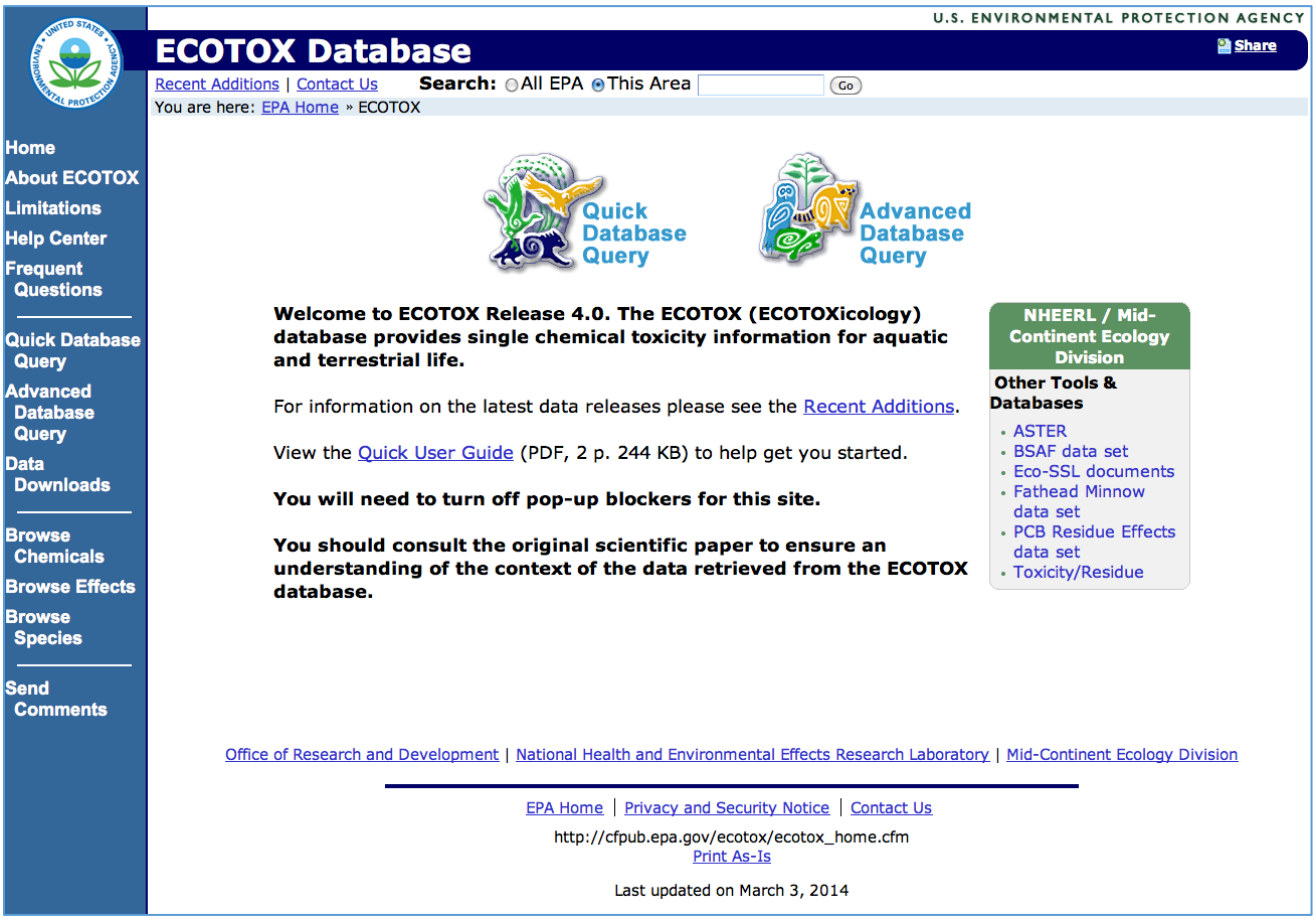
Column 7 of the spreadsheet contains the hazard assessment results, which agree with the information provided in the database. The spreadsheet indicates there are 33,835 chemicals in the database so, for those chemicals lacking important data, this database might help fill in many datagaps.

9. Ecological Toxicity (ECOTOX) Database

Updated: July 20, 2016

ECOTOX is a major source of ecological toxicity information. However, unlike many of the previous sources, EPA does not conduct detailed technical review of all of the information included in ECOTOX. There will be more variability in the quality of data found within. To address this concern, a 'weight of evidence' approach will be used to identify values to be used in a QCAT evaluation. In addition, the exposure hierarchy described in the HSDB section above (Salmonids followed by fathead minnow, followed by any other fish species) will be used during data evaluation.

The ECOTOX opening page appears as follows:



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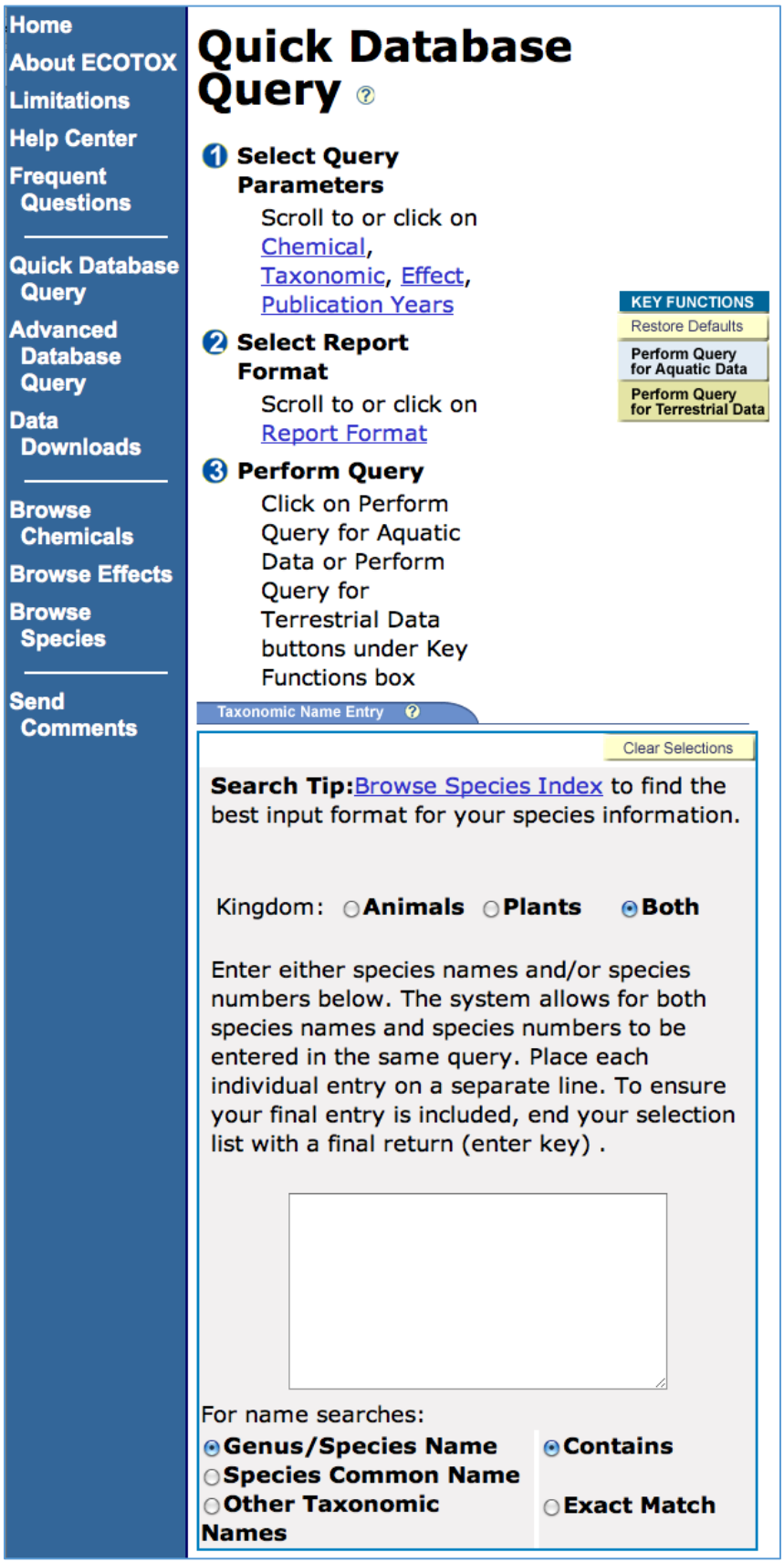
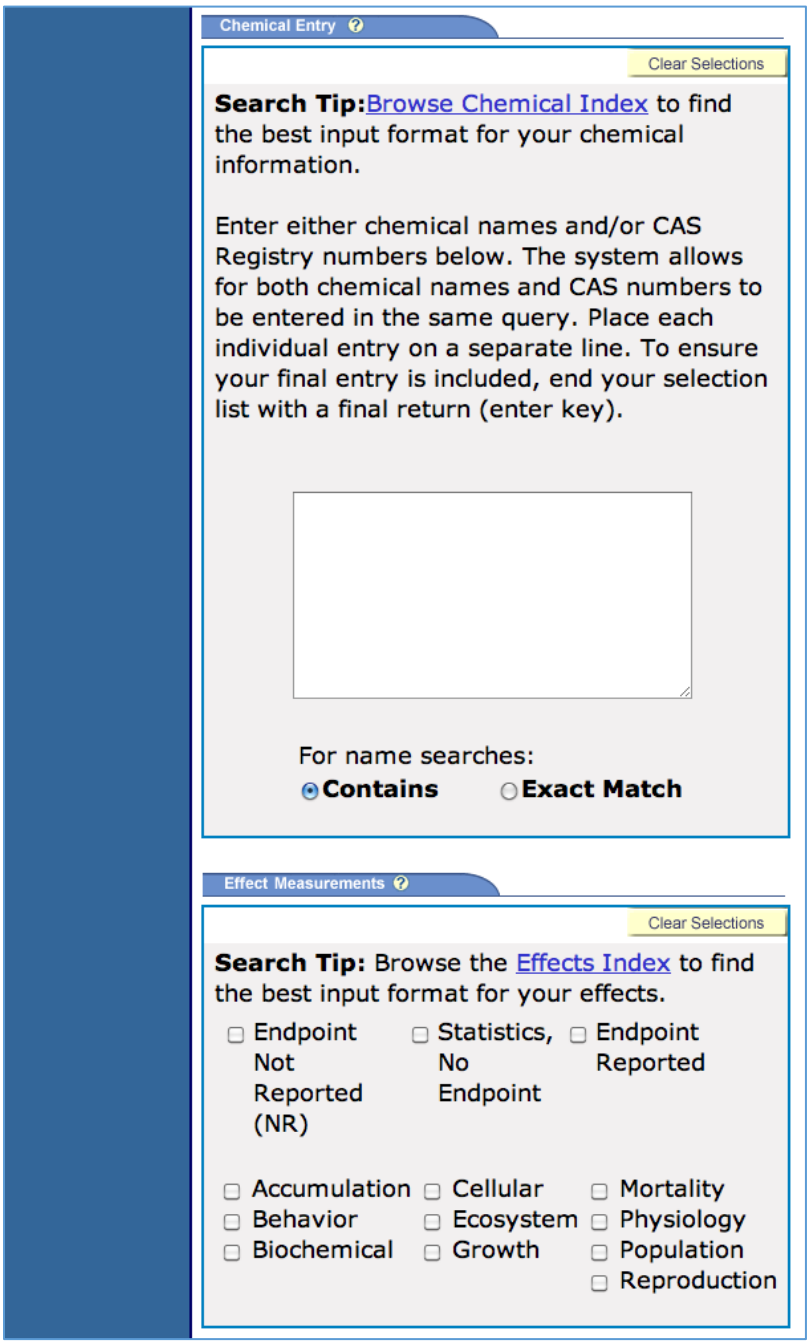
The easiest way to request information from the database is to select the ‘Quick Database Query’ Option’ which, once selected, appears as:



Screen capture continued on next page.

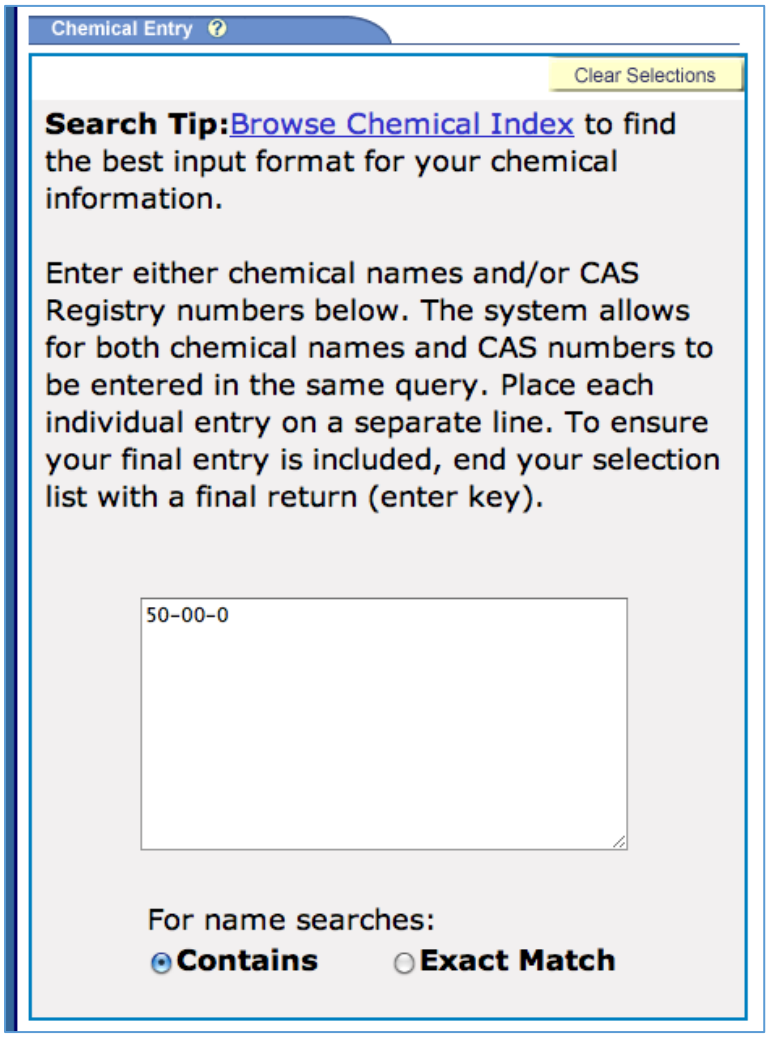
Updated: July 20, 2016



The screen captures above represent part of the information on the page. As can be seen, there are numerous ways to request data from ECOTOX. For most chemicals, there is limited information and the simplest method will work. In this instance, you enter the CAS number in the box labeled ‘Chemical Entry.’ No other changes are needed.

Updated: July 20, 2016

Using formaldehyde as an example, the entry would look like this:



Once the CAS number is entered into this box, the assessor clicks on the ‘Perform Query for Aquatic Data.’ A separate window will open that lists all of the information available in ECOTOX.

Updated: July 20, 2016

For example:

U.S. ENVIRONMENTAL PROTECTION AGENCY

ECOTOX: Aquatic Report

USEPA/ORD/NHEERL - Mid-Continent Ecology Division

E-mail: ecotox.support@epa.gov Telephone: 218-529-5225

It is recommended that users consult the original scientific paper to ensure an understanding of the context of the data retrieved from the ECOTOX database.

Report Generated: Sun Mar 2 21:33:48 2014

Aquatic Search Results: 566 Records

1 2 3 4 5 6 7 8 Next>> References **Page 1 of 9**

Spec. Sci. Name / Spec. Common Name	Exp. Type / Chem. Anal.	Media Type / Loc	Resp. Site / Obs. Dur. (Days)	Endpoint / BCF	Trend / Eff %	Effect / Effect Meas.	Conc (Standardized) / Appl. Rate	Stat. Signif. / Sig. Level	Ref#	View Details
CAS #/Chemical: 50000 - Formalin										
Algae, Moss, Fungi										
Chlorococcales Green Algae Order	S	FW	1	EC10		PHY ASML	F 2500 ug/L		56359	View Details
Chlorococcales Green Algae Order	S	FW	1	EC50		PHY ASML	F 6500 ug/L		56359	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP BMAS	F 3480 (3450-3520) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP BMAS	F 4440 (4420-4460) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP GPOP/	F 3540 (3210-3890) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP GPOP/	F 4450 (4140-4790) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP PGRT	F 4890 (2740-8690) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP PGRT	F 6420 (4450-9250) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP PGRT	F 6610 (4560-9570) ug/L		69554	View Details
Desmodesmus subspicatus Green Algae	S U	FW LAB	3	EC50	DEC	POP PGRT	F 6720 (5120-8830) ug/L		69554	View Details
Desmodesmus subspicatus	S U	FW LAB	3	EC50	DEC	POP PGRT	F 7410 (4000-13800) ug/L		69554	View Details

1 2 3 4 5 6 7 8 Next>> References **Page 1 of 9**

Last updated on Monday, March 3rd, 2014
URL: http://cfpub.epa.gov/ecotox/report.cfm

Formaldehyde contains numerous acute aquatic toxicity (LC_{50}) entries for Rainbow Trout. An excerpt of this data follows on the next page.

Aquatic Search Results: 566 Records

<<Prev 1 2 3 4 5 6 7 8 Next>> References

Spec. Sci. Name / Spec. Common Name	Exp. Type / Chem. Anal.	Media Type / Loc	Resp. Site / Obs. Dur. (Days)	Endpoint / BCF	Trend / Eff %	Effect / Effect Meas.	Conc (Standardized) / Appl. Rate	Stat. Signif. / Sig. Level	Ref#	View Details
Oncorhynchus mykiss Rainbow Trout	F / U	FW / LAB	/ 0.333	LC50	INC	MOR / MORT	F 0.223 (0.128-0.318) ml/L		16992	View Details
Oncorhynchus mykiss Rainbow Trout	F / U	FW / LAB	/ 1	LC50	INC	MOR / MORT	F 0.162 (0.081-0.243) ml/L		16992	View Details
Oncorhynchus mykiss Rainbow Trout	F / U	FW / LAB	/ 2	LC50	INC	MOR / MORT	F 0.159 (0.011-0.247) ml/L		16992	View Details
Oncorhynchus mykiss Rainbow Trout	F / U	FW / LAB	/ 3	LC50	INC	MOR / MORT	F 0.149 (0.059-0.239) ml/L		16992	View Details
Oncorhynchus mykiss Rainbow Trout	F / U	FW / LAB	/ 4	LC50	INC	MOR / MORT	F 0.129 (0.032-0.226) ml/L		16992	View Details
Oncorhynchus mykiss Rainbow Trout	/ U	FW / LAB	/ 2	LC50	INC	MOR / MORT	F 50000 (42300-86000) ug/L		18459	View Details
Oncorhynchus mykiss Rainbow Trout	R / U	FW / LAB	/ 2	LC50	INC	MOR / MORT/	F 320000 ug/L		6573	View Details
Oncorhynchus mykiss Rainbow Trout	S	FW / LAB	/ 4	LC50		MOR / MORT	NC > 100000 ug/L		344	View Details
Oncorhynchus mykiss Rainbow Trout	S	FW / LAB	/ 4	LC50		MOR / MORT	NC > 100000 ug/L		344	View Details
Oncorhynchus mykiss Rainbow Trout	S	FW / LAB	/ 4	LC50		MOR / MORT	NC 118000 (99700-140000) ug/L		344	View Details
Oncorhynchus mykiss Rainbow Trout	S	FW / LAB	/ 4	LC50		MOR / MORT	NC 118000 (99700-140000) ug/L		344	View Details

<<Prev 1 2 3 4 5 6 7 8 Next>> References

Many of the LC_{50} results can be discarded because the test lasted less than 24 hours (0.333 days). The remaining tests which lasted anywhere from 1 to 4 days provided results ranging from 1,410 to 320,000 µg/L. However, the low values were found in a limited number of studies and a majority of the results were in the 100,000 to 200,000 µg/L range. Therefore a value of 150,000 micrograms per liter (equivalent to 150 mg/L) would be selected for the QCAT as being most representative of the data in ECOTOX.

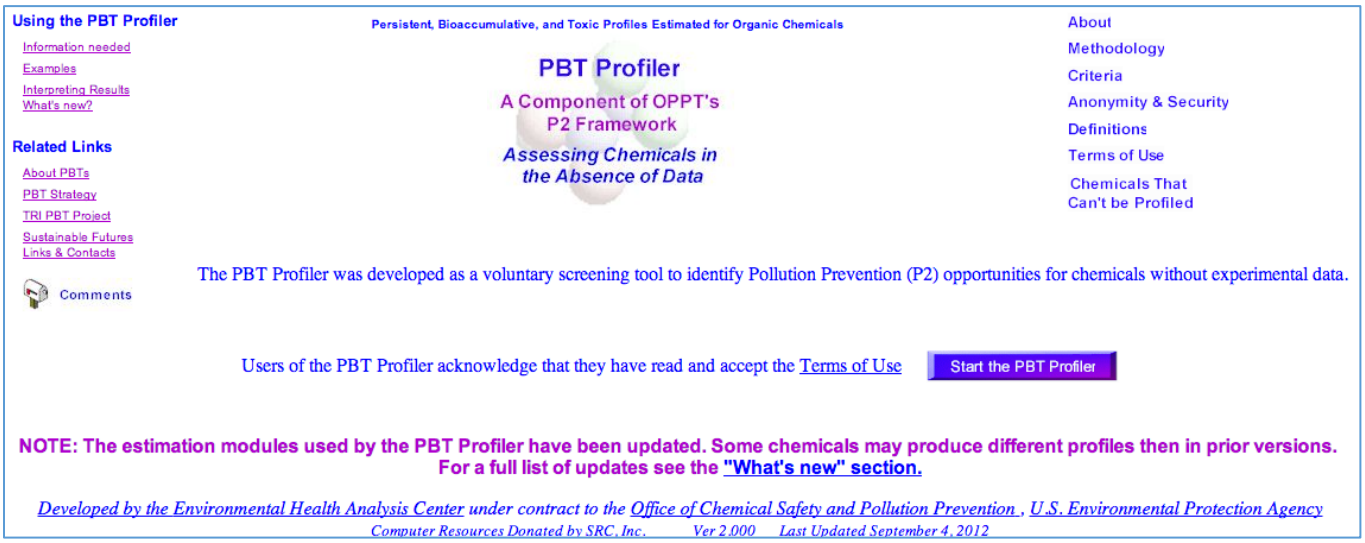
ECOTOX also contains information on a chemical's bioaccumulation factor. As with other information, the user must determine which BCF values to use. A 'weight of evidence' approach as shown in other examples in this document might be a preferred method. However, if bioaccumulation information cannot be found in the other sources or confirmatory values are needed, ECOTOX may prove a valuable source to determine whether or not a chemical bioaccumulates.

Updated: July 20, 2016

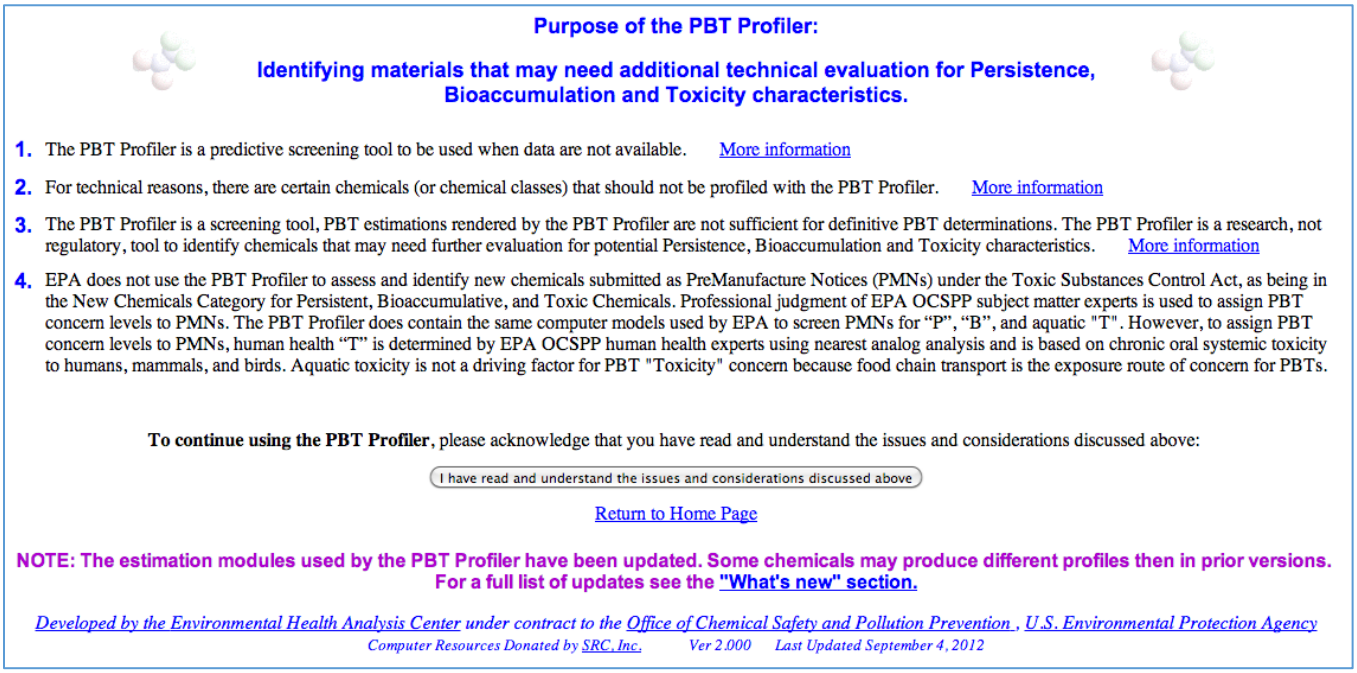
10. PBT Profiler

The U.S. EPA has developed a system for assessing chemicals for persistence and bioaccumulation when experimental data are absent. This system, the PBT Profiler, is used as screening tool to estimate persistence and bioaccumulation criteria and should only be used when other sources of information are not available.

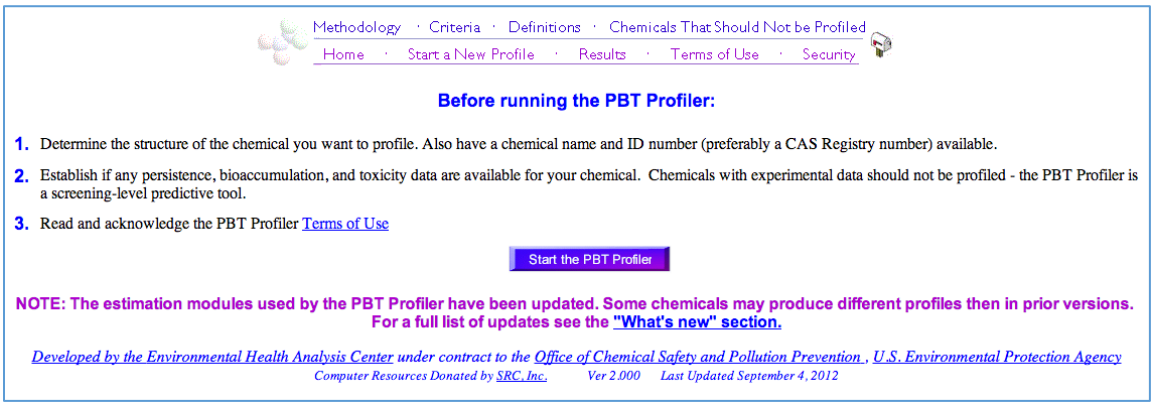
The initial screen of the PBT Profiler appears as:



Clicking on 'Start the PBT Profiler' takes you to the following page:



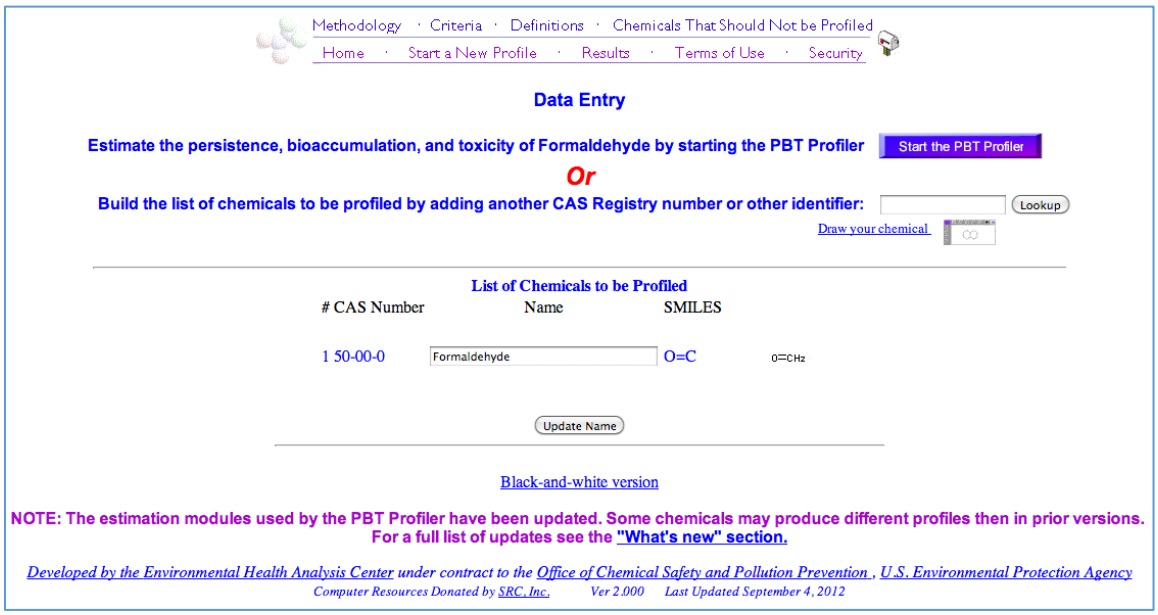
Agreeing to the issues and considerations takes you to the following page:



You may now actually start the PBT Profiler.

Using formaldehyde as an example, enter its CAS number into the box and click on ‘Lookup’. The following page appears:

Updated: July 20, 2016



Methodology · Criteria · Definitions · Chemicals That Should Not be Profiled

Home · Start a New Profile · Results · Terms of Use · Security

Data Entry

Estimate the persistence, bioaccumulation, and toxicity of Formaldehyde by starting the PBT Profiler Start the PBT Profiler

Or

Build the list of chemicals to be profiled by adding another CAS Registry number or other identifier: Lookup

Draw your chemical

List of Chemicals to be Profiled

#	CAS Number	Name	SMILES	
1	50-00-0	Formaldehyde	O=C	O=CH2

Update Name

Black-and-white version

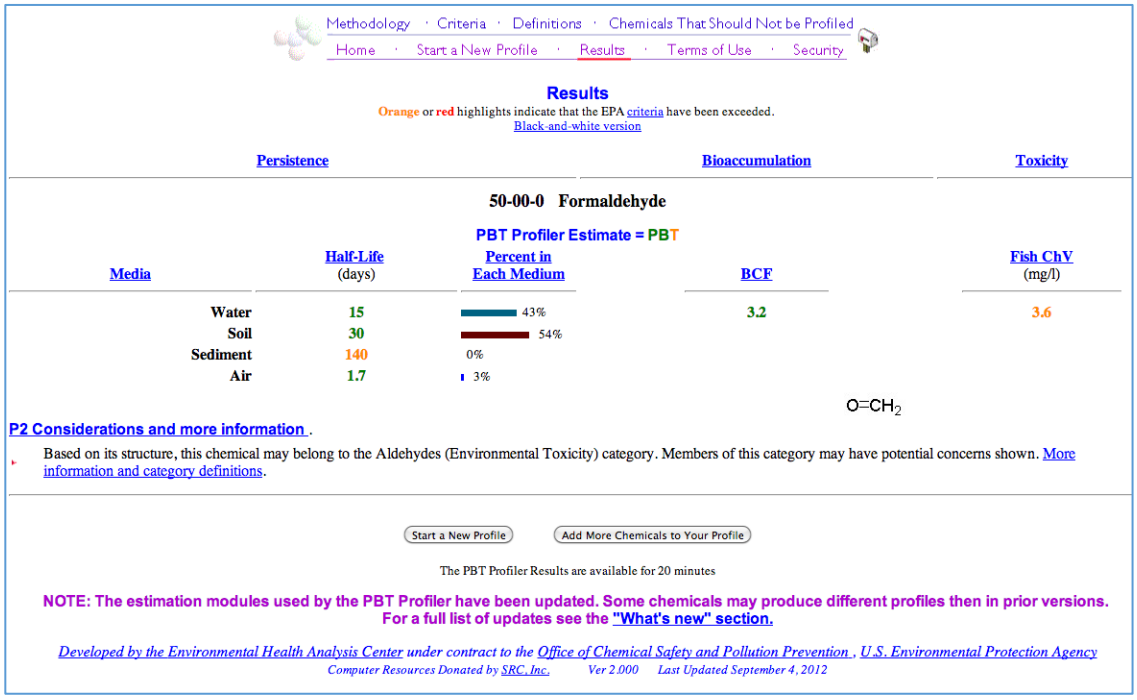
NOTE: The estimation modules used by the PBT Profiler have been updated. Some chemicals may produce different profiles then in prior versions. For a full list of updates see the "What's new" section.

Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention , U.S. Environmental Protection Agency

Computer Resources Donated by SRC, Inc. Ver 2.000 Last Updated September 4, 2012

Updated: July 20, 2016

Search for data on multiple chemicals by entering information on a second chemical and pressing ‘Lookup’ or look at the report on a single chemical by selecting the ‘Start the PBT Profiler’ option, which produces the following:



Methodology · Criteria · Definitions · Chemicals That Should Not be Profiled

Home · Start a New Profile · Results · Terms of Use · Security

Results

Orange or red highlights indicate that the EPA criteria have been exceeded.
Black-and-white version

Persistence			Bioaccumulation	Toxicity
50-00-0 Formaldehyde				
PBT Profiler Estimate = PBT				
Media	Half-Life (days)	Percent in Each Medium	BCF	Fish ChV (mg/l)
Water	15	43%	3.2	3.6
Soil	30	54%		
Sediment	140	0%		
Air	1.7	3%		

O=CH$_2$

P2 Considerations and more information .

Based on its structure, this chemical may belong to the Aldehydes (Environmental Toxicity) category. Members of this category may have potential concerns shown. More information and category definitions.

Start a New Profile | Add More Chemicals to Your Profile

The PBT Profiler Results are available for 20 minutes

NOTE: The estimation modules used by the PBT Profiler have been updated. Some chemicals may produce different profiles then in prior versions. For a full list of updates see the "What's new" section.

Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention , U.S. Environmental Protection Agency
Computer Resources Donated by SRC, Inc. Ver 2.000 Last Updated September 4, 2012

Various media including water, soil, sediment, and air display persistence results. When considering whether a chemical is persistent, it would be appropriate to consider what media is mostly likely to be the major factor for the chemical under evaluation. In the case of formaldehyde, the half-life values for water and soil are most important as these two media account for 97% of the media in which it is distributed. Sediment and air comprise only 3% and their half-life values are less likely to impact whether or not formaldehyde is persistent.

In addition to persistence, the PBT Profiler also includes information on bioaccumulation and toxicity. The bioaccumulation tendency is displayed as a projected bioaccumulation factor (BCF). This information may prove useful in filling in any gaps that remain for these criteria. The toxicity values, however, cannot be translated into a level of concern in QCAT using the DfE criteria and therefore are unlikely to help in the chemical assessment.

11. US EPA Characterization Criteria

As part of EPA's New Chemical Program, hazard endpoints were parsed into various levels of concern to assist EPA to better identify chemicals which may negatively impact human health or the environment. These criteria are used by EPA's Design for the Environment Program to assign a level of concern while conducting a chemical hazard assessment and were subsequently incorporated into the GreenScreen and QCAT methodologies.

Updated: July 20, 2016

The link provided in the QCAT Checklist takes the assessor directly to the criteria used by EPA's Design for the Environment Program (DfE) during their chemical hazard assessment process in support of their Alternatives Assessment Program. As DfE states:

> *For most endpoints, the criteria define "High," "Moderate," and "Low" concern. While many hazard classification criteria exist throughout the world, DfE has carefully chosen the criteria that form the Alternatives Assessment Criteria for Hazard Evaluation with the goal of creating a rigorous and useful system for differentiating among chemicals based on hazard. Authoritative sources – the United Nation's Globally Harmonized System (GHS) for the Classification and Labeling of Chemicals and U.S. EPA programs – are the basis for these distinctions. The criteria include endpoints used in the Screening Information Data Set (SIDS) [1], a set of endpoints internationally agreed upon for characterizing chemical hazards. In assigning a designation of Low, Moderate, or High concern for hazard, DfE uses the best information available, both experimental and modeled.*

Unlike the previous Step II sources, there is no actual data here that can help a QCAT assessor assign a level of concern for a chemical being evaluated. It was deemed important, however, that the QCAT explain the source of the Technical Criteria found in Appendix 8 to show that considerable thought had gone into separating data into different levels of concern.