Istituto superiore per la Ricerca e la Protezione Ambientale

Ministero del Lavoro, Salute e Politiche Sociali

In collaborazione con:

Ministero dell'Ambiente e della Tutela del Territorio e del Mare

Ministero dello Sviluppo Economico

Istituto Superiore di Sanità

(Q)SAR: una introduzione

Romualdo Benigni

ISS

Stima del rischio chimico:

La tossicologia tradizionale e' stata finora la principale fonte di informazione in EU

Nuove opportunita' per **metodi "alternativi"**

REACH: Registration, Evaluation and Assessment of Chemicals

*..Metodi alternativi, che includono **(Q)SAR**, **Read-Across** e **Categorie chimiche**, saranno usati piu' ampiamente e piu' sistematicamente che nella regolamentazione precedente…*

QSAR: Quantitative Structure-Activity Relationships

- **Read-Across / Analogue approach**: colmare i vuoti nei dati.

L'informazione esistente per una (o poche) sostanze usata per predizioni per la sostanza in esame, ritenuta simile chimicamente

- **Categoria chimica**:

Gruppo di sostanze le cui proprieta' fisico-chimiche e tossicologiche sono probabilmente simili, o seguono un andamento regolare come risultato di una similarita' strutturale

OECD Principles

- *To facilitate the consideration of a (Q)SAR model for regulatory purposes, it should be associated with the following information:*

- ***1) a defined endpoint***
- ***2) an unambiguous algorithm***
- ***3) a defined domain of applicability***
- ***4) appropriate measures of goodness-of–fit, robustness and predictivity***
- ***5) a mechanistic interpretation, if possible***

Un esempio: (Q)SAR per mutageni e cancerogeni

- Teoria piu' sviluppata che per altre tossicita' (meccanismi d'azione)

- Esempio di applicazione di vari metodi

Basi meccanicistiche della scienza e della regolamentazione di mutageni e cancerogeni chimici

- Reattivita' elettrofila dei cancerogeni (Miller)

- Modello in vitro dei meccanismi di cancerogenesi chimica (test di Ames, Salmonella)

- Modello teorico della cancerogenesi (Allerte Strutturali di Ashby)

Collection and Evaluation of (Q)SAR Models for Mutagenicity and Carcinogenicity

Romualdo Benigni, Cecilia Bossa, Tatiana Netzeva, Andrew Worth

PUBSY ID - EUR 22772 EN

2007

EUROPEAN COMMISSION
Joint Research Centre

ihcp

ECB

http://ecb.jrc.it/documents/QSAR/EUR_22772_EN.pdf

Relazioni Struttura-Attivita'

Applicazione a diversi problemi, con differenti approcci

A grana grossa: **Allerte Strutturali**

A grana fine**:** **QSAR**

Allerte Strutturali

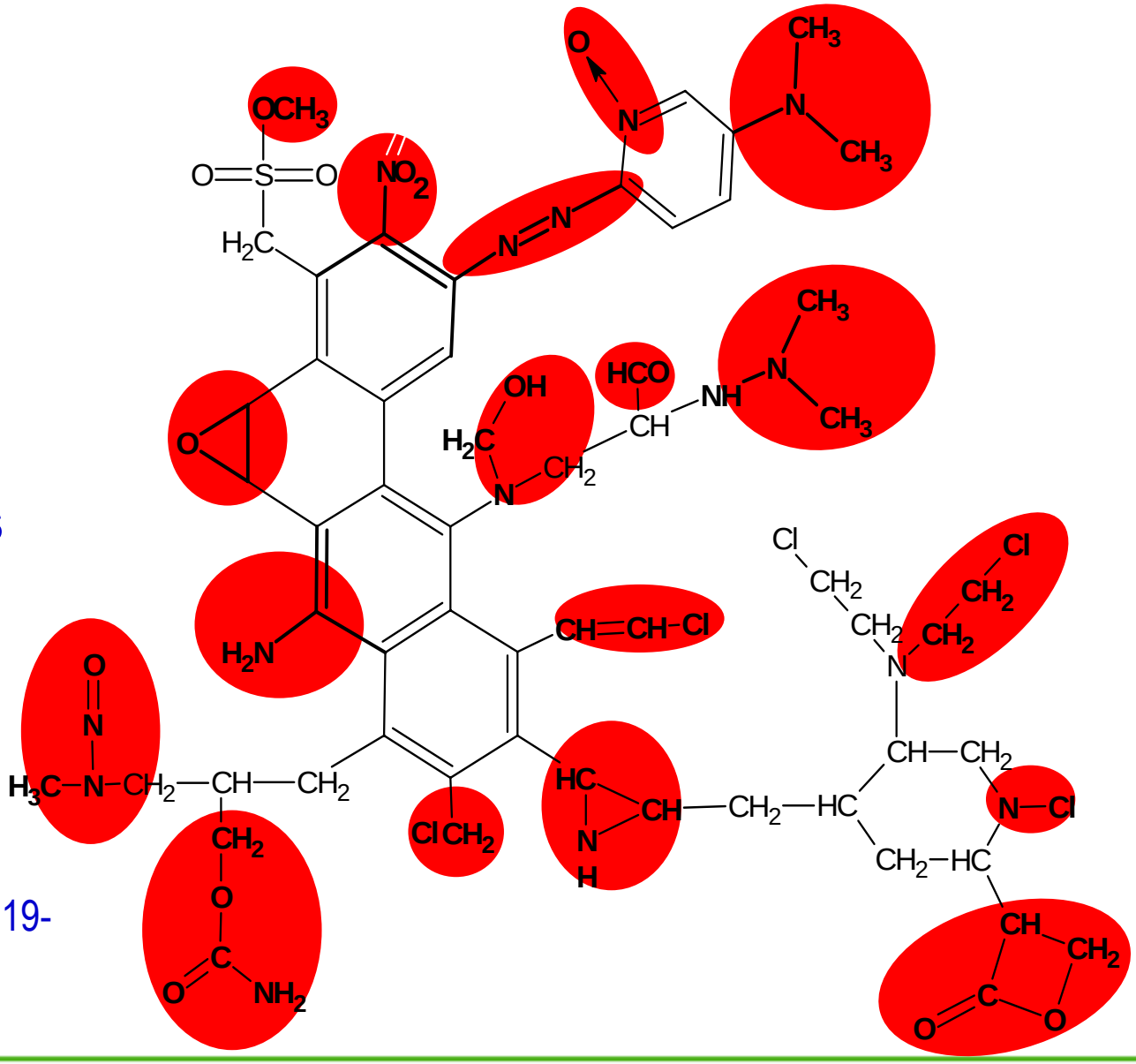
Gruppi funzionali o sottostrutture chimiche

legati agli

effetti tossici (mutagenesi / cancerogenesi) delle sostanze

Ashby's Poly-carcinogen

Some alerts accompanied by detoxifying (modulating) factors



Ashby (1995) Environ.Mutag. 7: 919-921

Allerte Strutturali; varie compilazioni

Ashby J
Environ Mutagen (1985) 7:919-921

Bailey AB, Chanderbhan N, Collazo-Braier N, Cheeseman MA, Twaroski ML
Regulat Pharmacol Toxicol (2005) 42:225-235

Kazius J, McGuire R, and Bursi R
J Med Chem (2005) 48:312-320

Kazius J, Nijssen S, Kok J, Back T, Ijzerman AP
J Chem Inf Model (2006) 46:597-605

Allerte Strutturali versus dati sperimentali

Banche dati:

- **Mutagenesi** (Toxnet, Kazius et al. 2005) *n=4337*

- **Canc / Mut** (CPDB in DSSTox) *n=1189*

http://www.epa.gov/ncct/dsstox/index.html

-**Canc / Mut** (ISSCAN) *n=890*

http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7

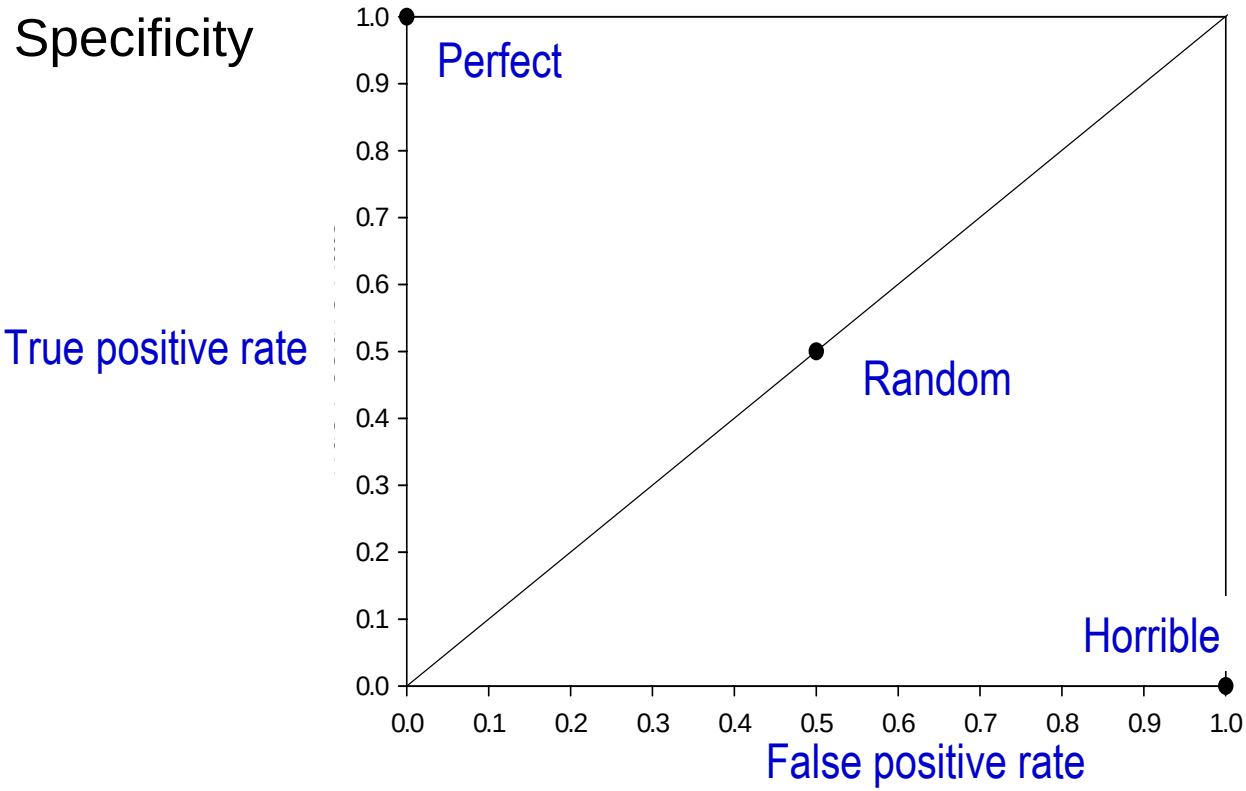
ROC graph: A simple, graphical way of comparing predictions with results

True positive rate = (Positives predicted as positive) / (Real positives)

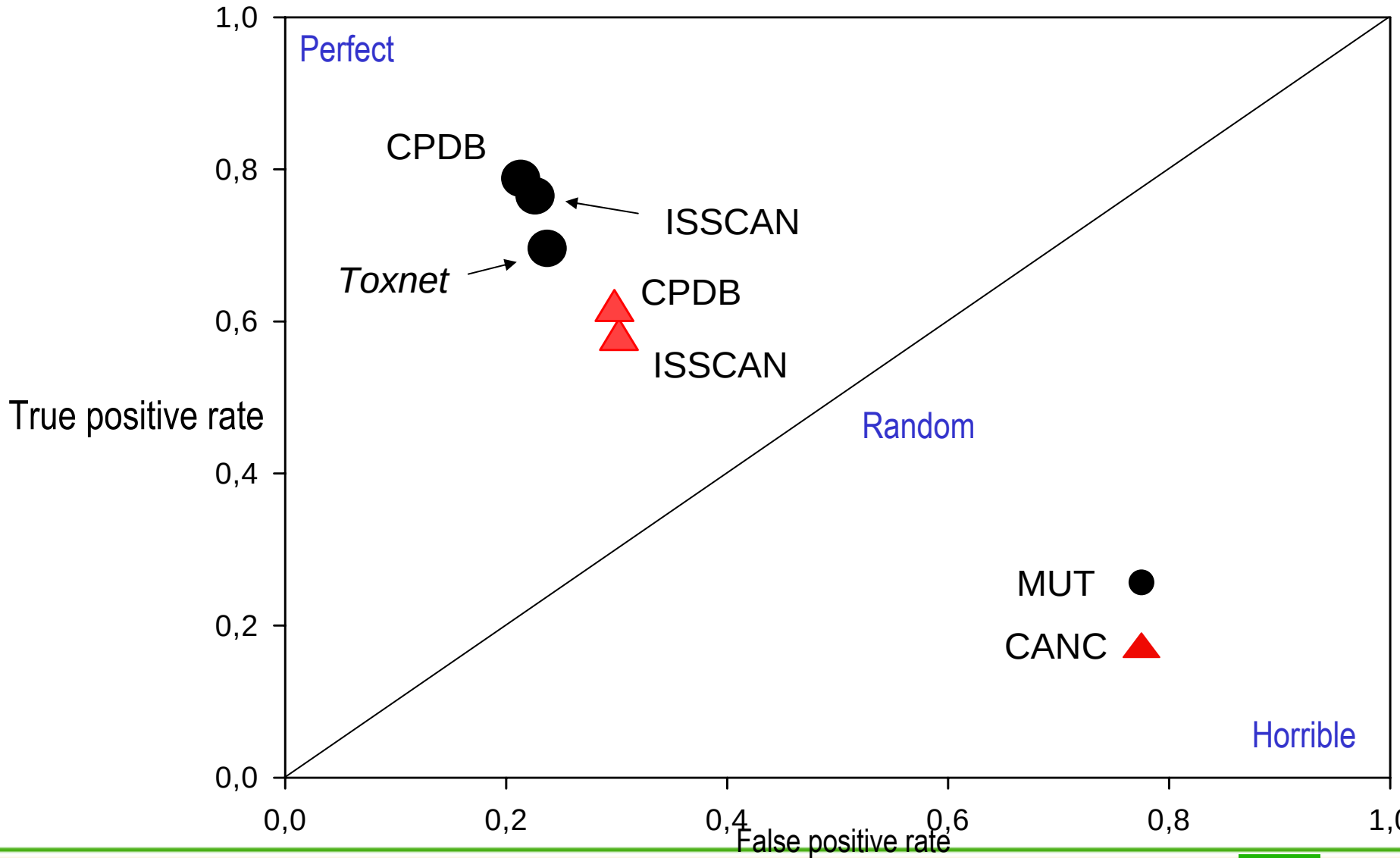
= Sensitivity

False Positive Rate = (Negatives predicted as positive) / (Real negatives)

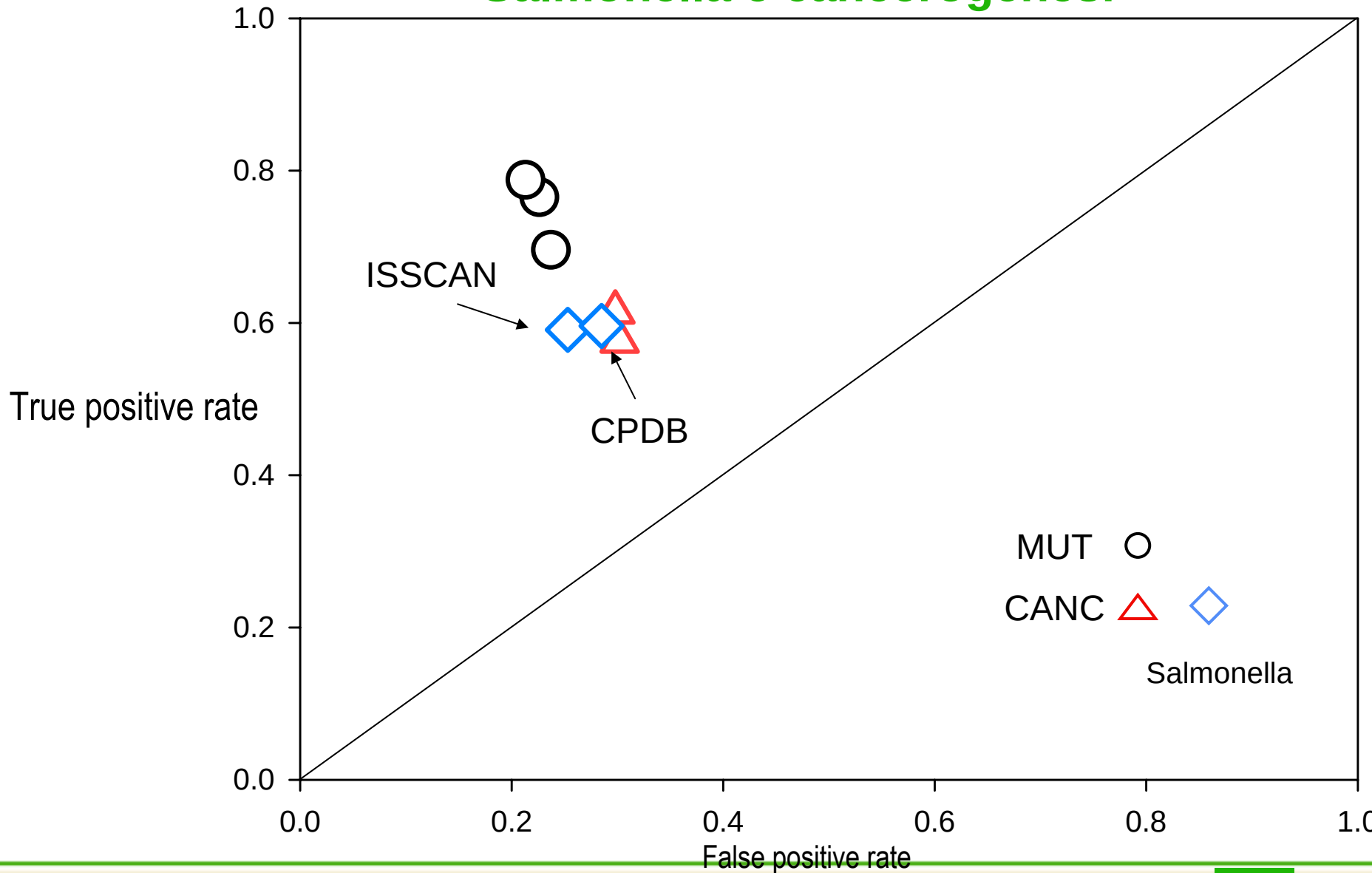
= 1 - Specificity



SA di Ashby, e mut / canc



Salmonella e cancerogenesi



Quale uso per le Allerte Strutturali ?

Una storia eccellente: priorita' nella sperimentazione NTP

400 sostanze provate da NCI / NTP:

- 2/3 scelte come sospetti cancerogeni (n=267)

68% cancerogeni (n=187)

- 1/3 scelte per criteri di quantita' / esposizione (n=133)

20% cancerogene (n=26), 6.8% positive in due specie (n=9)

Fung et al., 1995

Quale uso per le Allerte Strutturali ?

Strumento per la **caratterizzazione a grana grossa** delle sostanze

- Descrizione di gruppi di sostanze
- Caratterizzazione preliminare del rischio
- Formazione di categorie (per regolamentazione, per studi QSAR)
- Priorita’ (arricchimento del campione)

Limiti delle Allerte Strutturali

- Solo sostanze con sottostrutture potenzialmente reattive
- Niente predizione di negativi (solo per esclusione)
- Scarsa discriminazione all'interno di una classe chimica

Una generalizzazione piu' raffinata:

QSAR per classi congeneriche

- Uso di pochi parametri chimico-fisici
- Parametri scalati finemente per descrivere differenze sottili
- Predizioni sia per positivi e negativi

QSARs of Aromatic amines: mutagenic potency

Mutagenic potency in *Salmonella typhimurium* TA98 (+ S9)

Hydrophobic Electronic Steric

$$\log TA98 = 1.08\ \log P + 1.28\ HOMO - 0.73\ LUMO + 1.46\ I_L + 7.20$$

n=88 r=0.898 s=0.860

Mutagenic potency in *Salmonella typhimurium* TA100 (+ S9)

$$\log TA100 = 0.92\ \log P + 1.17\ HOMO - 1.18\ LUMO + 7.35$$

n = 67, r = 0.877, s = 0.708

Debnath et al., 1992

QSARs of Aromatic amines: mutagenic activity

Mutagenic **activity** in *Salmonella typhimurium* TA100 (+ S9)

Electronic ↓ Steric ↓

$$ActTA100 = 0.67\ HOMO - 0.75\ LUMO - 0.39\ MR_2 - 0.38\ MR_3 - 0.44\ MR_6 - 0.62\ Idist$$

n = 111 (- =47; + = 64) Correct Classification = 87. %

Mutagenic **activity** in *Salmonella typhimurium* TA98 (+ S9)

$$ActTA98 = 0.34\ HOMO - 0.86\ LUMO + 0.28\ MR_5 - 0.48\ MR_6 - 0.67\ Idist$$

n = 111 (- =25; + = 86) Correct Classification = 89. %

Benigni et al., 2007

Progetto ISS – ECB

Selezione di QSAR di buona qualita' per congeneri:

- Interpretabili scientificamente (meccanismi)
- Buona statistica interna
- Provata la predittivita' esterna

Controllato il dominio di applicabilita' (*gruppi funzionali, intervalli dei parametri, similarita' chimica*)

Regression-based QSARs for Potency (positives) : fit and predictivity

	--------training set----------				*-----test set-----*	
QSAR	**rtra**	**q^2**	**q^2_10**	**lever**	**rte**	**accte**
Amm TA98	.90	.78	.71	.06	.41	.36
Amm TA100	.88	.74	.66	.06	.68	.57
Amm mouse	.91	.58	.0	.25	.56	.58
Amm rat	.93	.81	.79	.15	.48	.71
Nitro TA98	.90	.89	.80	.04	-.23	.43
Nitro TA100	.88	.77	.73	.05	.36	.32

Amm: aromatic ammines; **Nitro**: nitroarenes

Training set:

rtra: corr.coeff.; **q^2**: r^2 cross-val (LOO); **q^2_10**: q^2 L-10-O; **lever**: mean leverage

Test set:

rte: corr.coeff.; **accte**: accuracy (within 1 log activity unit)

Discriminant QSARs for Activity (+/-): fit and predictivity

	--------*training set*----------			----*test set*-----
QSAR	sqcc	acctra	acc10	accte
Amm rodent	0.38	0.88	0.75	0.67
Amm rodent	0.50	0.94	0.78	0.70
Amm TA98	0.46	0.89	0.88	0.69
Amm TA100	0.52	0.87	0.87	0.81
Ald TA100	0.61	1.0	0.85	1.0

Amm: aromatic ammines; Ald: α-β unsaturated aldehydes

Training set: Sqcc: Squared Canonical Corr.; acctra: Accuracy;
acc10: Accuracy L-10%-O;

Test set: Accte: Accuracy

QSAR per congeneri: sommario

Scientificamente accettabili, buona statistica interna, ma diversi per predittivita' esterna

- QSAR per la potenza tossica: 30 – 70 % predittivita' esterna
- QSAR per l'attivita' tossica (si/no): 70 -100 % predittivita' esterna

Stima di intervalli piu' affidabile della stima di punti

Quale uso per gli QSAR per congenerici ?

- **Predittivita' esterna dello stesso ordine di grandezza della variabilita' sperimentale dei test**

Riproducibilita' sperimentale del test di Ames: 80 – 85 %

Predittivita' di QSAR per attivita': 70 – 100 %

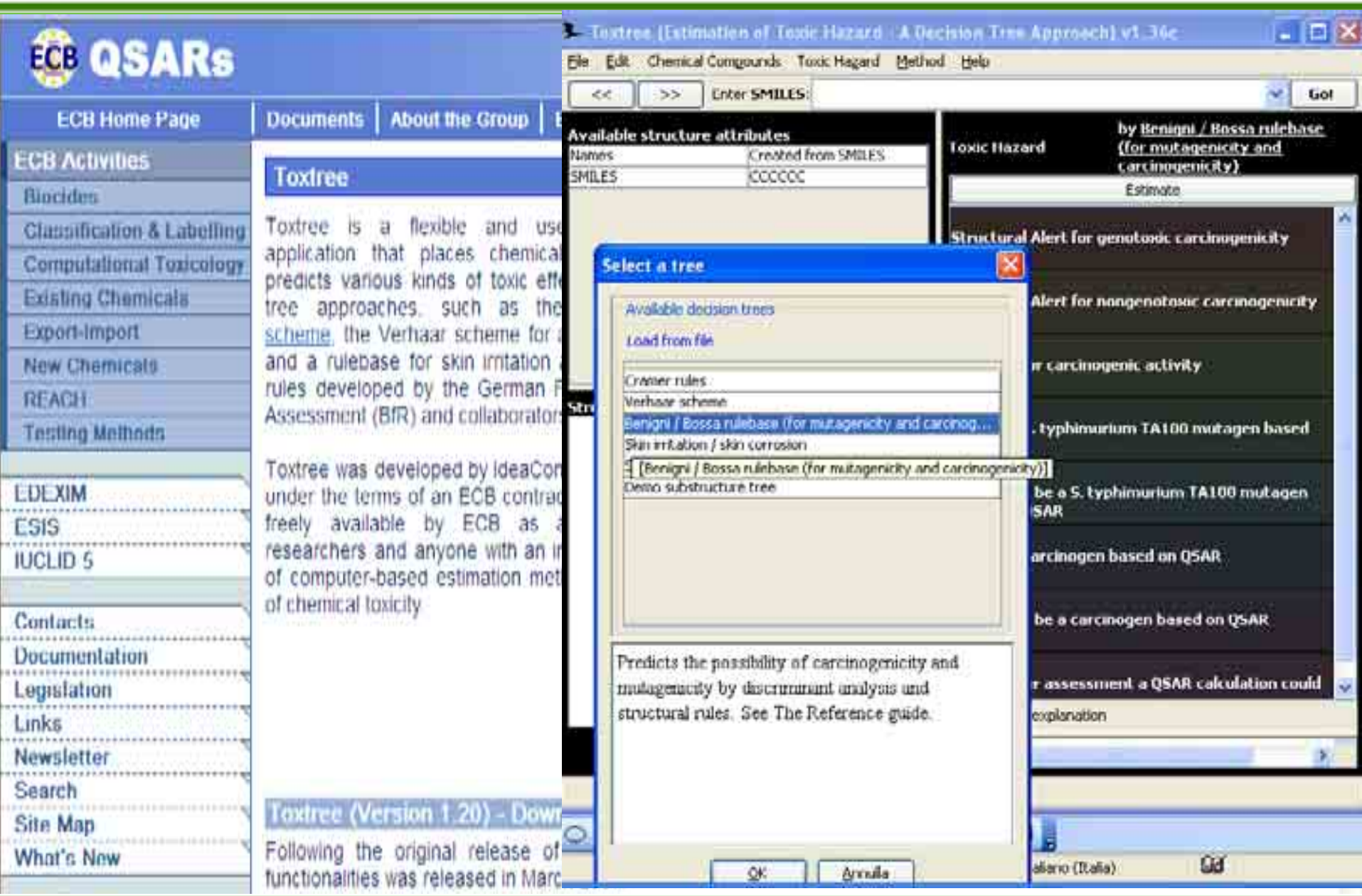
Usare le conoscenze dallo studio ISS – ECB

Toxtree

Strumento informatico sviluppato da ECB, attraverso IdeaConsult Ltd. e ISS

Stima diverse tossicita' applicando regole strutturali

Disponibile liberamente da ECB http://ecb.jrc.it/QSAR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Computational Toxicology
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EDEXIM
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What's New
Toxtree
Toxtree is a flexible and use
application that places chemical
predicts various kinds of toxic effe
tree approaches, such as the
scheme, the Verhaar scheme for
and a rulebase for skin irritation
rules developed by the German F
Assessment (BfR) and collaborator
Toxtree was developed by IdeaCon
under the terms of an ECB contrac
freely available by ECB as
researchers and anyone with an i
of computer-based estimation met
of chemical toxicity
Toxtree (Version 1.20) - Down
Following the original release of
functionalities was released in Marc
Toxtree [Estimation of Toxic Hazard - A Decision Tree Approach] v1.36c
File Edit Chemical Compounds Toxic Hazard Method Help
<< >> Enter SMILES: Go!
Available structure attributes
Names Created from SMILES
SMILES CCCCCC
Toxic Hazard
by Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
Estimate
Structural Alert for genotoxic carcinogenicity
Alert for nongenotoxic carcinogenicity
r carcinogenic activity
. typhimurium TA100 mutagen based
be a S. typhimurium TA100 mutagen
SAR
arcinogen based on QSAR
be a carcinogen based on QSAR
r assessment a QSAR calculation could
explanation
Select a tree
Available decision trees
Load from file
Cramer rules
Verhaar scheme
Benigni / Bossa rulebase (for mutagenicity and carcinog...
Skin irritation / skin corrosion
[Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)]
Demo substructure tree
Predicts the possibility of carcinogenicity and mutagenicity by discriminant analysis and structural rules. See The Reference guide.
OK
Annulla

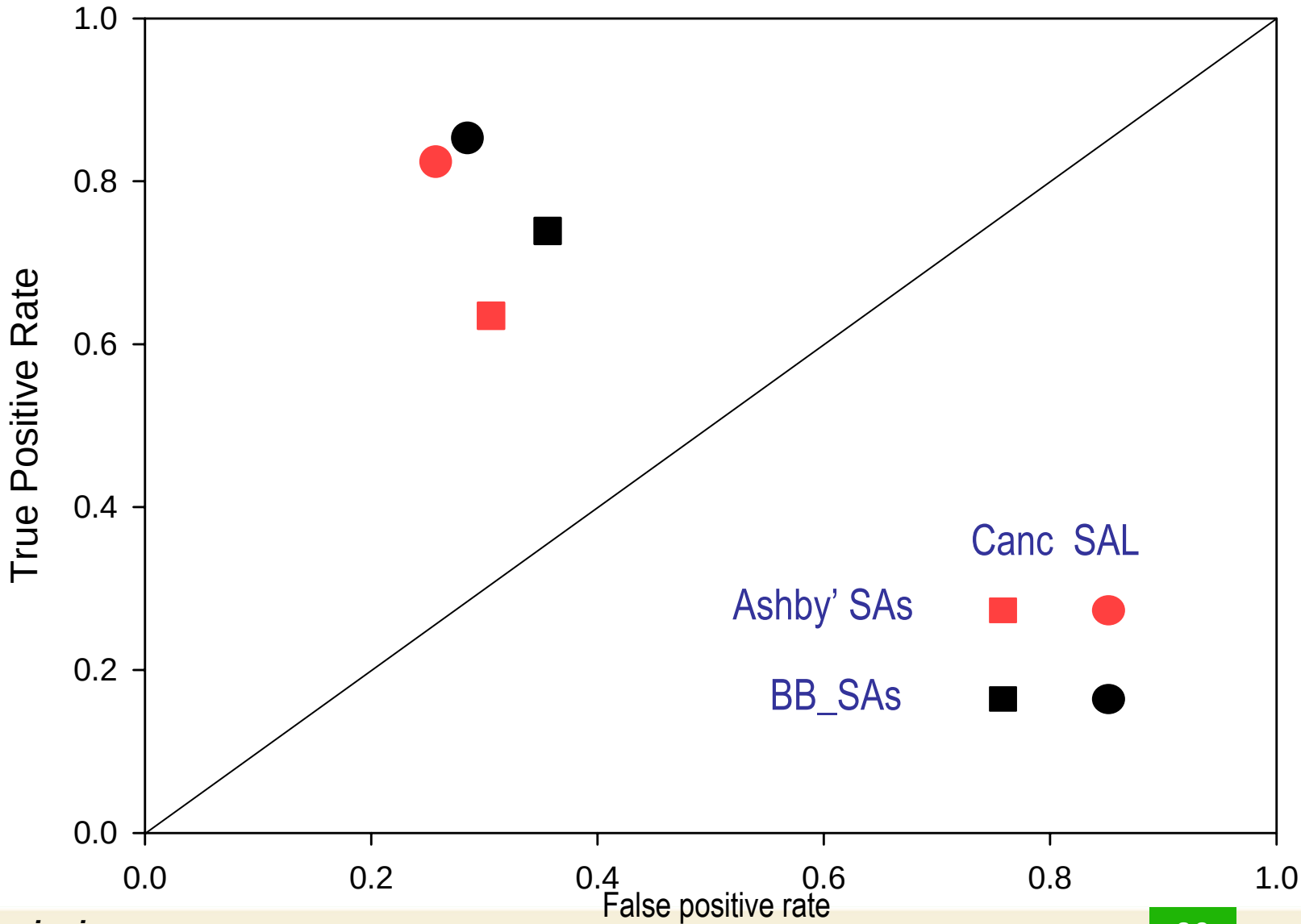
Toxtree 1.5 Base di regole per mutageni / cancerogeni

Metodo basato su regole strutturali, con:

- Nuova compilazione (ISS) di Allerte Strutturali
- Tre QSAR per classi congeneriche (ammine aromatiche, aldeidi)

Manuale in: ***http://ecb.jrc.it/documents/QSAR/EUR_23241_EN.pdf***

SA: Ashby e ISS



Toxtree (Estimation of Toxic Hazard - A Decision Tree Approach) v1.40

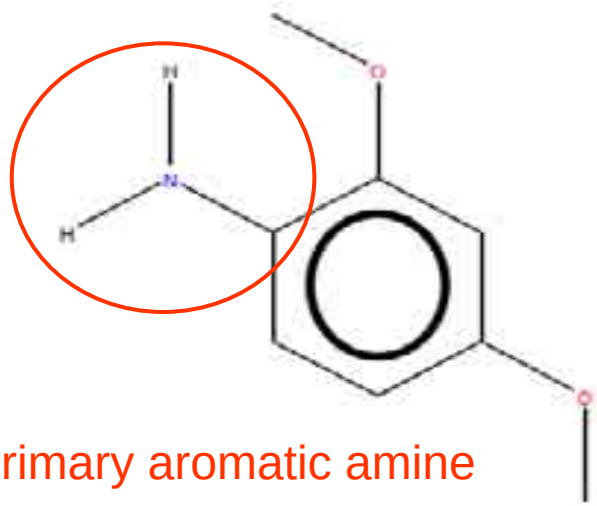
File Edit Chemical Compounds Toxic Hazard Method Help

<< >> Enter SMILES: CCC Go!

Available structure attributes

BSSTM1	1,0000
Benigni / Bossa rulebase (For mutagenicity a...	,*sA1N,*sA2N,*sA3N,*sA4N,*sA5N,*sA6N,*sA7N,...
EHOMO	-8,1427
ELUMO	0,3737
For a better assessment a QSAR calculation ...	NO
I(An)	true
I(BBr)	false
I(NO2)	false
Idist	0
LSTM1	2,0600
MR2	0,7900

Structure diagram



Primary aromatic amine

First Prev 1 / 1 Next Last

Toxic Hazard — by Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)

Estimate

Structural Alert for genotoxic carcinogenicity

Structural Alert for nongenotoxic carcinogenicity

No alerts for carcinogenic activity

Potential S. typhimurium TA100 mutagen based on QSAR

Unlikely to be a S. typhimurium TA100 mutagen based on QSAR

Potential carcinogen based on QSAR

Unlikely to be a carcinogen based on QSAR

For a better assessment a QSAR calculation could be applied.

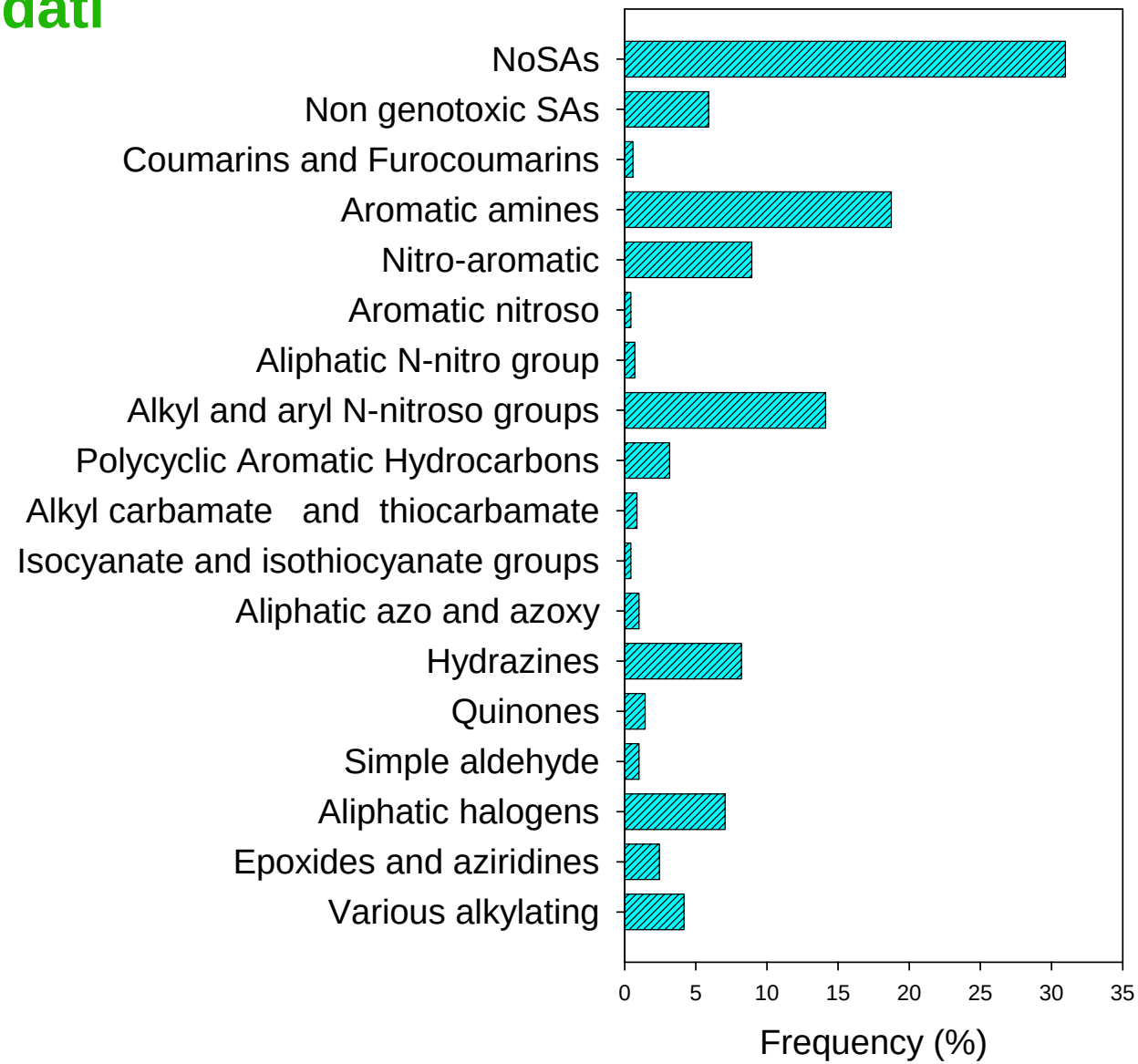
Verbose explanation

Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)

```
QSA1.Acyl halides          No
QSA2.Alkyl (C<5) or benzyl ester of sulphonic or phosphonic a
QSA3.N-methylol derivatives      No
QSA4.Monohaloalkene        No
QSA5.S or N mustard        No
QSA6.Propiolactones and propiosultones  No
```

Completed.

Profilo di una banca dati di cancerogeni via Toxtree

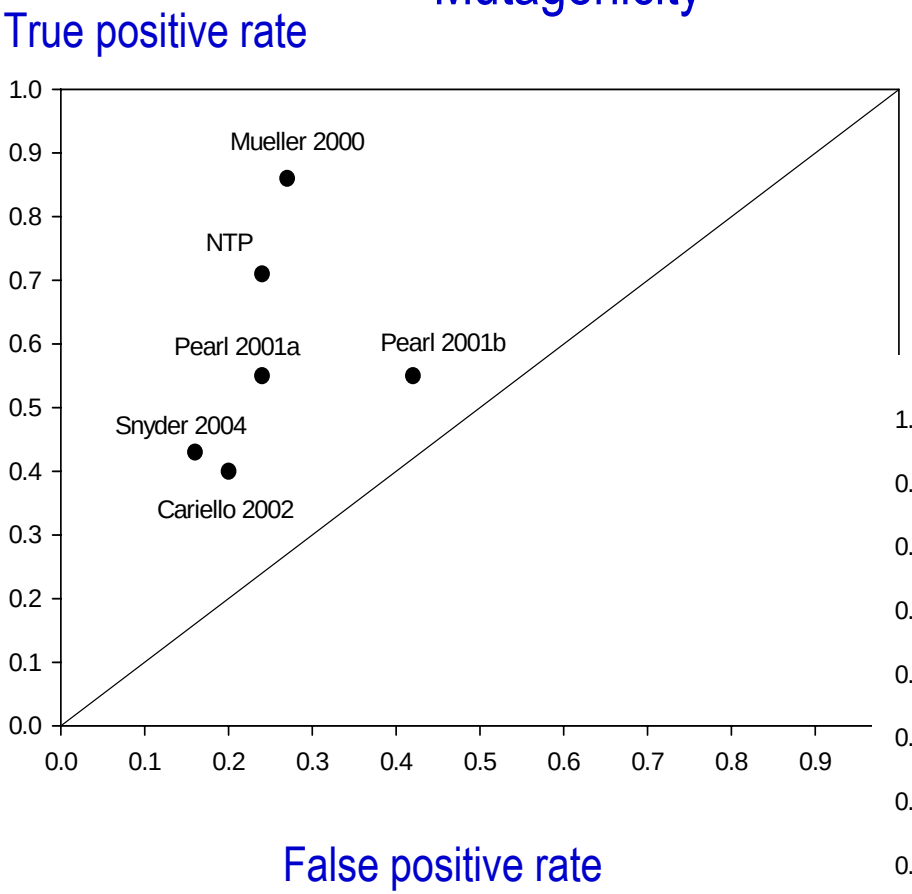


Un’altra classe di modelli: QSAR per non congenerici

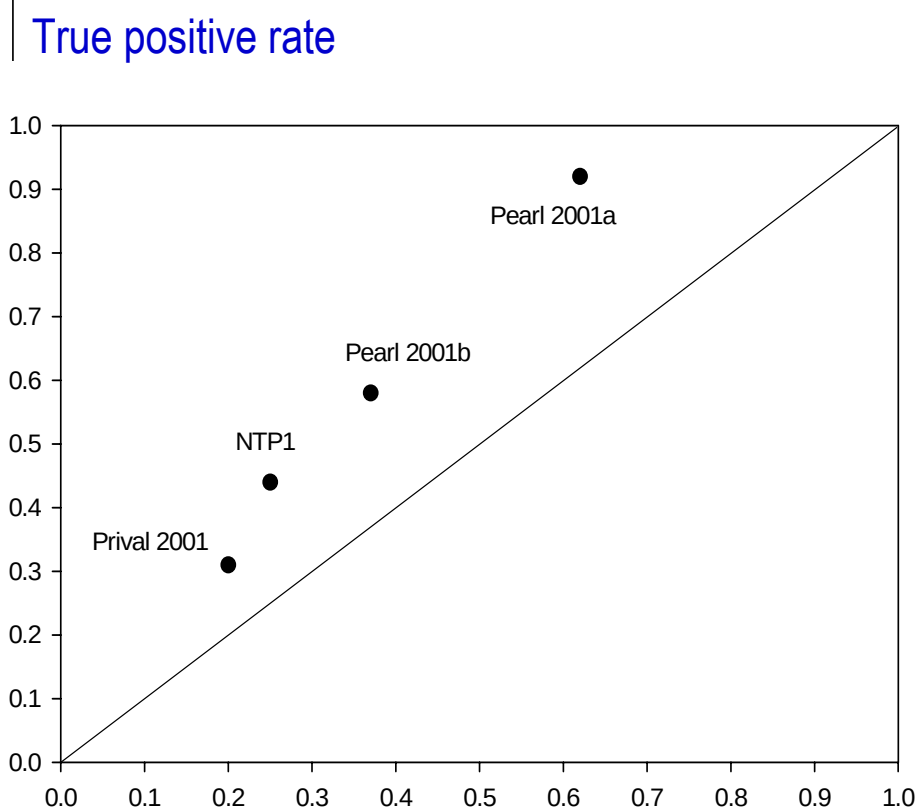
- Modificazione di QSAR per congenerici
- Modellizzazione simultanea di tutte (??) le classi chimiche
- Sistemi commerciali
- Spesso descrittori non meccanicistici
- Spesso impossibile interpretazione
- Validati per lo piu’ internamente

TOPKAT: Validazione esterna

Mutagenicity

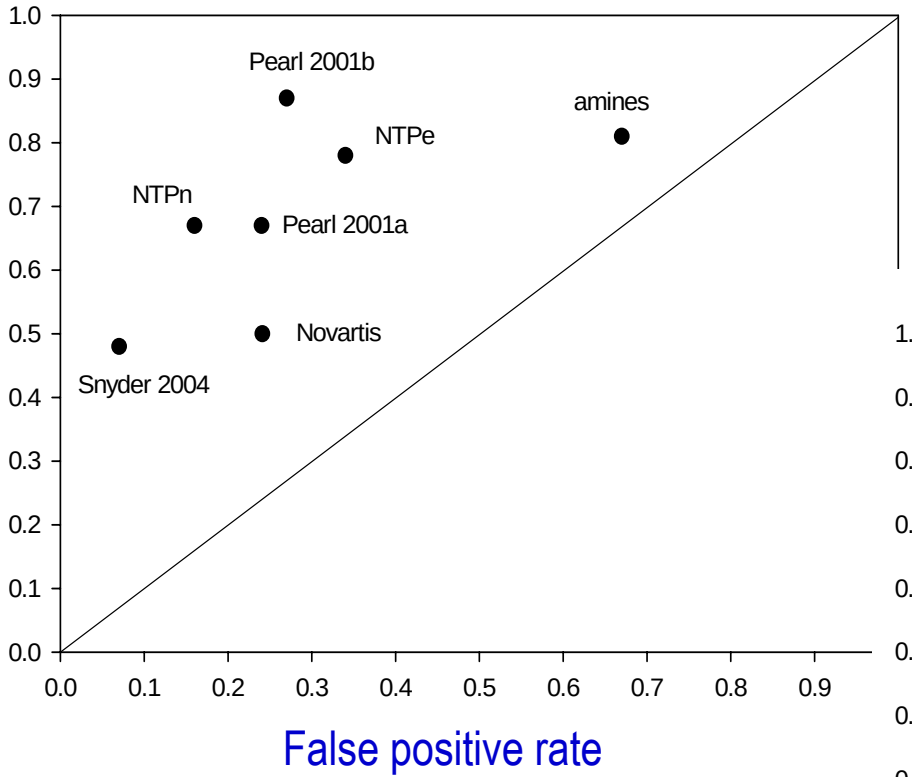


Carcinogenicity

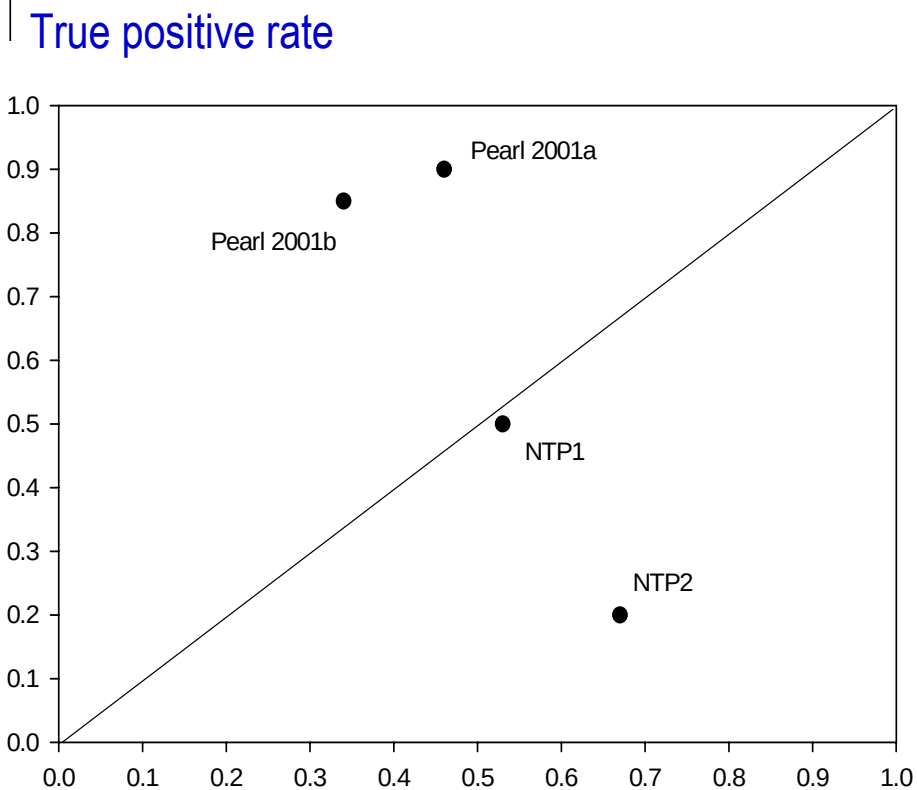


MULTICASE: Validazione esterna

Mutagenicity

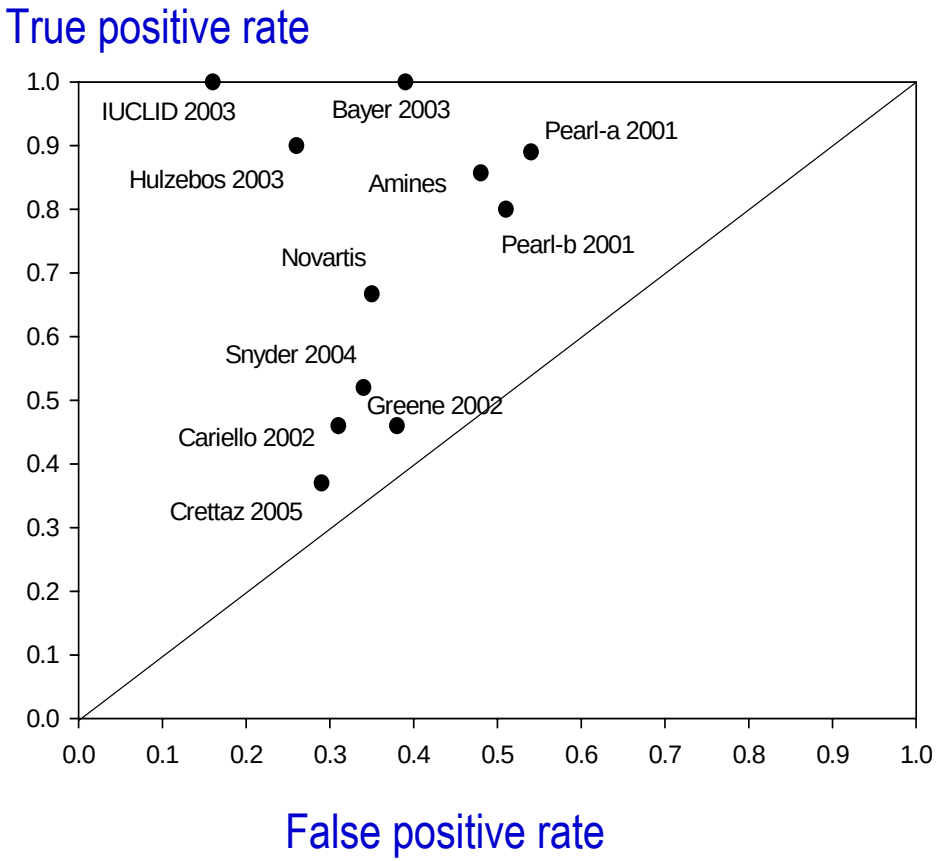


Carcinogenicity

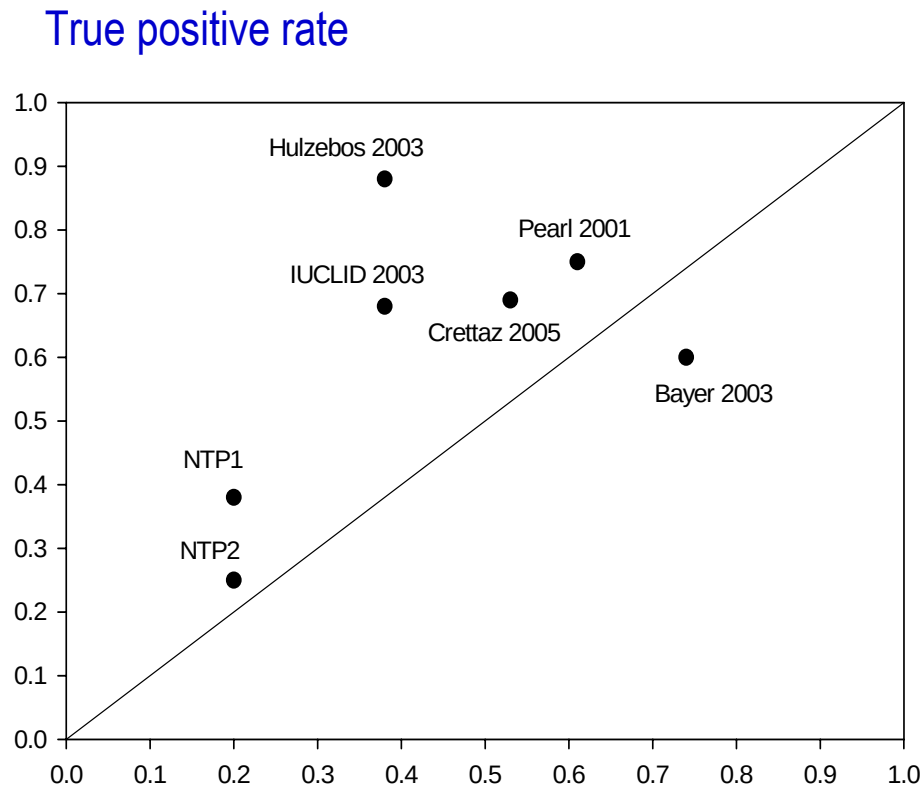


DEREK: Validazione esterna

Mutagenicity



Carcinogenicity



(Q)SAR non sostituiscono la realta' ma forniscono un aiuto potente

"...As the drug discovery process is of a very complex nature, effective drug design requires an entire spectrum of techniques in which QSAR methods still play an important role. …

The real power of drug design methods is to ***extract and synthesize information from data to obtain hypotheses that can be put to experimental test***. No dramatic overnight discoveries of wonder drug will result, but an ***increase in the chance of success due to indications of promising directions*** is a realistic expectation…."

Franke and Gruska, 2003

Bibliografia essenziale

Hansch,C., Hoekman,D., Leo,A., Weininger,D., and Selassie,C.D. (2002): Chem-bioinformatics: comparative QSAR at the interface between chemistry and biology. *Chem.Revs.*, 102:783-812.

Benigni,R. and Bossa,C. (2008): Predictivity and reliability of QSAR models: the case of mutagens and carcinogens. *Toxicol.Mechanisms Meth.*, 18:137-147.

Worth, A. P., Bassan, A., Gallegos, A., Netzeva, T. I., Patlewicz, G., Pavan, M., Tsakovska, I., and Vracko, M. The characterisation of (Quantitative) Structure-Activity Relationships: Preliminary guidance. JRC report EUR 21866 EN. 2005. Ispra, European Chemicals Bureau, Joint Research Centre, European Commission.

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Istituto Superiore di Sanità

(Q)SAR: strumenti

Romualdo Benigni

ISS

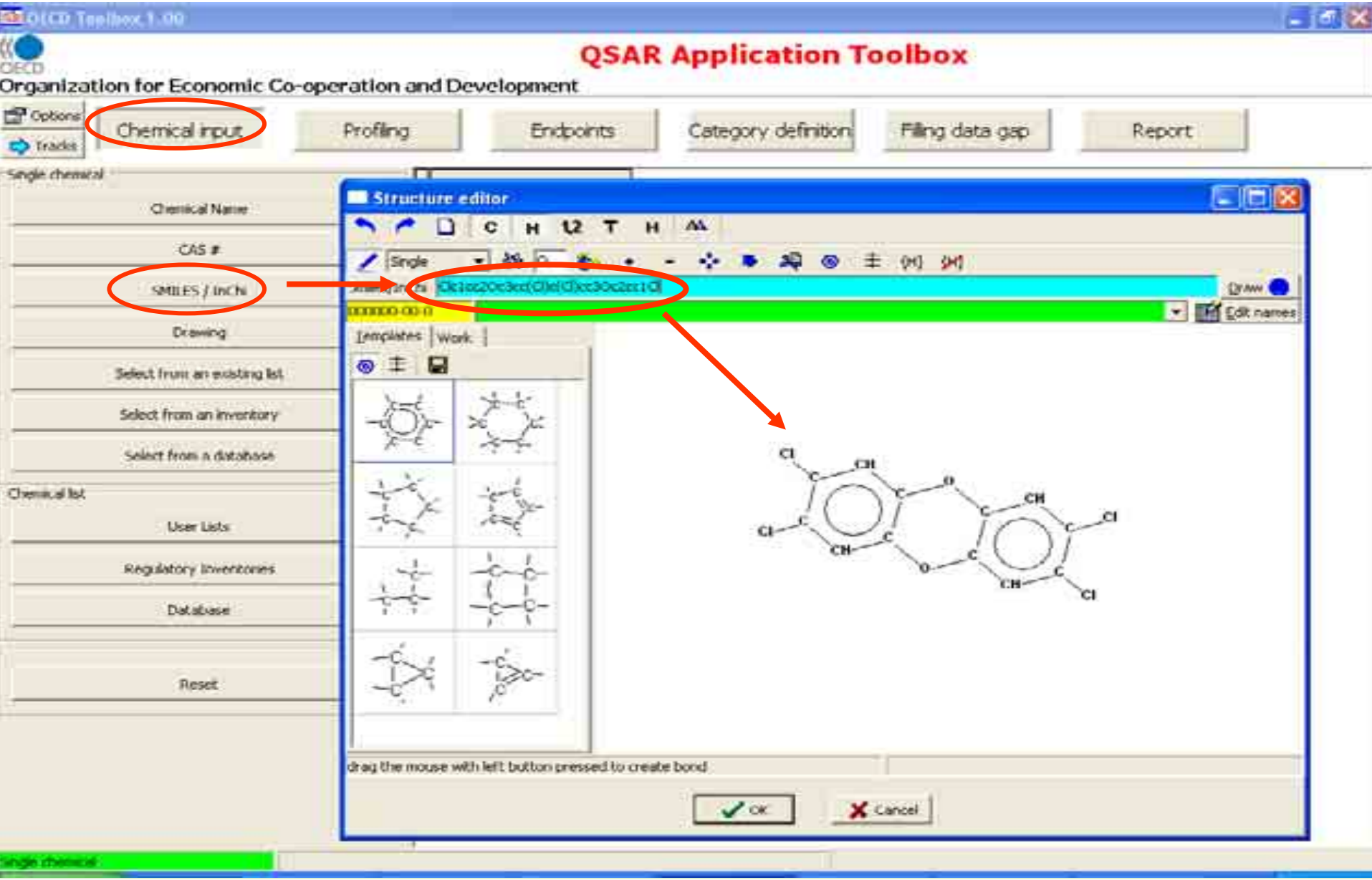
OECD Toolbox

Programma informatico sviluppato per regolatori, industria chimica ed altri soggetti interessati per:
Riempire i vuoti nell'informazione (eco)tossicologica per le sostanze chimiche

• Informazione e strumenti da varie fonti, raccolti in un flusso logico

• Read-across / analogue approach, categorie chimiche, (Q)SAR

Disponibile pubblicamente: www.oecd.org/env/existingchemicals/qsar


QSAR Application Toolbox
Organization for Economic Co-operation and Development
Chemical input
Profiling
Endpoints
Category definition
Filling data gap
Report
Chemical Name
CAS #
SMILES / InChi
Drawing
Select from an existing list
Select from an inventory
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Regulatory Inventories
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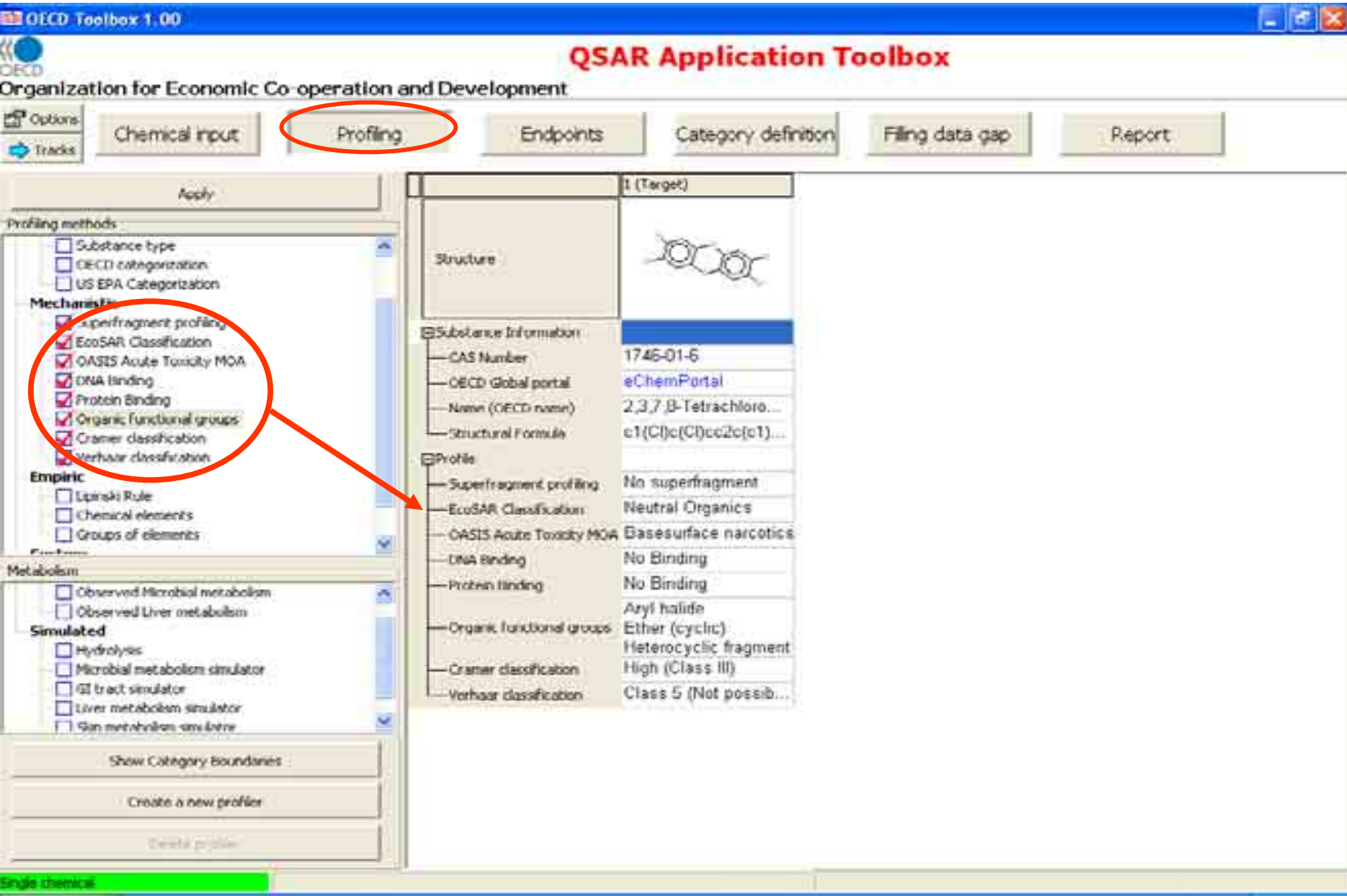
Reset
Structure editor
drag the mouse with left button pressed to create bond
OK
Cancel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QSAR Application Toolbox
Organization for Economic Co-operation and Development
Options
Tracks
Chemical input
Profiling
Endpoints
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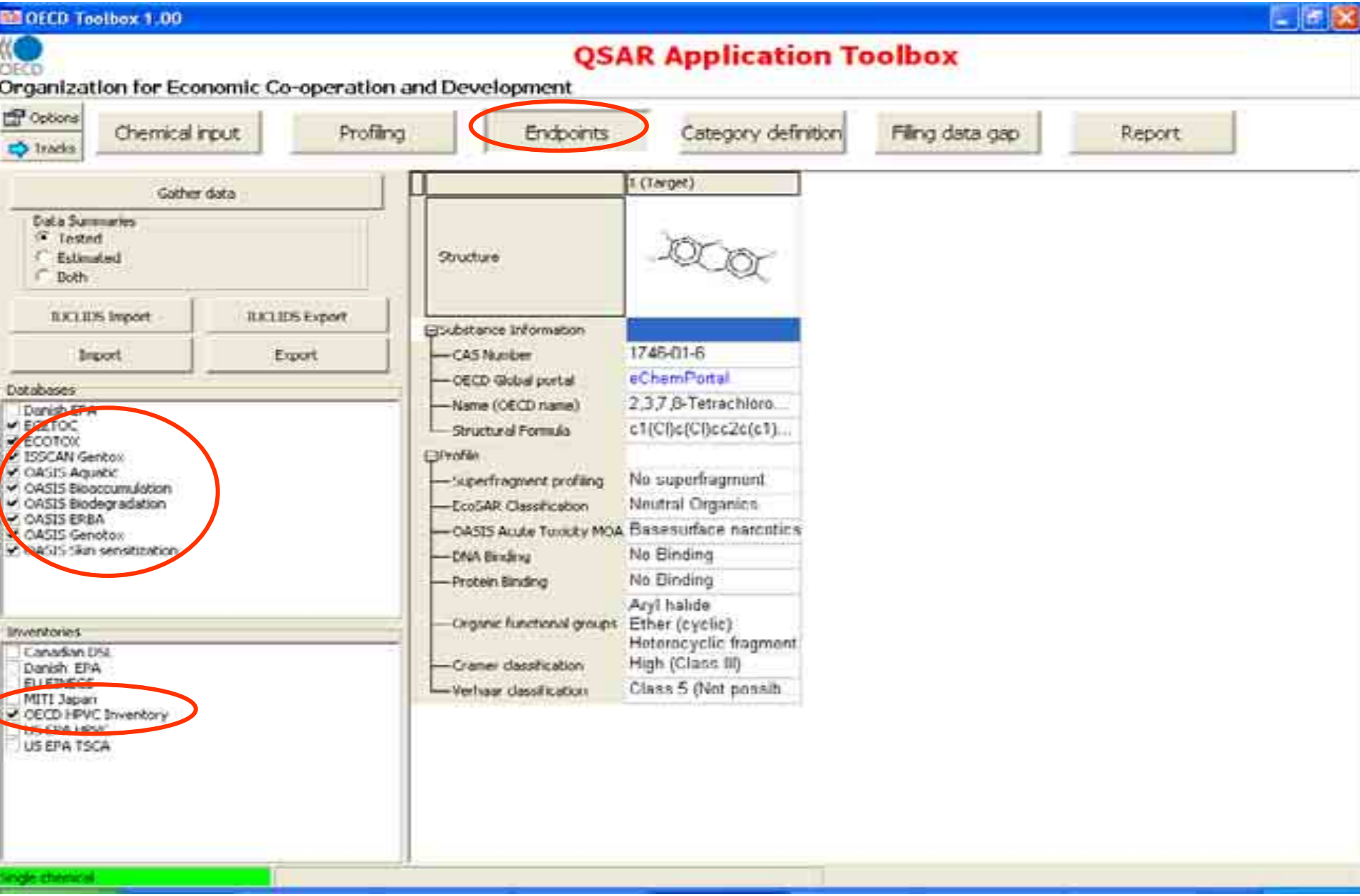
Report
Apply
Profiling methods
Substance type
OECD categorization
US EPA Categorization
Mechanistic
Superfragment profiling
EcoSAR Classification
OASIS Acute Toxicity MOA
DNA Binding
Protein Binding
Organic functional groups
Cramer classification
Verhaar classification
Empiric
Lipinski Rule
Chemical elements
Groups of elements
Metabolism
Observed Microbial metabolism
Observed Liver metabolism
Simulated
Hydrolysis
Microbial metabolism simulator
GI tract simulator
Liver metabolism simulator
Skin metabolism simulator
Show Category Boundaries
Create a new profiler
Delete profiler
t (Target)
Structure
Substance Information
CAS Number 1746-01-6
OECD Global portal eChemPortal
Name (OECD name) 2,3,7,8-Tetrachloro...
Structural Formula c1(Cl)c(Cl)cc2c(c1)...
Profile
Superfragment profiling No superfragment
EcoSAR Classification Neutral Organics
OASIS Acute Toxicity MOA Basesurface narcotics
DNA Binding No Binding
Protein Binding No Binding
Organic functional groups Aryl halide
Ether (cyclic)
Heterocyclic fragment
Cramer classification High (Class III)
Verhaar classification Class 5 (Not possib...
Single chemical


OECD Toolbox 1.00
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Options
Tasks
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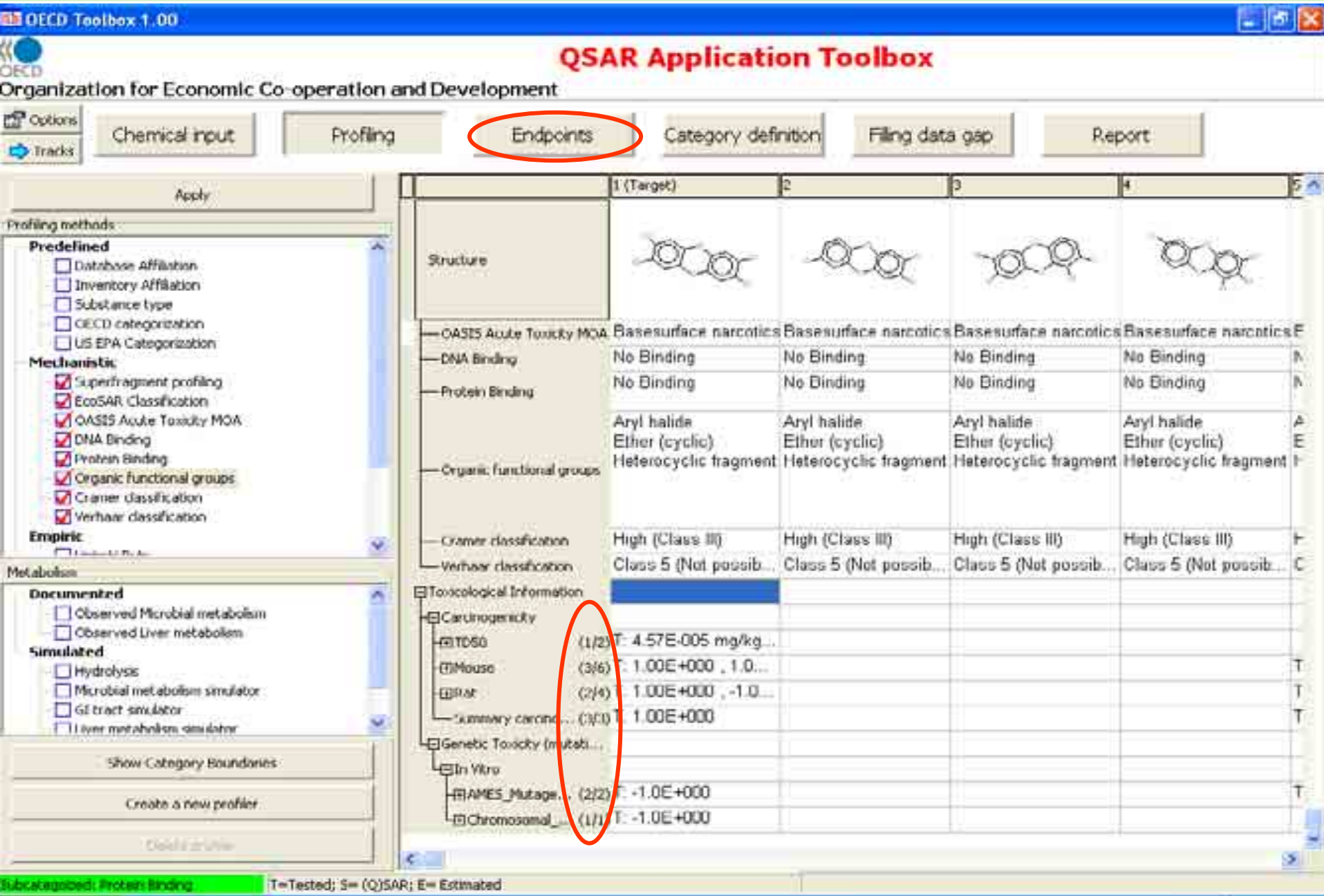
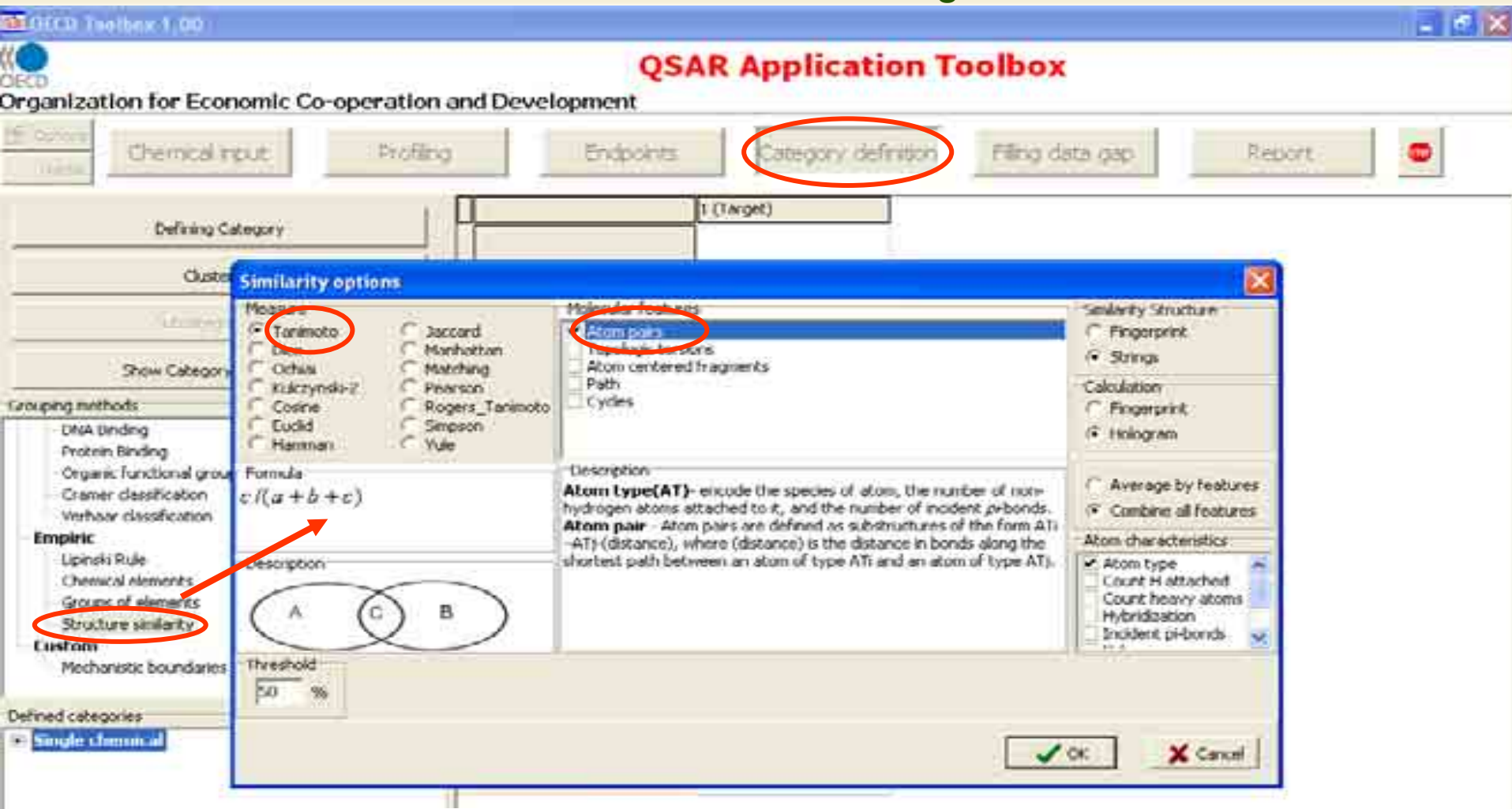
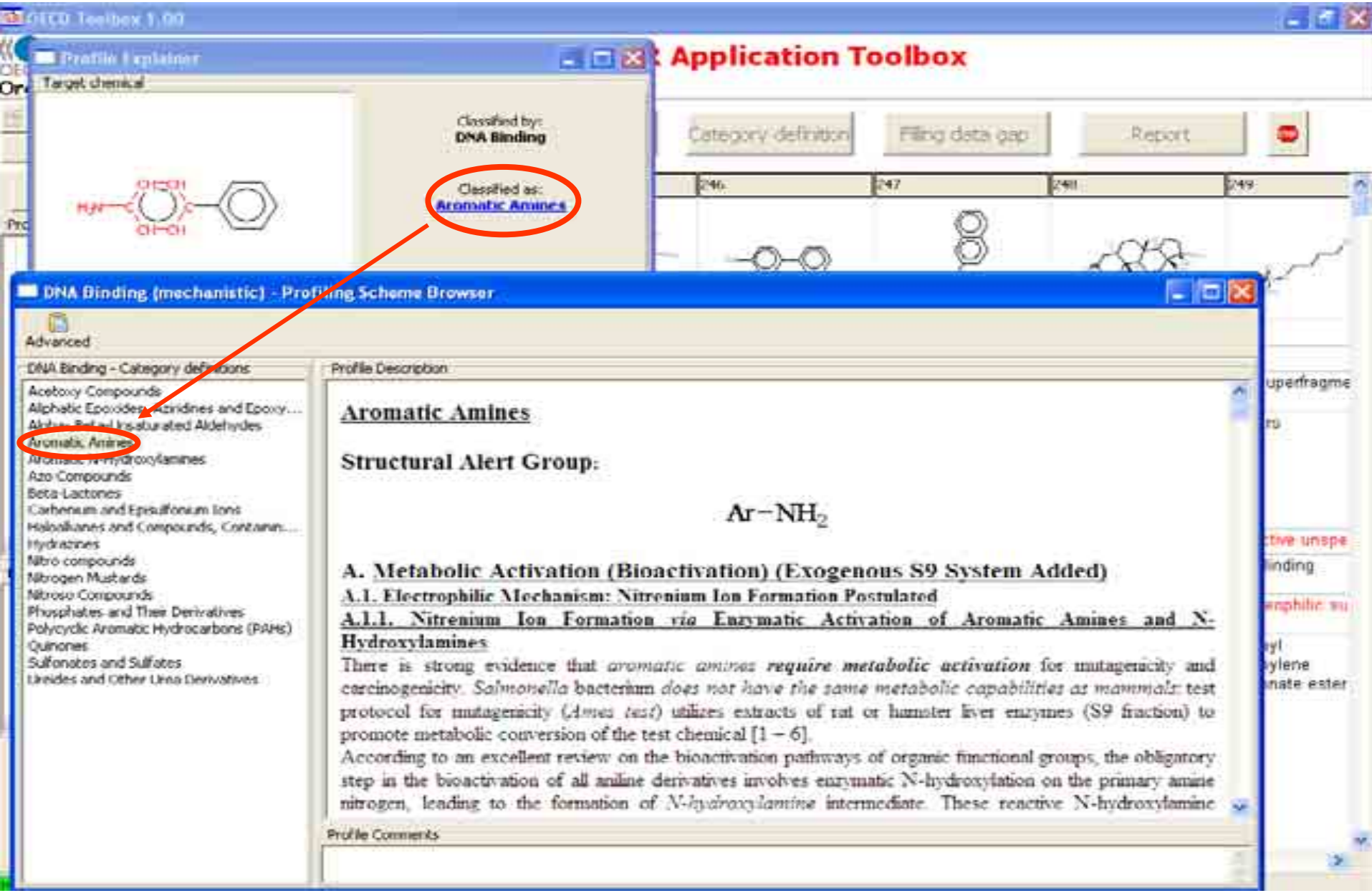
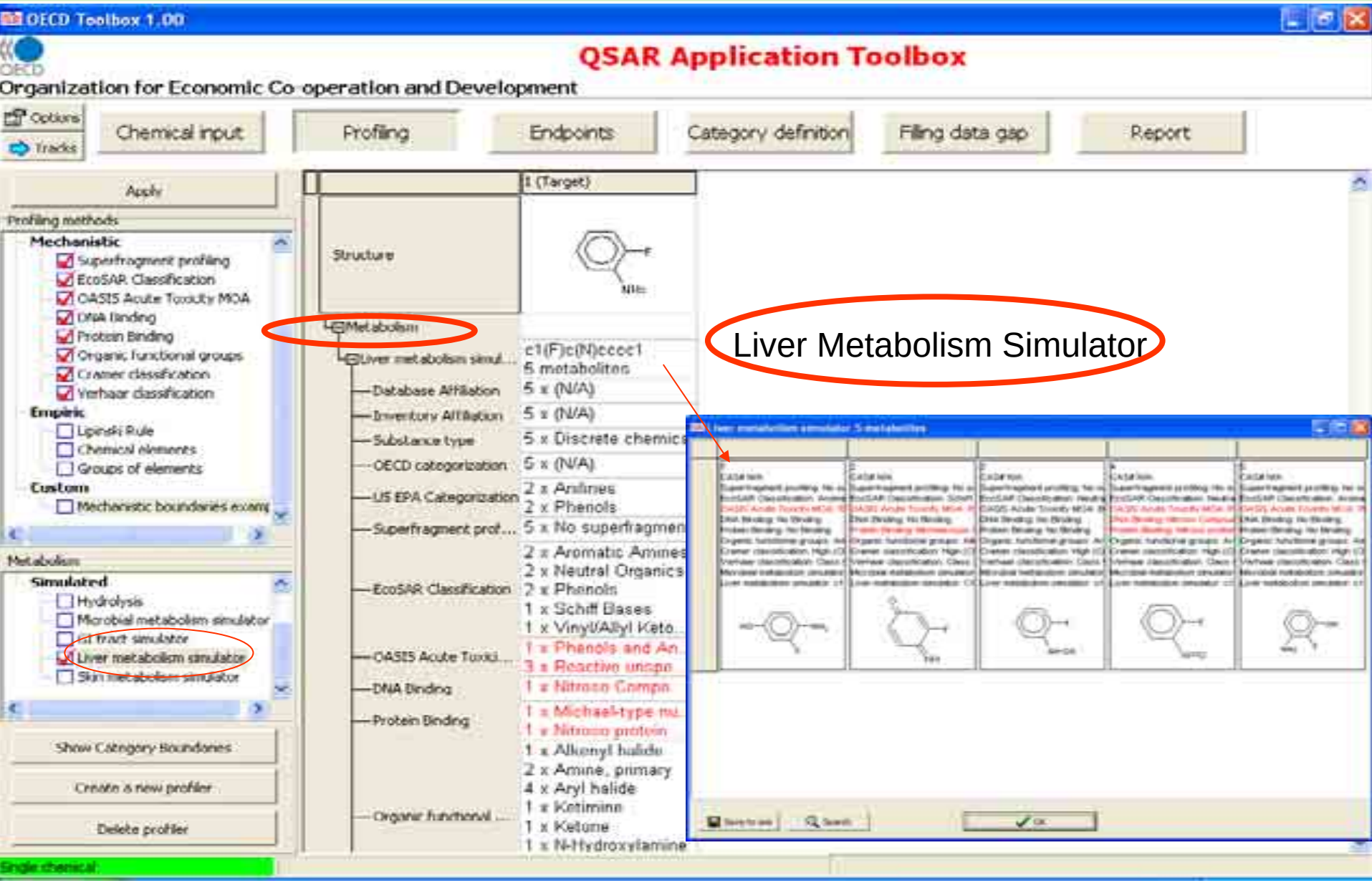
Category definition
Filing data gap
Report
Gather data
Data Summaries
Tested
Estimated
Both
IUCLID5 Import
IUCLID5 Export
Import
Export
Databases
Danish EPA
EPIWIN
ECOTOX
ISSCAN Genotox
OASIS Aquatic
OASIS Bioaccumulation
OASIS Biodegradation
OASIS ERBA
OASIS Genotox
OASIS Skin sensitization
Inventories
Canadian DSL
Danish EPA
EU ESIS
MITI Japan
OECD HPVC Inventory
US EPA HPVC
US EPA TSCA
1 (Target)
Structure
Substance Information
CAS Number
1746-01-6
OECD Global portal
eChemPortal
Name (OECD name)
2,3,7,8-Tetrachloro...
Structural Formula
c1(Cl)c(Cl)cc2c(c1)...
Profiles
Superfragment profiling
No superfragment
EcoSAR Classification
Neutral Organics
OASIS Acute Toxicity MOA
Basesurface narcotics
DNA Binding
No Binding
Protein Binding
No Binding
Organic functional groups
Aryl halide
Ether (cyclic)
Heterocyclic fragment
Cramer classification
High (Class III)
Verhaar classification
Class 5 (Not possib
Single chemical


OECD Toolbox 1.00
QSAR Application Toolbox
Organization for Economic Co-operation and Development
Options
Tracks
Chemical input
Profiling
Endpoints
Category definition
Filing data gap
Report
Apply
Profiling methods
Predefined
Database Affiliation
Inventory Affiliation
Substance type
OECD categorization
US EPA Categorization
Mechanistic
Superfragment profiling
EcoSAR Classification
OASIS Acute Toxicity MOA
DNA Binding
Protein Binding
Organic functional groups
Cramer classification
Verhaar classification
Empiric
Metabolism
Documented
Observed Microbial metabolism
Observed Liver metabolism
Simulated
Hydrolysis
Microbial metabolism simulator
GI tract simulator
Liver metabolism simulator
Show Category Boundaries
Create a new profiler
1 (Target)
2
3
4
Structure
OASIS Acute Toxicity MOA
Basesurface narcotics
DNA Binding
No Binding
Protein Binding
Organic functional groups
Aryl halide
Ether (cyclic)
Heterocyclic fragment
Cramer classification
High (Class III)
Verhaar classification
Class 5 (Not possib...
Toxicological Information
Carcinogenicity
TD50
(1/2)
T: 4.57E-005 mg/kg...
Mouse
(3/6)
T: 1.00E+000 , 1.0...
Rat
(2/4)
T: 1.00E+000 , -1.0...
Summary carcino...
(3/3)
T: 1.00E+000
Genetic Toxicity (mutati...
In Vitro
AMES_Mutage...
(2/2)
T: -1.0E+000
Chromosomal_...
(1/1)
T: -1.0E+000
Subcategorized: Protein Binding
T=Tested; S= (Q)SAR; E= Estimated



We choose a Structure Similarity based on Tanimoto measure


OECD Toolbox 1.00
Application Toolbox
Profile Explainer
Target chemical
Classified by:
DNA Binding
Classified as:
Aromatic Amines
Category definition
Filing data gap
Report
DNA Binding (mechanistic) - Profiling Scheme Browser
Advanced
DNA Binding - Category definitions
Acetoxy Compounds
Aromatic Amines
Azo Compounds
Beta-Lactones
Hydrazines
Nitro compounds
Nitrogen Mustards
Nitroso Compounds
Phosphates and Their Derivatives
Polycyclic Aromatic Hydrocarbons (PAHs)
Quinones
Sulfonates and Sulfates
Profile Description
Aromatic Amines
Structural Alert Group:
Ar−NH2
A. Metabolic Activation (Bioactivation) (Exogenous S9 System Added)
A.1. Electrophilic Mechanism: Nitrenium Ion Formation Postulated
A.1.1. Nitrenium Ion Formation via Enzymatic Activation of Aromatic Amines and N-Hydroxylamines
There is strong evidence that aromatic amines require metabolic activation for mutagenicity and carcinogenicity. Salmonella bacterium does not have the same metabolic capabilities as mammals: test protocol for mutagenicity (Ames test) utilizes extracts of rat or hamster liver enzymes (S9 fraction) to promote metabolic conversion of the test chemical [1 – 6].
According to an excellent review on the bioactivation pathways of organic functional groups, the obligatory step in the bioactivation of all aniline derivatives involves enzymatic N-hydroxylation on the primary amine nitrogen, leading to the formation of N-hydroxylamine intermediate. These reactive N-hydroxylamine
Profile Comments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QSAR Application Toolbox
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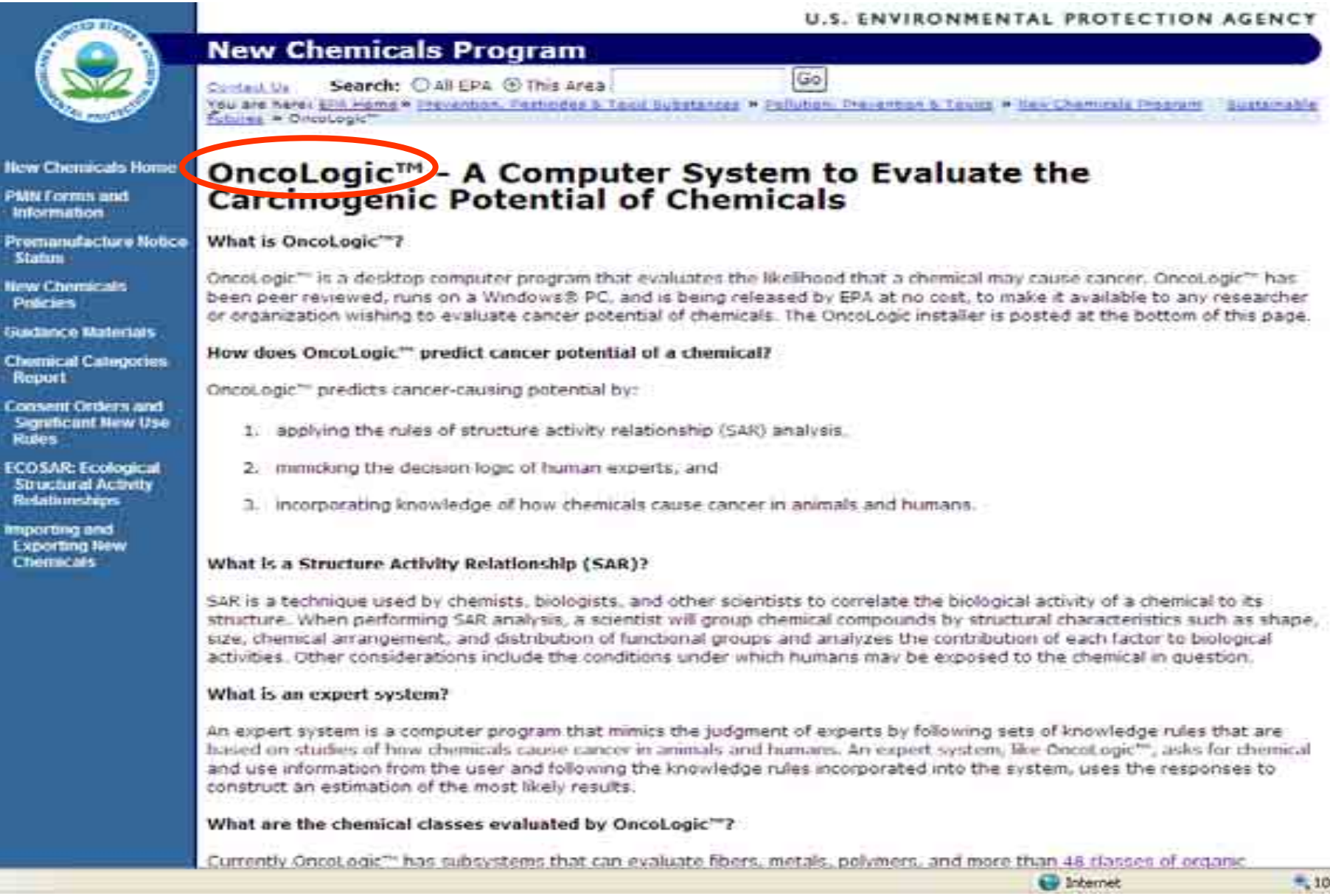
OASIS Acute Toxicity MOA
DNA Binding
Protein Binding
Organic functional groups
Cramer classification
Verhaar classification
Empiric
Lipinski Rule
Chemical elements
Groups of elements
Custom
Mechanistic boundaries examp
Metabolism
Simulated
Hydrolysis
Microbial metabolism simulator
Liver metabolism simulator
Skin metabolism simulator
Show Category Boundaries
Create a new profiler
Delete profiler
Single chemical
1 (Target)
Structure
Metabolism
Liver metabolism simul...
c1(F)c(N)cccc1
6 metabolites
Database Affiliation
5 x (N/A)
Inventory Affiliation
5 x (N/A)
Substance type
5 x Discrete chemics
OECD categorization
5 x (N/A)
US EPA Categorization
2 x Anilines
2 x Phenols
Superfragment prof...
5 x No superfragment
2 x Aromatic Amines
2 x Neutral Organics
EcoSAR Classification
2 x Phenols
1 x Schiff Bases
1 x Vinyl/Allyl Keto...
OASIS Acute Toxici...
1 x Phenols and An...
3 x Reactive unspe...
DNA Binding
1 x Nitroso Compo...
Protein Binding
1 x Michael-type ac...
1 x Nitroso protein
1 x Alkenyl halide
2 x Amine, primary
4 x Aryl halide
Organic functional ...
1 x Ketimine
1 x Ketone
1 x N-Hydroxylamine
Liver Metabolism Simulator

ONCOLOGIC

Sistema esperto dell' US EPA per **predire i cancerogeni chimici**

- Riproduce il ragionamento di esperti umani
- Basato su regole strutturali (allerte + fattori modificanti): assegna un livello di base di pericolosita', e considera come i sostituenti lo modificano

Disponibile pubblicamente:
http://www.epa.gov/oppt/newchems/tools/oncologic.htm



U.S. ENVIRONMENTAL PROTECTION AGENCY

New Chemicals Program

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You are here: EPA Home » Prevention, Pesticides & Toxic Substances » Pollution Prevention & Toxics » New Chemicals Program » Sustainable Futures » OncoLogic™

New Chemicals Home
PMN Forms and Information
Premanufacture Notice Status
New Chemicals Policies
Guidance Materials
Chemical Categories Report
Consent Orders and Significant New Use Rules
ECOSAR: Ecological Structural Activity Relationships
Importing and Exporting New Chemicals

OncoLogic™ - A Computer System to Evaluate the Carcinogenic Potential of Chemicals

What is OncoLogic™?

OncoLogic™ is a desktop computer program that evaluates the likelihood that a chemical may cause cancer. OncoLogic™ has been peer reviewed, runs on a Windows® PC, and is being released by EPA at no cost, to make it available to any researcher or organization wishing to evaluate cancer potential of chemicals. The OncoLogic installer is posted at the bottom of this page.

How does OncoLogic™ predict cancer potential of a chemical?

OncoLogic™ predicts cancer-causing potential by:

1. applying the rules of structure activity relationship (SAR) analysis,
2. mimicking the decision logic of human experts, and
3. incorporating knowledge of how chemicals cause cancer in animals and humans.

What is a Structure Activity Relationship (SAR)?

SAR is a technique used by chemists, biologists, and other scientists to correlate the biological activity of a chemical to its structure. When performing SAR analysis, a scientist will group chemical compounds by structural characteristics such as shape, size, chemical arrangement, and distribution of functional groups and analyzes the contribution of each factor to biological activities. Other considerations include the conditions under which humans may be exposed to the chemical in question.

What is an expert system?

An expert system is a computer program that mimics the judgment of experts by following sets of knowledge rules that are based on studies of how chemicals cause cancer in animals and humans. An expert system, like OncoLogic™, asks for chemical and use information from the user and following the knowledge rules incorporated into the system, uses the responses to construct an estimation of the most likely results.

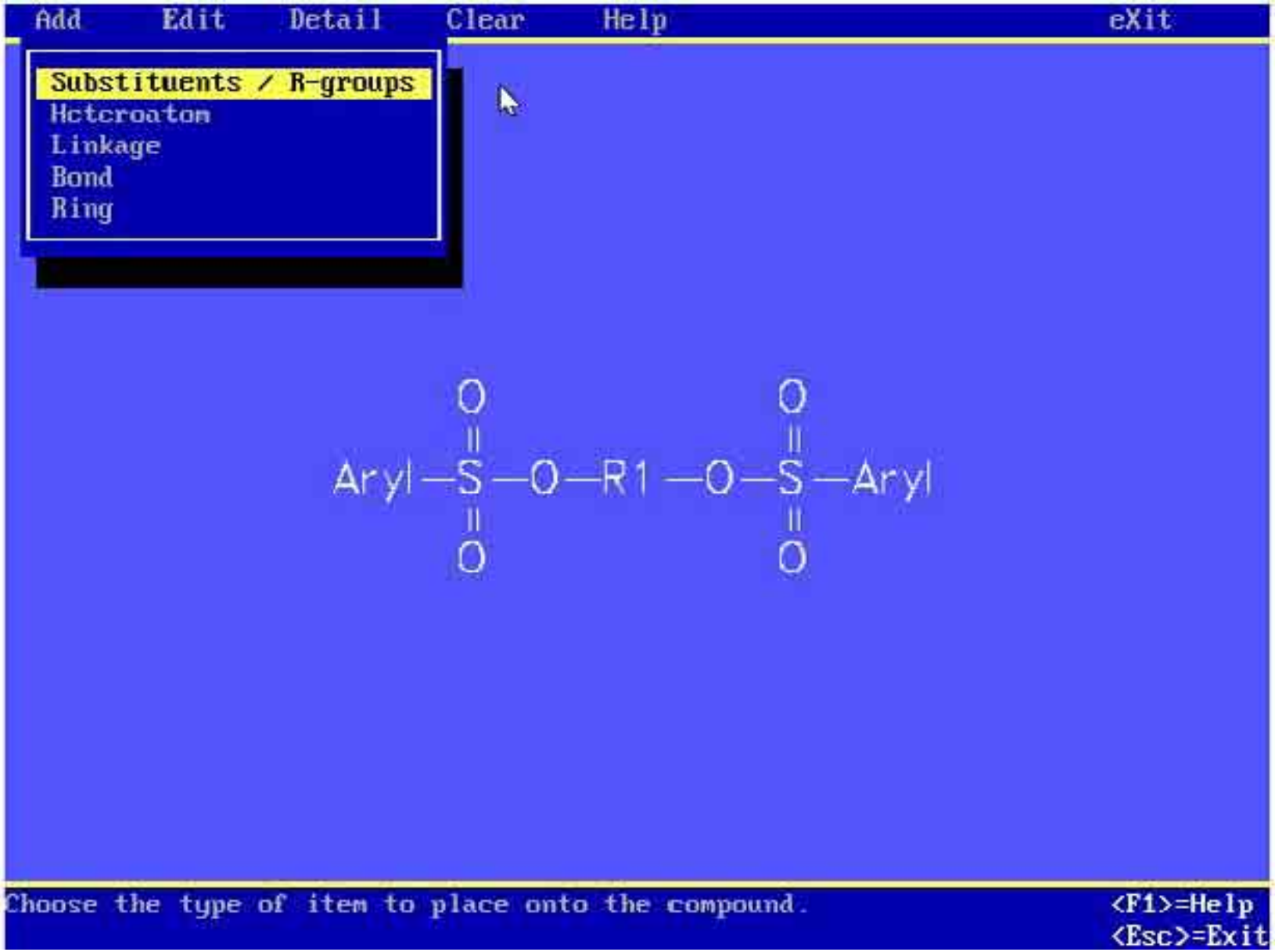
What are the chemical classes evaluated by OncoLogic™?

Currently OncoLogic™ has subsystems that can evaluate fibers, metals, polymers, and more than 46 classes of organic

Internet 100%

OncoLogic Concern	Definition
Low	Unlikely to be carcinogenic
Marginal	Likely to have equivocal carcinogenic activity
Low – Moderate	Likely to be weakly carcinogenic
Moderate	Likely to be a moderately active carcinogen
Moderate – High	Highly likely to be a moderately active carcinogen
High	Highly likely to be a potent carcinogen


ORGANIC CLASSES
Acylating Agents
Acyl and Benzoyl Halides
Acrylamides
Acrylates and Related Compounds
Aflatoxins and Microbial Toxins
Aldehydes
Aliphatic Azo and Azoxy Compounds
Alkanesulfonoxy Esters
Alkenylbenzenes
Alkyl Sulfates and Alkyl Alkanesulfonates
Anhydride Compounds
Aromatic Amines
Arylazo Compounds
Aryldiazonium Salts
C-Nitroso Compounds and Oximes
Carbamates
Carbamyl Halides
Coumarins
Dicarbonyls
Direct-Acting Alkylating Agents
Direct-Acting Arylating Agents
Epoxides
Ethyleneimines
Furocoumarins
alpha-Haloalkylamines
alpha-/beta-Haloethers
Halogenated Aromatic Hydrocarbons
Halogenated Cycloalkanes and Cycloalkenes
Select the appropriate class.
<F1>=Help <Esc>=Exit


Add Edit Detail Clear Help eXit
Substituents / R-groups
Hetcroatom
Linkage
Bond
Ring
Aryl—S—O—R1—O—S—Aryl
O
O
O
O
Choose the type of item to place onto the compound.
<F1>=Help
<Esc>=Exit

Compound Display

Justification Report

SUMMARY:

CODE NUMBER: chem125

SUBSTANCE ID: test1

The final level of carcinogenicity concern for this arylsulfonoxy ester, when the anticipated route of exposure is inhalation or injection, is LOW-MODERATE.

The final level of carcinogenicity concern for this arylsulfonoxy

<F1>=Help <ESC>=Exit

OncoLogic Justification Report

Bifunctional alkanesulfonoxy esters, consisting of an alkyl chain capped by two alkanesulfonoxy or arylsulfonoxy groups at both ends, are potential crosslinking agents which may initiate/exert carcinogenic action by causing DNA-DNA or DNA-protein crosslinks. The crosslinking activity is dependent on the nature of the reactive alkane-/aryl-sulfonoxy groups and the distance between the two reactive functional groups. In general, p-toluenesulfonoxy and methanesulfonoxy groups are good leaving groups whereas unmethylated arylsulfonoxy groups are poorer leaving groups. An intergroup distance of 2 to 6 atoms appears to be the most favorable range for carcinogenic activity, while the distances outside this range are less favorable, or may even reduce the level of concern.

The baseline level of concern for this arylsulfonoxy ester is MARGINAL.

The distance of three carbon atoms between the two sulfonoxy groups is within the optimum range for crosslinking activity, and is therefore expected to raise the level of concern.

Therefore, the level of concern is raised to LOW-MODERATE.

In general, inhalation and injection provide the best chance of delivering the largest possible amount of direct-acting reactive chemicals to target tissue because of a lesser absorption barrier and better chance of avoiding detoxification by protective nucleophiles such as glutathione. Exposure to the compound by inhalation is expected to raise the level of concern to MODERATE.

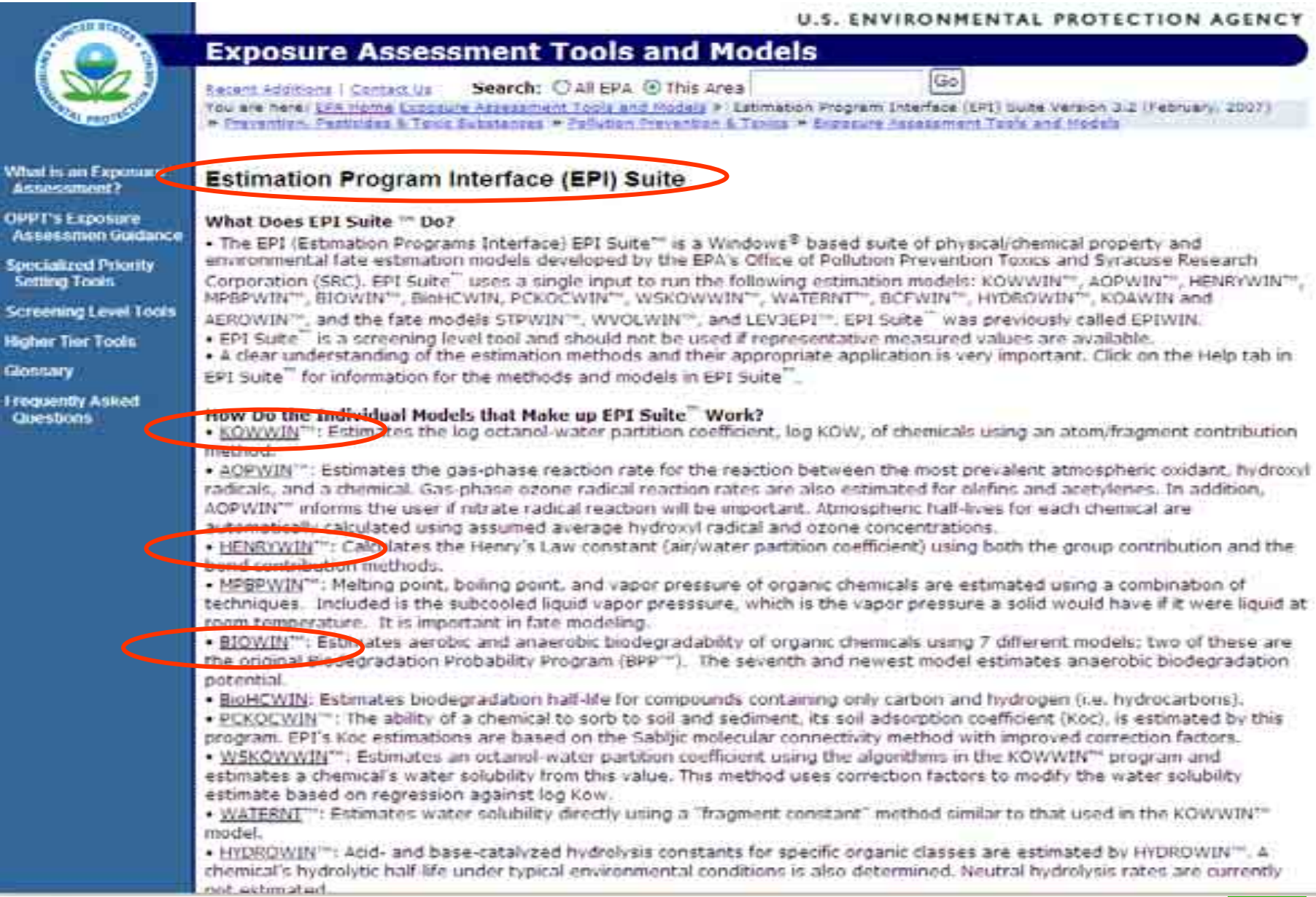
The final level of carcinogenicity concern for this arylsulfonoxy ester, when the anticipated route of exposure is inhalation, is MODERATE.

EPI Suite

Software dell' US EPA per **stimare proprieta' chimico-fisiche**

Disponibile:
http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

Anche in Toolbox



U.S. ENVIRONMENTAL PROTECTION AGENCY

Exposure Assessment Tools and Models

Recent Additions | Contact Us Search: All EPA This Area Go

You are here: EPA Home > Exposure Assessment Tools and Models > Estimation Program Interface (EPI) Suite Version 3.2 (February, 2007) > Prevention, Pesticides & Toxic Substances > Pollution Prevention & Toxics > Exposure Assessment Tools and Models

- What is an Exposure Assessment?
- OPPT's Exposure Assessment Guidance
- Specialized Priority Setting Tools
- Screening Level Tools
- Higher Tier Tools
- Glossary
- Frequently Asked Questions

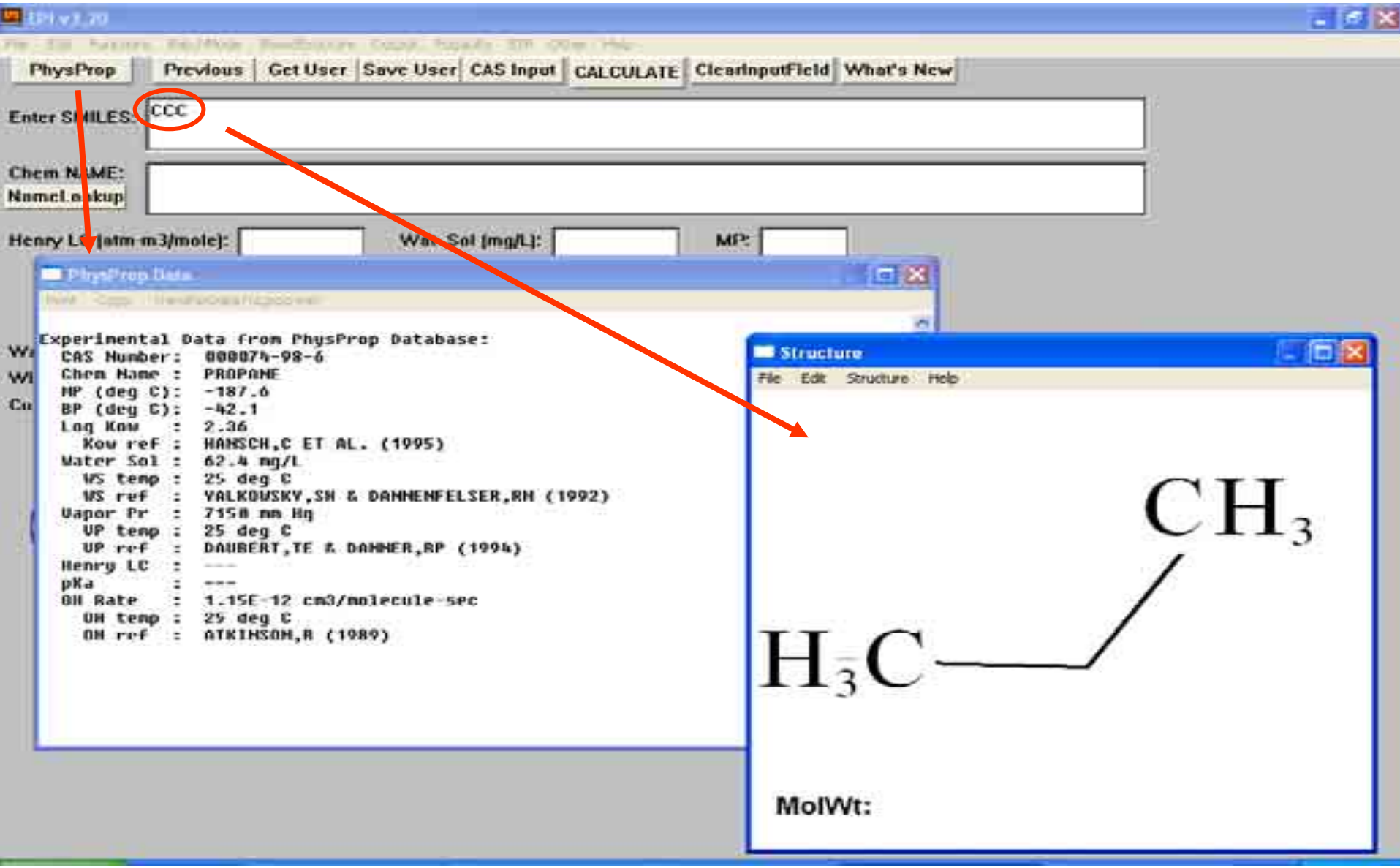
Estimation Program Interface (EPI) Suite

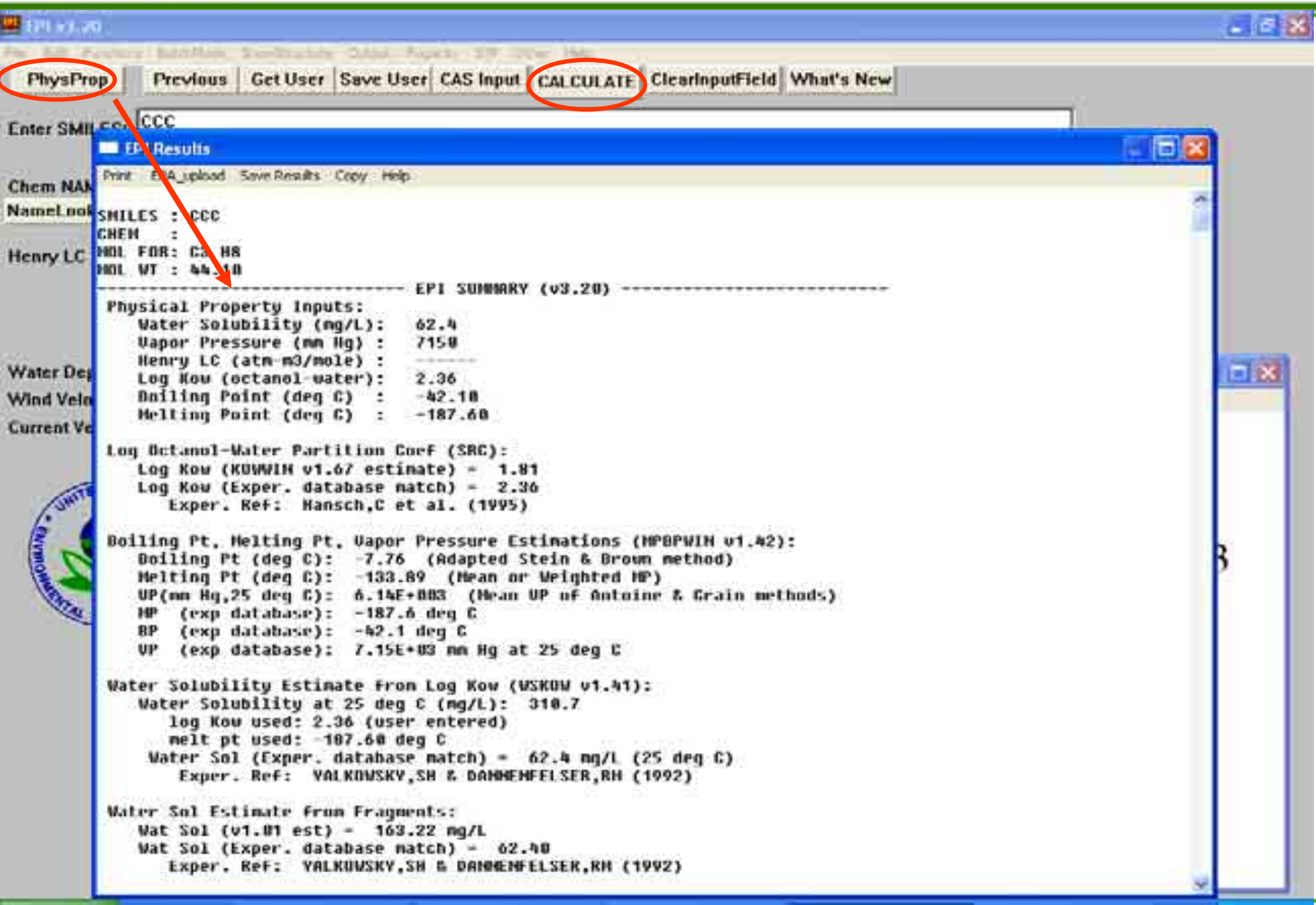
What Does EPI Suite™ Do?

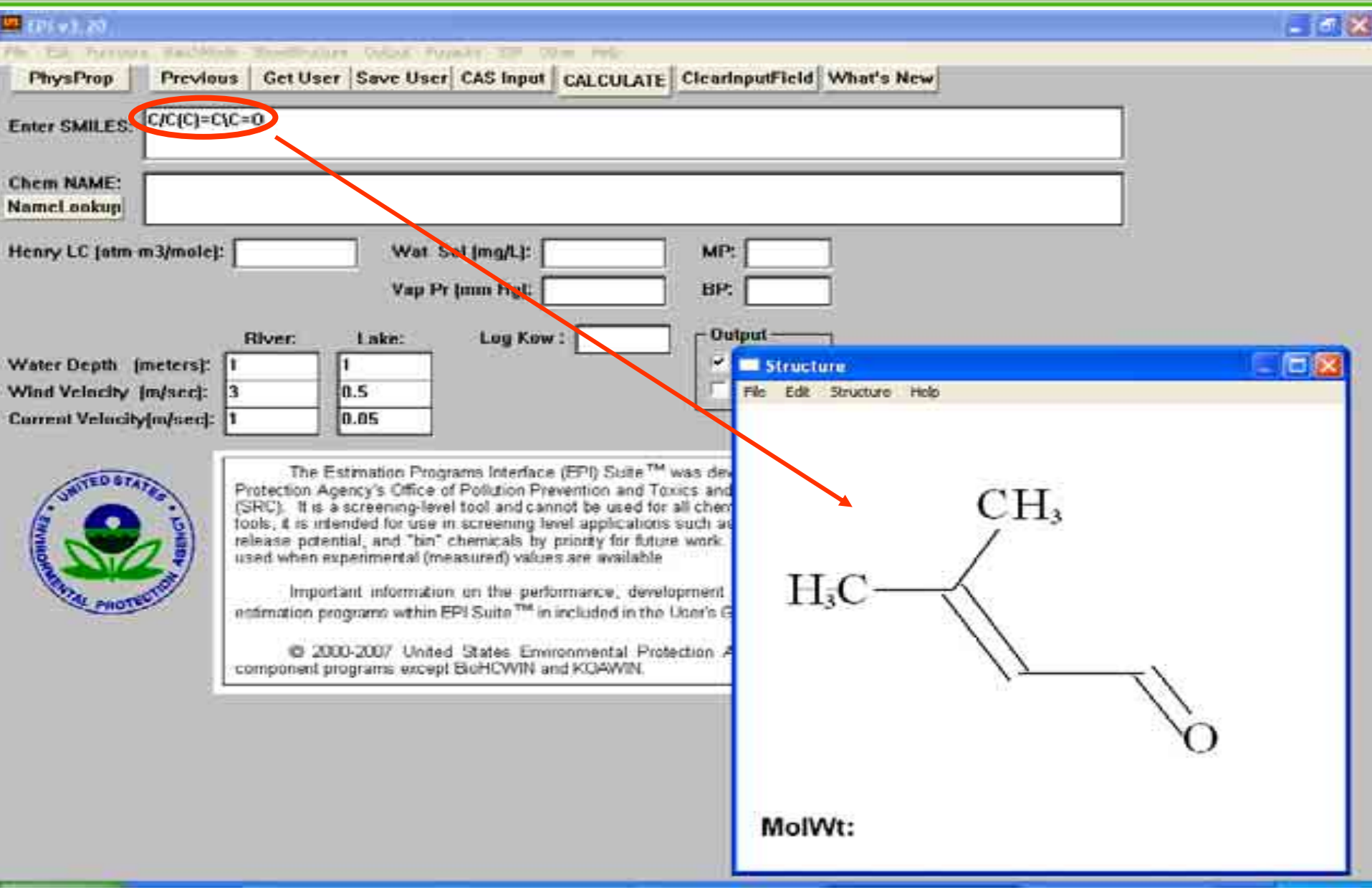
- The EPI (Estimation Programs Interface) EPI Suite™ is a Windows® based suite of physical/chemical property and environmental fate estimation models developed by the EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). EPI Suite™ uses a single input to run the following estimation models: KOWWIN™, AOPWIN™, HENRYWIN™, MPBPWIN™, BIOWIN™, BioHCWIN, PCKOCWIN™, WSKOWWIN™, WATERNT™, BCFWIN™, HYDROWIN™, KOAWIN and AEROWIN™, and the fate models STPWIN™, WVOLWIN™, and LEV3EPI™. EPI Suite™ was previously called EPIWIN.
- EPI Suite™ is a screening level tool and should not be used if representative measured values are available.
- A clear understanding of the estimation methods and their appropriate application is very important. Click on the Help tab in EPI Suite™ for information for the methods and models in EPI Suite™.

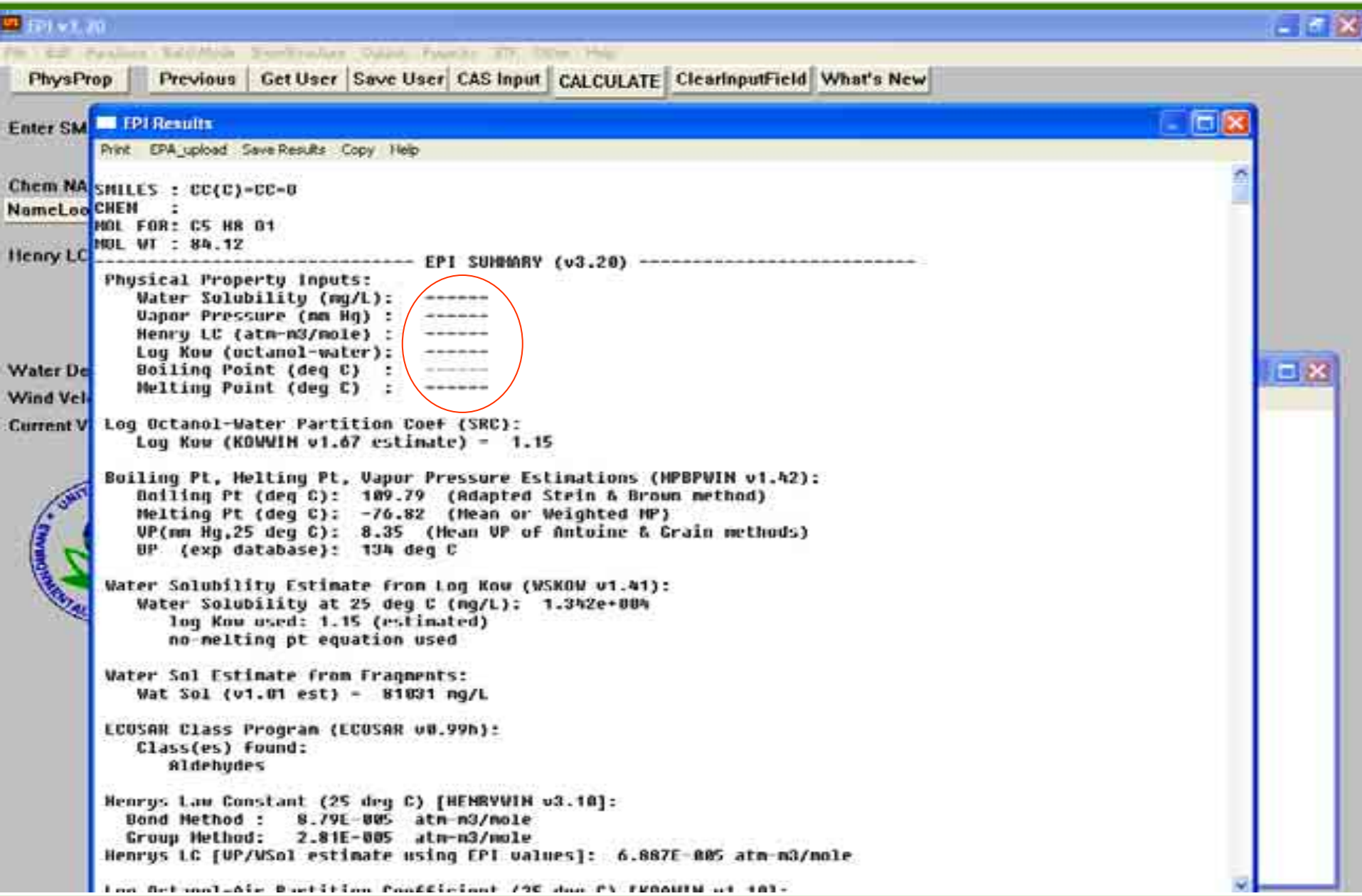
How Do the Individual Models that Make up EPI Suite™ Work?

- KOWWIN™: Estimates the log octanol-water partition coefficient, log KOW, of chemicals using an atom/fragment contribution method.
- AOPWIN™: Estimates the gas-phase reaction rate for the reaction between the most prevalent atmospheric oxidant, hydroxyl radicals, and a chemical. Gas-phase ozone radical reaction rates are also estimated for olefins and acetylenes. In addition, AOPWIN™ informs the user if nitrate radical reaction will be important. Atmospheric half-lives for each chemical are automatically calculated using assumed average hydroxyl radical and ozone concentrations.
- HENRYWIN™: Calculates the Henry's Law constant (air/water partition coefficient) using both the group contribution and the bond contribution methods.
- MPBPWIN™: Melting point, boiling point, and vapor pressure of organic chemicals are estimated using a combination of techniques. Included is the subcooled liquid vapor presssure, which is the vapor pressure a solid would have if it were liquid at room temperature. It is important in fate modeling.
- BIOWIN™: Estimates aerobic and anaerobic biodegradability of organic chemicals using 7 different models; two of these are the original Biodegradation Probability Program (BPP™). The seventh and newest model estimates anaerobic biodegradation potential.
- BioHCWIN: Estimates biodegradation half-life for compounds containing only carbon and hydrogen (i.e. hydrocarbons).
- PCKOCWIN™: The ability of a chemical to sorb to soil and sediment, its soil adsorption coefficient (Koc), is estimated by this program. EPI's Koc estimations are based on the Sabljic molecular connectivity method with improved correction factors.
- WSKOWWIN™: Estimates an octanol-water partition coefficient using the algorithms in the KOWWIN™ program and estimates a chemical's water solubility from this value. This method uses correction factors to modify the water solubility estimate based on regression against log Kow.
- WATERNT™: Estimates water solubility directly using a "fragment constant" method similar to that used in the KOWWIN™ model.
- HYDROWIN™: Acid- and base-catalyzed hydrolysis constants for specific organic classes are estimated by HYDROWIN™. A chemical's hydrolytic half-life under typical environmental conditions is also determined. Neutral hydrolysis rates are currently not estimated.


PhysProp
Previous
Get User
Save User
CAS Input
CALCULATE
ClearInputField
What's New
Enter SMILES:
CCC
Chem NAME:
Namelookup
Henry LC (atm-m3/mole):
Wat Sol (mg/L):
MP:
PhysProp Data
Experimental Data from PhysProp Database:
CAS Number: 000074-98-6
Chem Name : PROPANE
MP (deg C): -187.6
BP (deg C): -42.1
Log Kow : 2.36
Kow ref : HANSCH,C ET AL. (1995)
Water Sol : 62.4 mg/L
WS temp : 25 deg C
WS ref : YALKOWSKY,SH & DANNENFELSER,RM (1992)
Vapor Pr : 7158 mm Hg
VP temp : 25 deg C
VP ref : DAUBERT,TE & DANNER,RP (1994)
Henry LC : ---
pKa : ---
OH Rate : 1.15E-12 cm3/molecule-sec
OH temp : 25 deg C
OH ref : ATKINSON,R (1989)
Structure
File Edit Structure Help
CH3
H3C
MolWt:


PhysProp
Previous
Get User
Save User
CAS Input
CALCULATE
ClearInputField
What's New
Enter SMILES:
CCC
EPI Results
Print
EPA_upload
Save Results
Copy
Help
SMILES : CCC
CHEM :
MOL FOR: C3 H8
MOL WT : 44.10
---------- EPI SUMMARY (v3.20) ----------
Physical Property Inputs:
Water Solubility (mg/L): 62.4
Vapor Pressure (mm Hg) : 7150
Henry LC (atm-m3/mole) :
Log Kow (octanol-water): 2.36
Boiling Point (deg C) : -42.10
Melting Point (deg C) : -187.60
Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.67 estimate) = 1.81
Log Kow (Exper. database match) = 2.36
Exper. Ref: Hansch,C et al. (1995)
Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.42):
Boiling Pt (deg C): -7.76 (Adapted Stein & Brown method)
Melting Pt (deg C): -133.89 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 6.14E+003 (Mean VP of Antoine & Grain methods)
MP (exp database): -187.6 deg C
BP (exp database): -42.1 deg C
VP (exp database): 7.15E+03 mm Hg at 25 deg C
Water Solubility Estimate from Log Kow (WSKOW v1.41):
Water Solubility at 25 deg C (mg/L): 310.7
log Kow used: 2.36 (user entered)
melt pt used: -187.60 deg C
Water Sol (Exper. database match) = 62.4 mg/L (25 deg C)
Exper. Ref: YALKOWSKY,SH & DANNENFELSER,RH (1992)
Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 163.22 mg/L
Wat Sol (Exper. database match) = 62.40
Exper. Ref: YALKOWSKY,SH & DANNENFELSER,RH (1992)
Chem NAM
NameLook
Henry LC
Water Dep
Wind Velo
Current Ve


PhysProp
Previous
Get User
Save User
CAS Input
CALCULATE
ClearInputField
What's New
Enter SMILES:
C/C(C)=C\C=O
Chem NAME:
NameLookup
Henry LC [atm-m3/mole]:
Wat Sol [mg/L]:
MP:
Vap Pr [mm Hg]:
BP:
Log Kow :
Output
River:
Lake:
Water Depth [meters]:
1
1
Wind Velocity [m/sec]:
3
0.5
Current Velocity[m/sec]:
1
0.05
The Estimation Programs Interface (EPI) Suite™ was dev
Protection Agency's Office of Pollution Prevention and Toxics and
(SRC). It is a screening-level tool and cannot be used for all chem
tools; it is intended for use in screening level applications such a
release potential, and "bin" chemicals by priority for future work.
used when experimental (measured) values are available
Important information on the performance, development
estimation programs within EPI Suite™ is included in the User's G
© 2000-2007 United States Environmental Protection A
component programs except BioHCWIN and KOAWIN.
Structure
File
Edit
Structure
Help
CH3
H3C
O
MolWt:


PhysProp
Previous
Get User
Save User
CAS Input
CALCULATE
ClearInputField
What's New
EPI Results
Print
EPA_upload
Save Results
Copy
Help
SMILES : CC(C)=CC=O
CHEM :
MOL FOR: C5 H8 O1
MOL WT : 84.12
EPI SUMMARY (v3.20)
Physical Property Inputs:
Water Solubility (mg/L): ------
Vapor Pressure (mm Hg) : ------
Henry LC (atm-m3/mole) : ------
Log Kow (octanol-water): ------
Boiling Point (deg C) : ------
Melting Point (deg C) : ------
Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.67 estimate) = 1.15
Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.42):
Boiling Pt (deg C): 109.79 (Adapted Stein & Brown method)
Melting Pt (deg C): -76.82 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 8.35 (Mean VP of Antoine & Grain methods)
BP (exp database): 134 deg C
Water Solubility Estimate from Log Kow (WSKOW v1.41):
Water Solubility at 25 deg C (mg/L): 1.342e+004
log Kow used: 1.15 (estimated)
no melting pt equation used
Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 81031 mg/L
ECOSAR Class Program (ECOSAR v0.99h):
Class(es) found:
Aldehydes
Henrys Law Constant (25 deg C) [HENRYWIN v3.10]:
Bond Method : 8.79E-005 atm-m3/mole
Group Method: 2.81E-005 atm-m3/mole
Henrys LC [VP/WSol estimate using EPI values]: 6.887E-005 atm-m3/mole

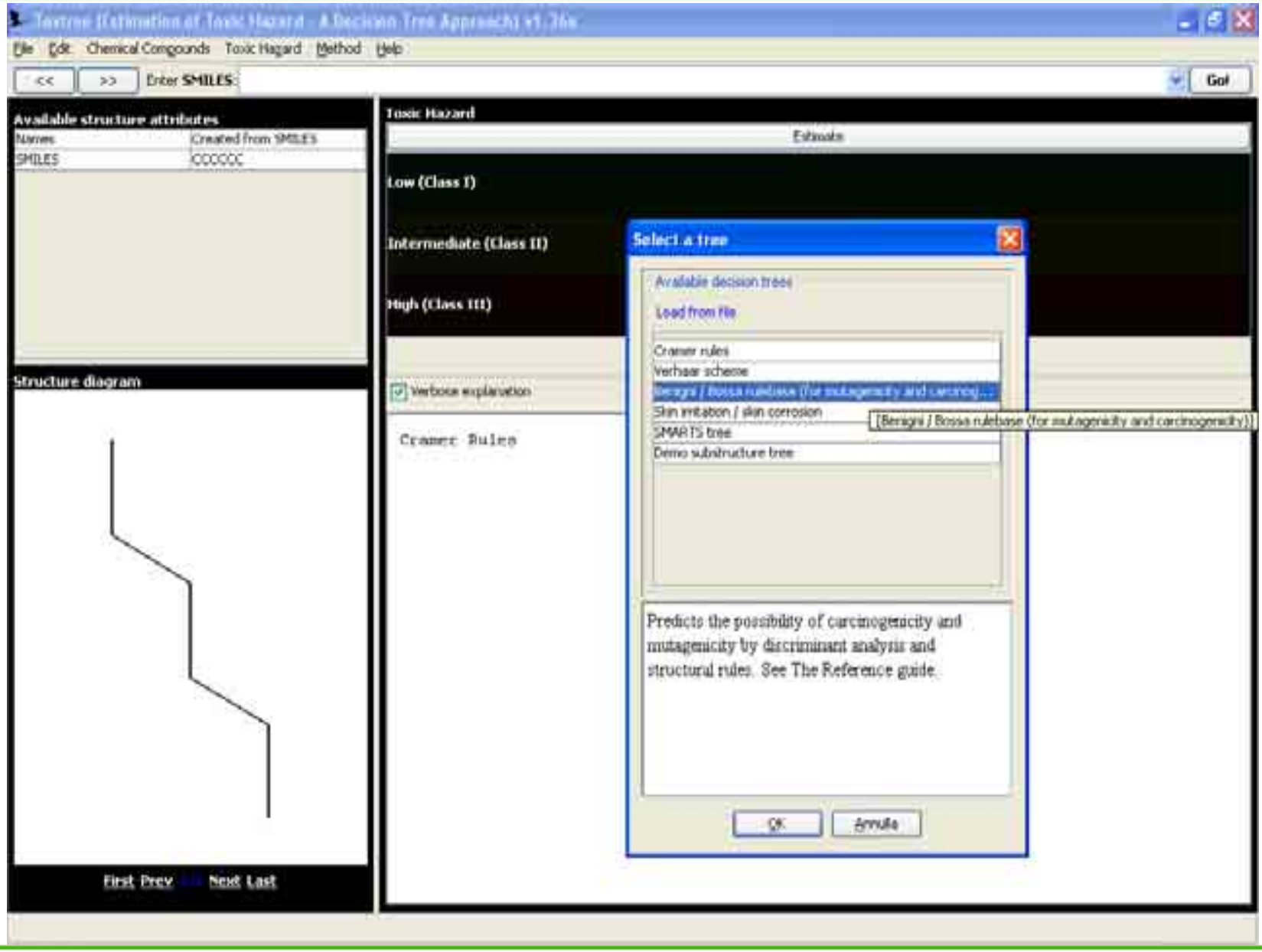
Toxtree

Sistema esperto dell' European Chemicals Bureau (ora Institute for Health and Consumer Protection)

Stima varie tossicita' in base a regole srutturali

http://ecb.jrc.it/QSAR

Anche in Toolbox


File Edit Chemical Compounds Toxic Hazard Method Help
<< >> Enter SMILES: Go!
Available structure attributes
Names Created from SMILES
SMILES CCCCCC
Structure diagram
First Prev Next Last
Toxic Hazard
Estimate
Low (Class I)
Intermediate (Class II)
High (Class III)
Verbose explanation
Cramer Rules
Select a tree
Available decision trees
Load from file
Cramer rules
Verhaar scheme
Benigni / Bossa rulebase (for mutagenicity and carcinog...
Skin irritation / skin corrosion
SMARTS tree
Demo substructure tree
[Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)]
Predicts the possibility of carcinogenicity and mutagenicity by discriminant analysis and structural rules. See The Reference guide.
OK
Annulla

Cramer rules

- Structure-based approach to the ***Threshold of Toxicological Concern*** (TTC) concept

- ***Subchronic, chronic and reproductive*** effects; carcinogenic or mutagenic endpoints not considered

Three classes:

• Class I: simple chemical structures with efficient modes of metabolism, suggesting a low order of oral toxicity;
• Class III: may suggest significant toxicity; reactive functional groups;
• Class II: intermediate

Verhaar scheme

- Structure-based; Mode of Action for ***Aquatic Toxicity***

Class 1: *non-polar narcosis* or baseline toxicity

Class 2: *polar narcosis,* less inert compounds

Class 3: *reactive chemicals* (un-selective towards proteins and other macromolecules)

Class 4: *specifically acting chemicals* (e.g., towards receptors)

Class 5: No classification possible

(LogP calculated)

Skin irritation/corrosion rules

- structural rules, plus

- ***physicochemical properties***: MW, LogP, melting point, water solubility, lipid solubility and surface tension

(MW, LogP calculated; other data requested)

Categories:

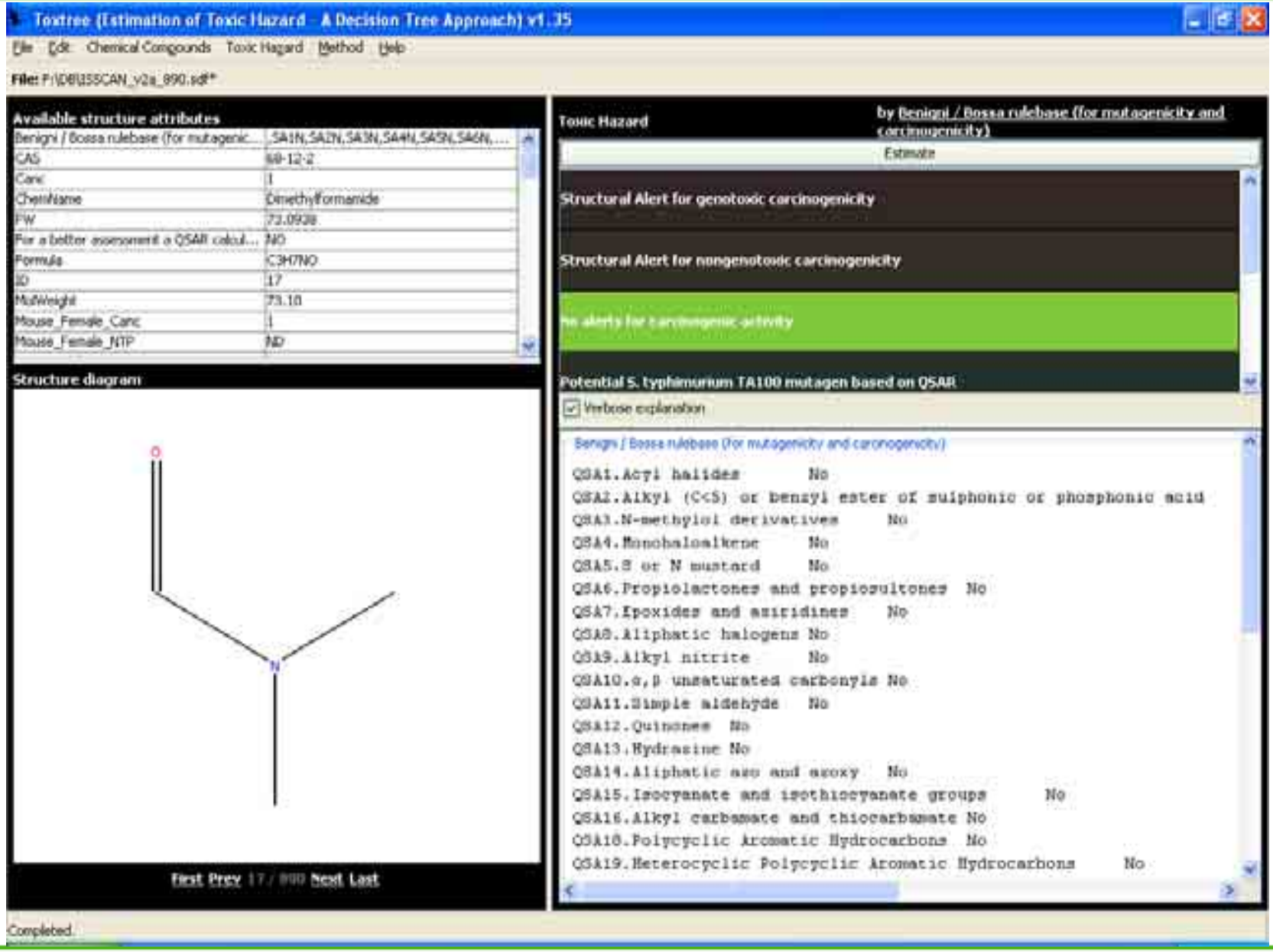
- Not Corrosive
- Not Irritating Or Corrosive
- Not Irritating
- Irritating
- Corrosive
- Irritating Or Corrosive
- Unknown

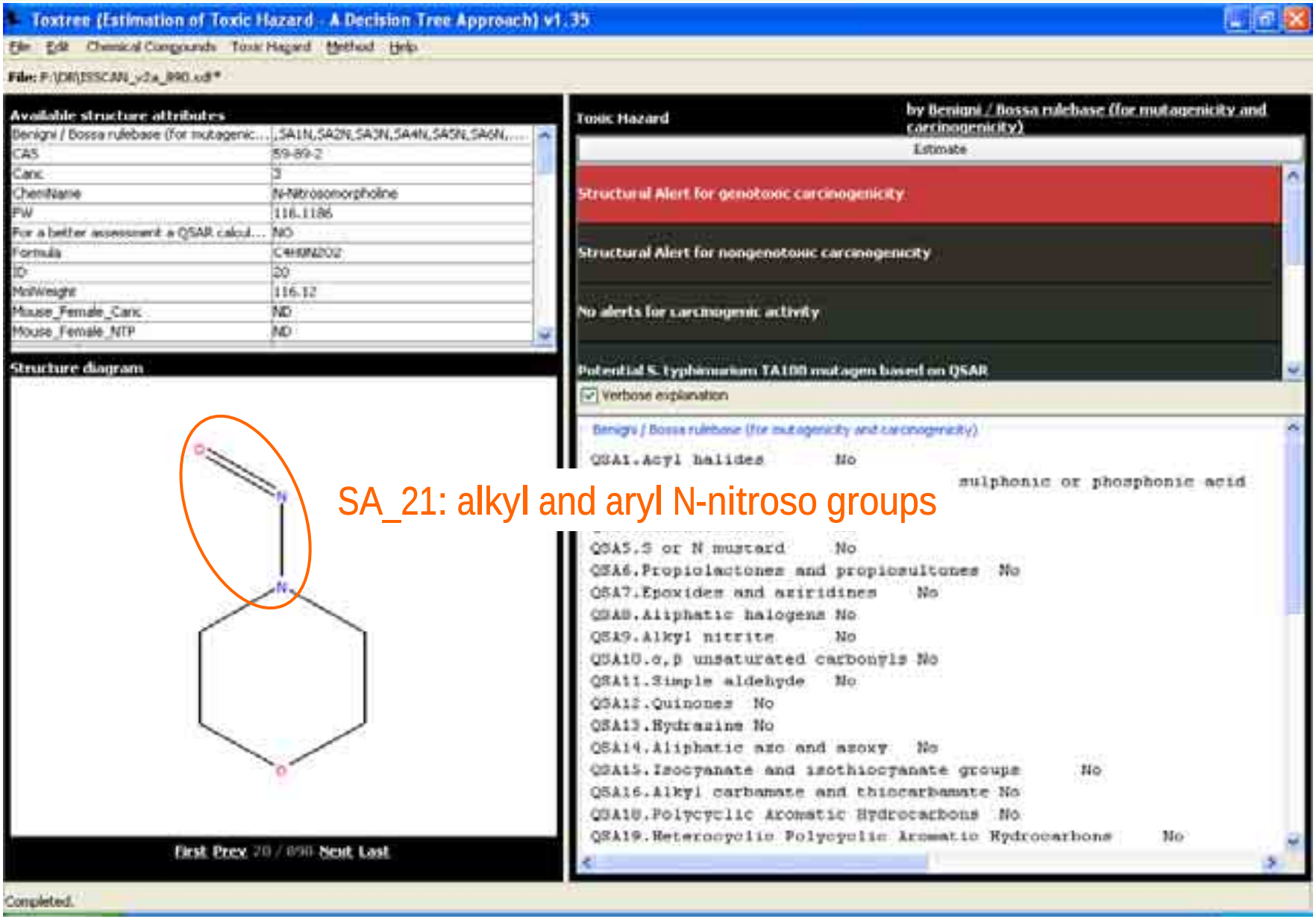
Toxtree 1.5 Base di regole per mutageni / cancerogeni

Metodo basato su regole strutturali, con:

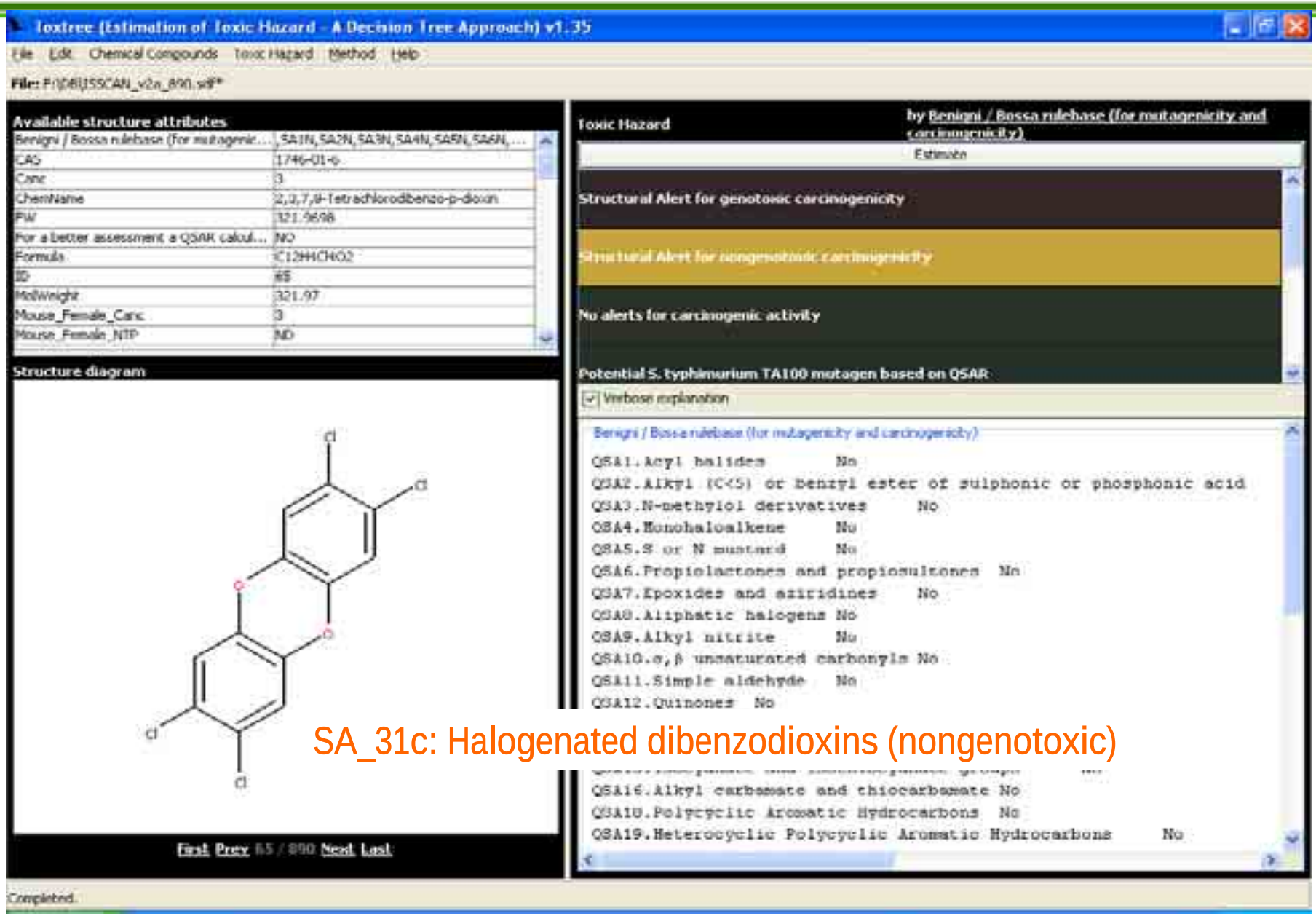
- Nuova compilazione (ISS) di Allerte Strutturali
- Tre QSAR per classi congeneriche (ammine aromatiche, aldeidi)

Manuale in: ***http://ecb.jrc.it/documents/QSAR/EUR_23241_EN.pdf***

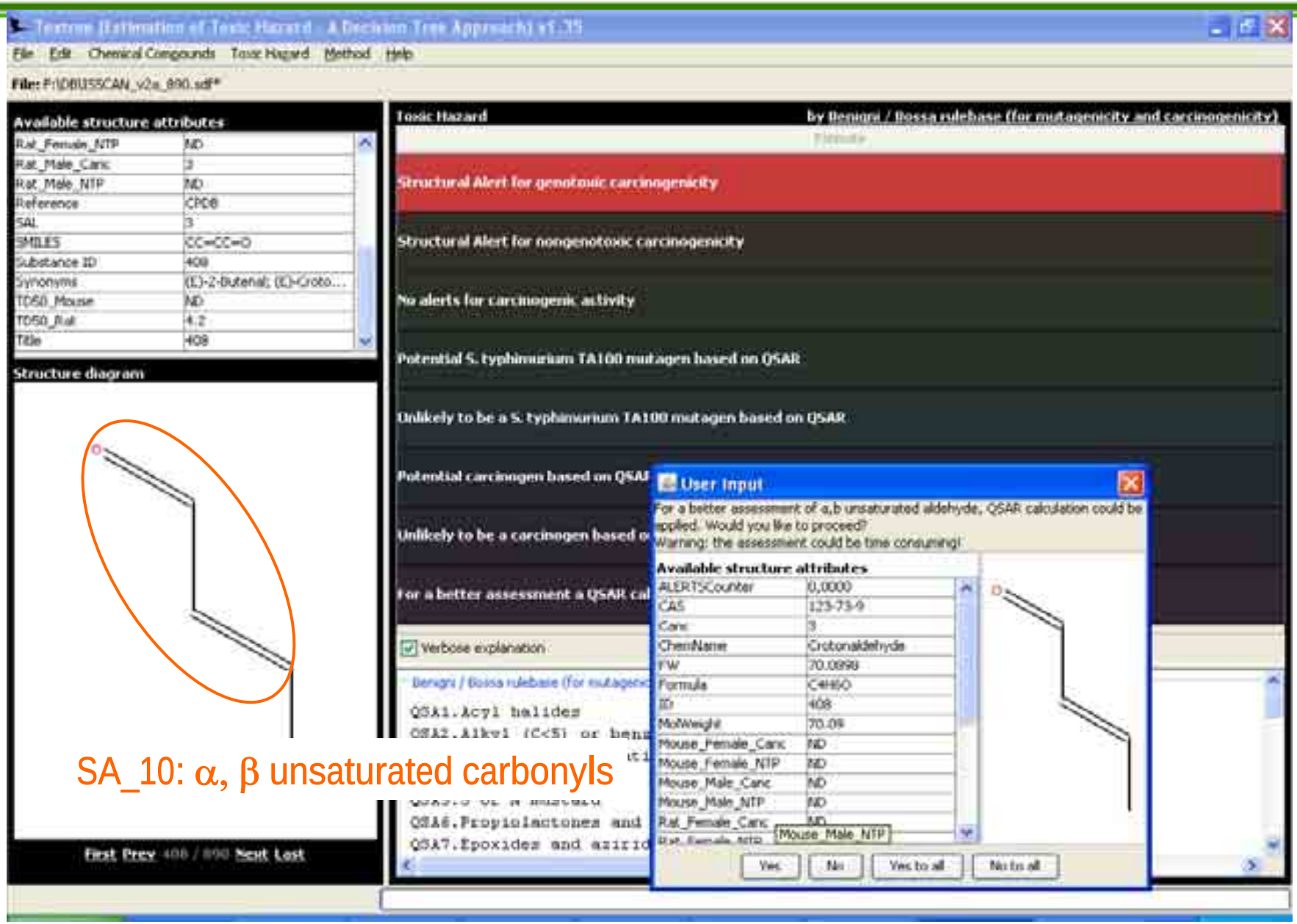

Toxtree (Estimation of Toxic Hazard – A Decision Tree Approach) v1.35
File Edit Chemical Compounds Toxic Hagard Method Help
File: F:\DB\USSCAN_v2a_890.sdf*
Available structure attributes
Benigni / Bossa rulebase (for mutagenic... ,SA1N,SA2N,SA3N,SA4N,SA5N,SA6N,...
CAS 68-12-2
Canc 1
ChemName Dimethylformamide
FW 73.0938
For a better assessment a QSAR calcul... NO
Formula C3H7NO
ID 17
MolWeight 73.10
Mouse_Female_Canc 1
Mouse_Female_NTP ND
Structure diagram
First Prev 17 / 890 Next Last
Toxic Hazard
by Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
Estimate
Structural Alert for genotoxic carcinogenicity
Structural Alert for nongenotoxic carcinogenicity
no alerts for carcinogenic activity
Potential S. typhimurium TA100 mutagen based on QSAR
Verbose explanation
Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
QSA1.Acyl halides No
QSA2.Alkyl (C<5) or benzyl ester of sulphonic or phosphonic acid
QSA3.N-methylol derivatives No
QSA4.Monohaloalkene No
QSA5.S or N mustard No
QSA6.Propiolactones and propiosultones No
QSA7.Epoxides and aziridines No
QSA8.Aliphatic halogens No
QSA9.Alkyl nitrite No
QSA10.α,β unsaturated carbonyls No
QSA11.Simple aldehyde No
QSA12.Quinones No
QSA13.Hydrazine No
QSA14.Aliphatic azo and azoxy No
QSA15.Isocyanate and isothiocyanate groups No
QSA16.Alkyl carbamate and thiocarbamate No
QSA18.Polycyclic Aromatic Hydrocarbons No
QSA19.Heterocyclic Polycyclic Aromatic Hydrocarbons No
Completed



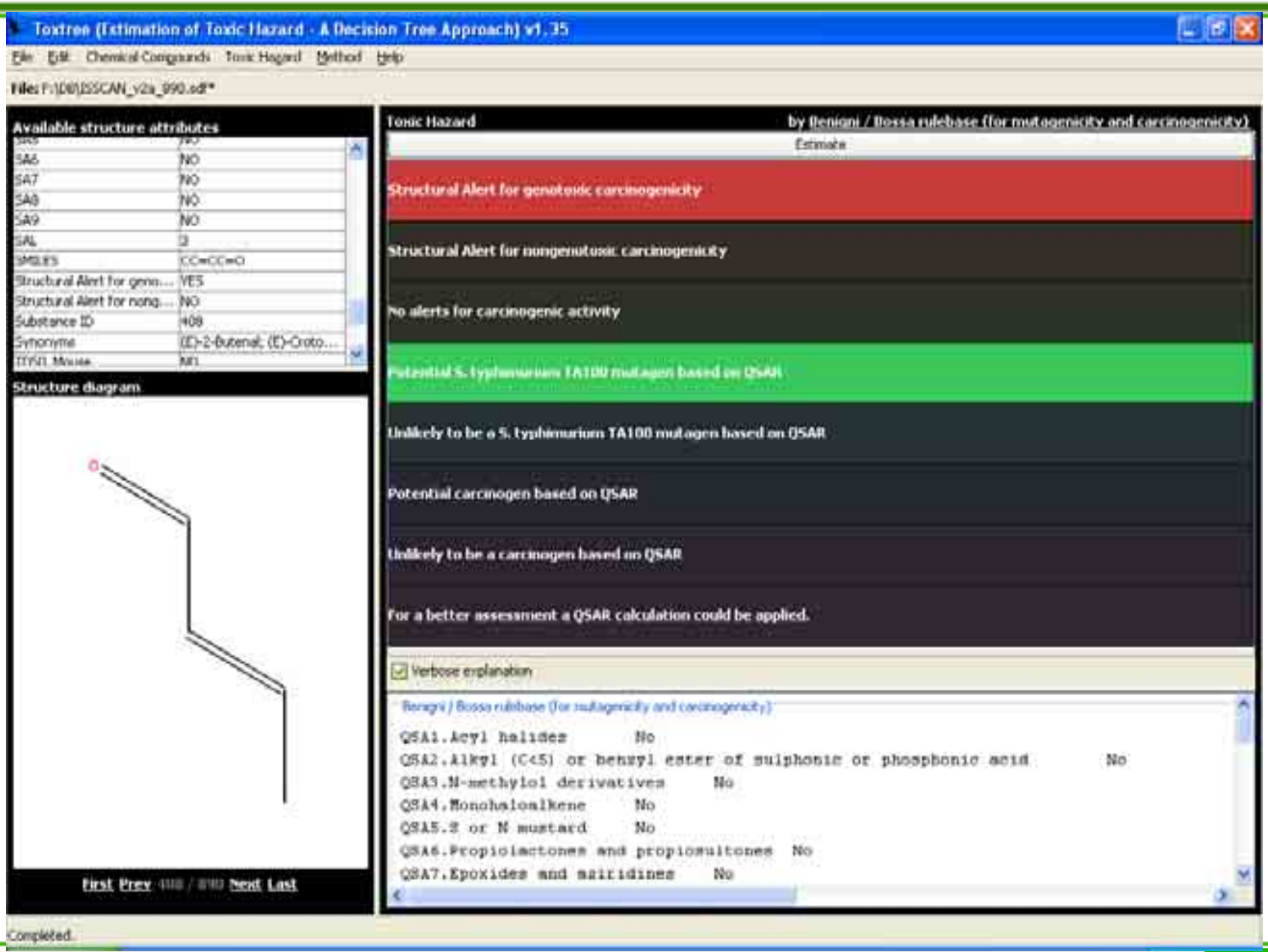
SA_21: alkyl and aryl N-nitroso groups

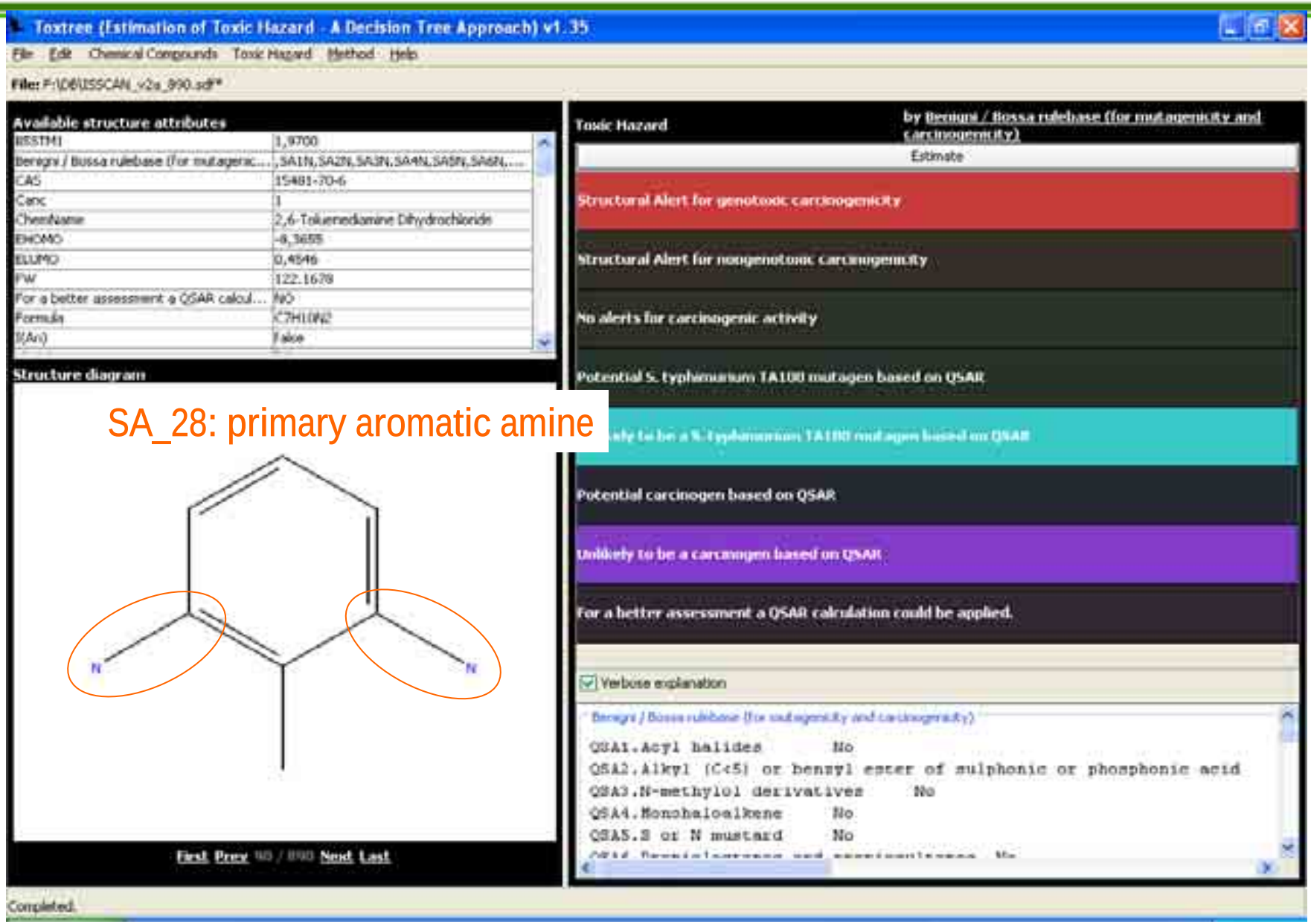


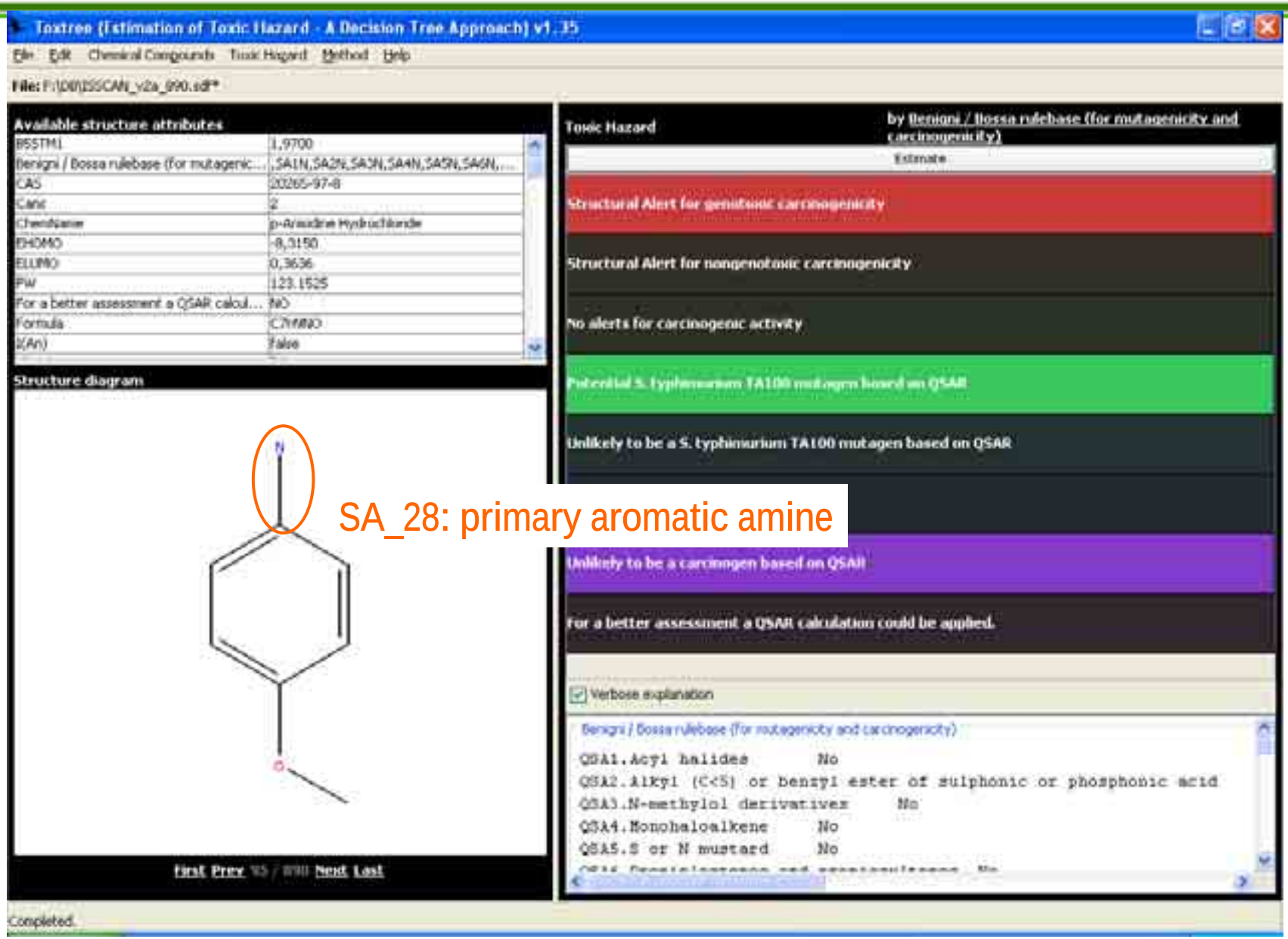
SA_31c: Halogenated dibenzodioxins (nongenotoxic)



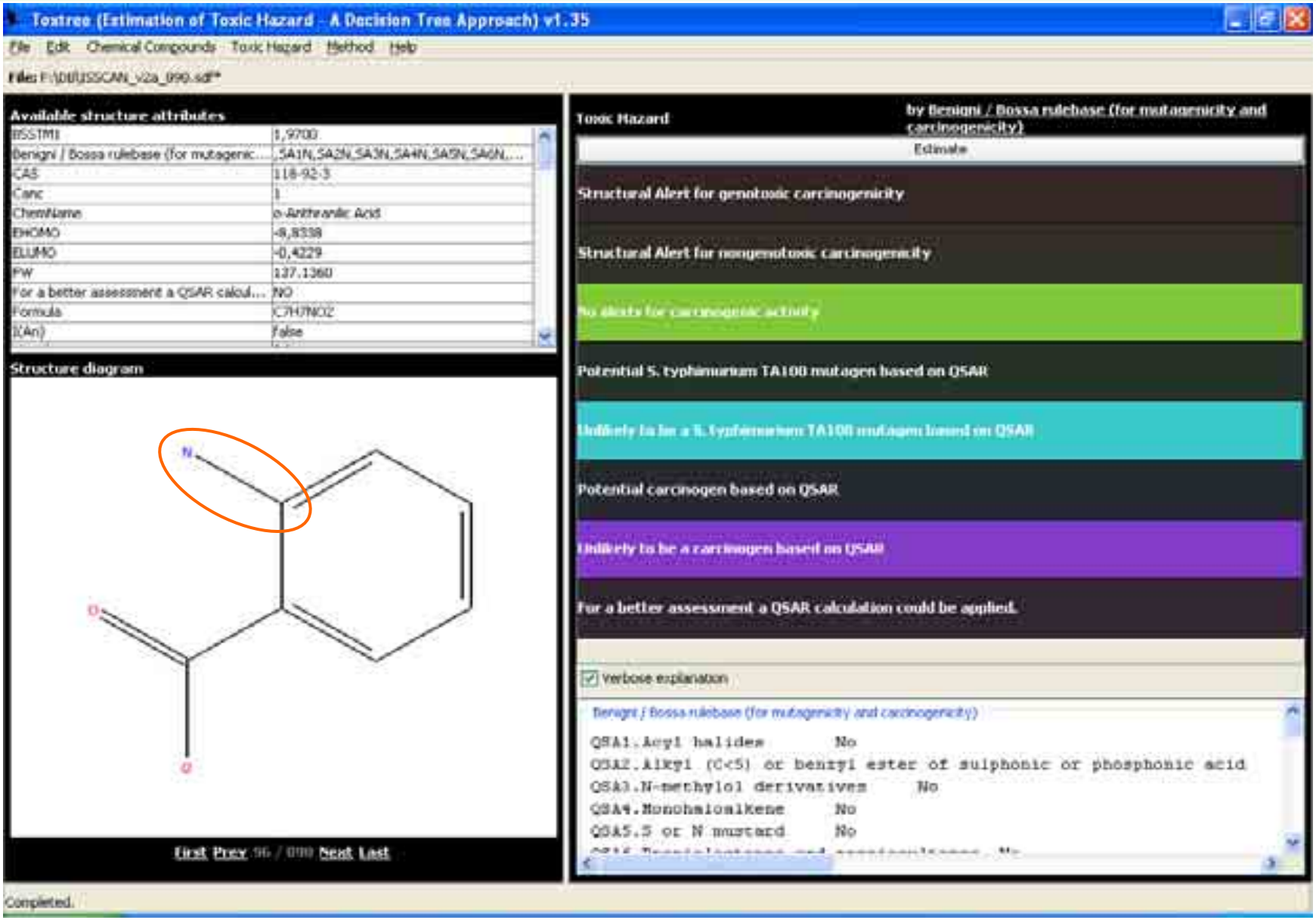
SA_10: α, β unsaturated carbonyls


Toxtree (Estimation of Toxic Hazard - A Decision Tree Approach) v1.35
File Edit Chemical Compounds Toxic Hazard Method Help
Files: F:\DB\DSSCAN_v2a_990.sd*
Available structure attributes
SA6 NO
SA7 NO
SA8 NO
SA9 NO
SAL 0
SMILES CC=CC=O
Structural Alert for geno... YES
Structural Alert for nong... NO
Substance ID 408
Synonyms (E)-2-Butenal; (E)-Croto...
Structure diagram
First Prev Next Last
Toxic Hazard
by Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
Estimate
Structural Alert for genotoxic carcinogenicity
Structural Alert for nongenotoxic carcinogenicity
No alerts for carcinogenic activity
Potential S. typhimurium TA100 mutagen based on QSAR
Unlikely to be a S. typhimurium TA100 mutagen based on QSAR
Potential carcinogen based on QSAR
Unlikely to be a carcinogen based on QSAR
For a better assessment a QSAR calculation could be applied.
Verbose explanation
Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
QSA1.Acyl halides No
QSA2.Alkyl (C<5) or benzyl ester of sulphonic or phosphonic acid No
QSA3.N-methylol derivatives No
QSA4.Monohaloalkene No
QSA5.S or N mustard No
QSA6.Propiolactones and propiosultones No
QSA7.Epoxides and aziridines No
Completed.

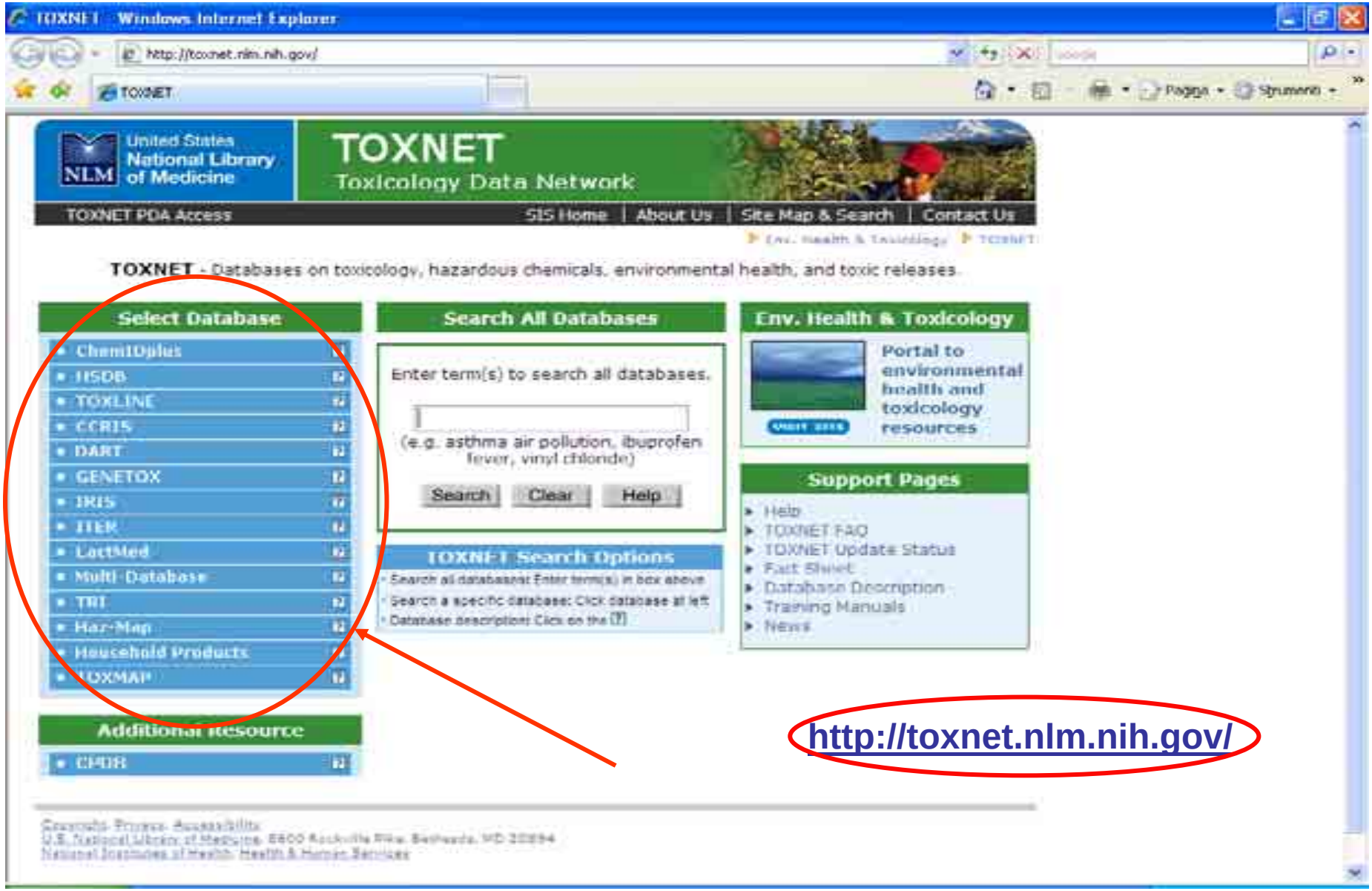

Toxtree (Estimation of Toxic Hazard - A Decision Tree Approach) v1.35
File Edit Chemical Compounds Toxic Hazard Method Help
File: F:\DB\ISSCAN_v2a_890.sdf*
Available structure attributes
Structure diagram
SA_28: primary aromatic amine
First Prev Next Last
Toxic Hazard
by Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
Estimate
Structural Alert for genotoxic carcinogenicity
Structural Alert for nongenotoxic carcinogenicity
No alerts for carcinogenic activity
Potential S. typhimurium TA100 mutagen based on QSAR
Potential carcinogen based on QSAR
Unlikely to be a carcinogen based on QSAR
For a better assessment a QSAR calculation could be applied.
Verbose explanation
QSA1.Acyl halides No
QSA2.Alkyl (C<5) or benzyl ester of sulphonic or phosphonic acid
QSA3.N-methylol derivatives No
QSA4.Monohaloalkene No
QSA5.S or N mustard No
Completed.

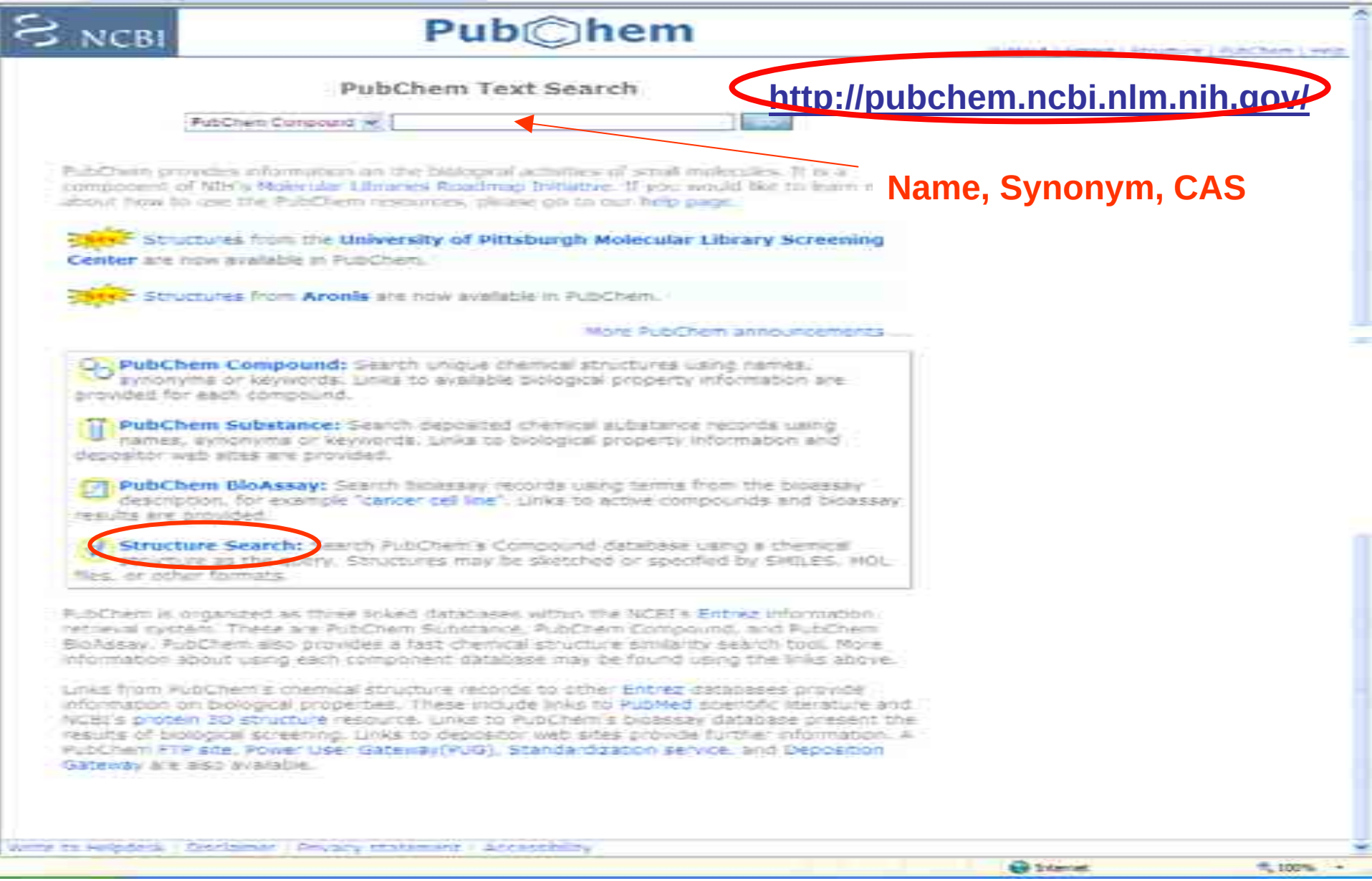


SA_28: primary aromatic amine

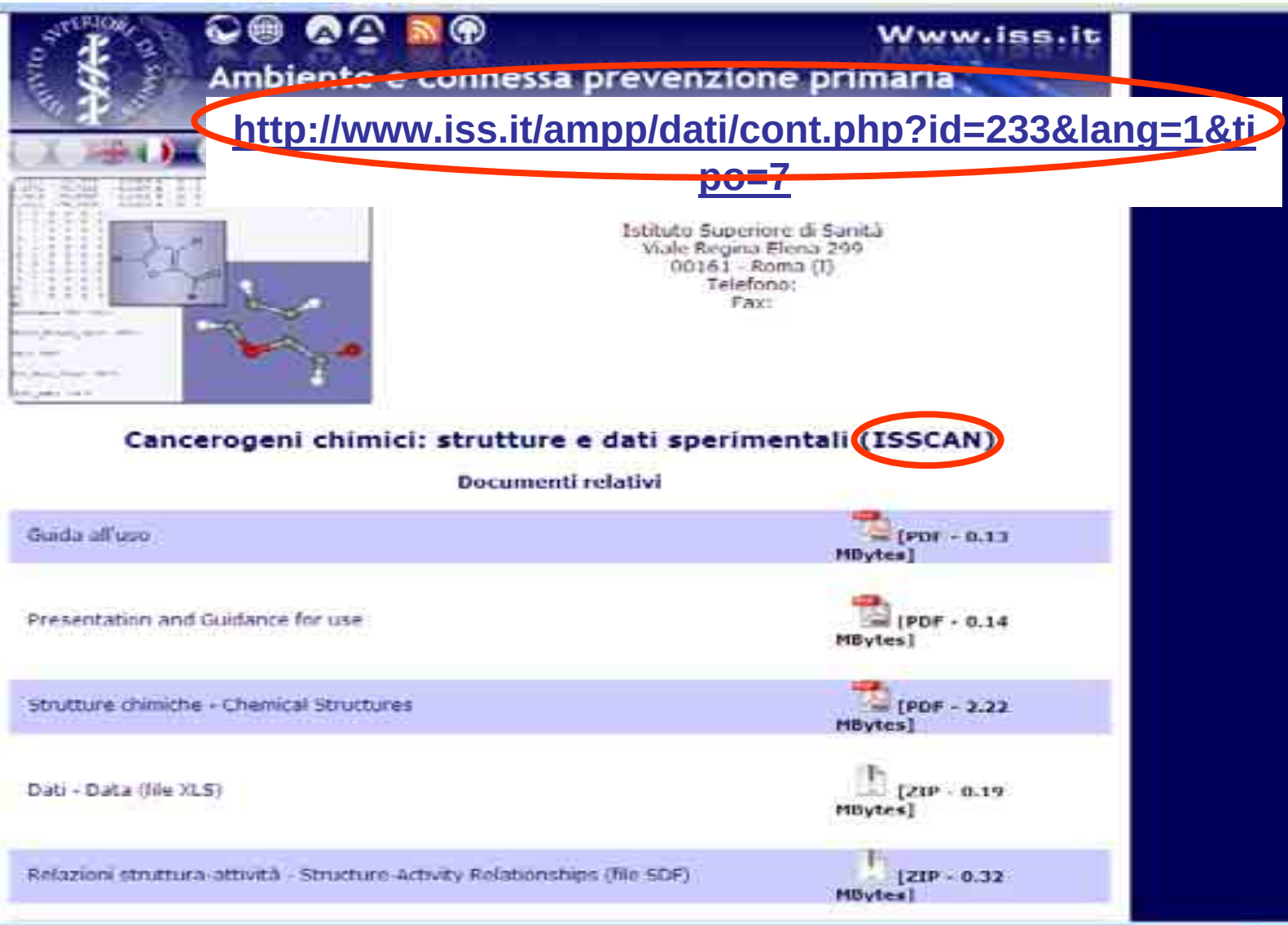

Toxtree (Estimation of Toxic Hazard - A Decision Tree Approach) v1.35
File Edit Chemical Compounds Toxic Hazard Method Help
File: F:\DIUSSCAN_v2a_099.sdf*
Available structure attributes
BSSTMI 1,9700
Benigni / Bossa rulebase (for mutagenic... ,SA1N,SA2N,SA3N,SA4N,SA5N,SA6N,...
CAS 118-92-3
Canc 1
ChemName o-Anthranilic Acid
EHOMO -8,8338
ELUMO -0,4229
FW 137.1360
For a better assessment a QSAR calcul... NO
Formula C7H7NO2
I(An) False
Structure diagram
First Prev Next Last
Toxic Hazard
by Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
Estimate
Structural Alert for genotoxic carcinogenicity
Structural Alert for nongenotoxic carcinogenicity
No alerts for carcinogenic activity
Potential S. typhimurium TA100 mutagen based on QSAR
Unlikely to be a S. typhimurium TA100 mutagen based on QSAR
Potential carcinogen based on QSAR
Unlikely to be a carcinogen based on QSAR
For a better assessment a QSAR calculation could be applied.
Verbose explanation
Benigni / Bossa rulebase (for mutagenicity and carcinogenicity)
QSA1.Acyl halides No
QSA2.Alkyl (C<5) or benzyl ester of sulphonic or phosphonic acid
QSA3.N-methylol derivatives No
QSA4.Monohaloalkene No
QSA5.S or N mustard No
Completed.

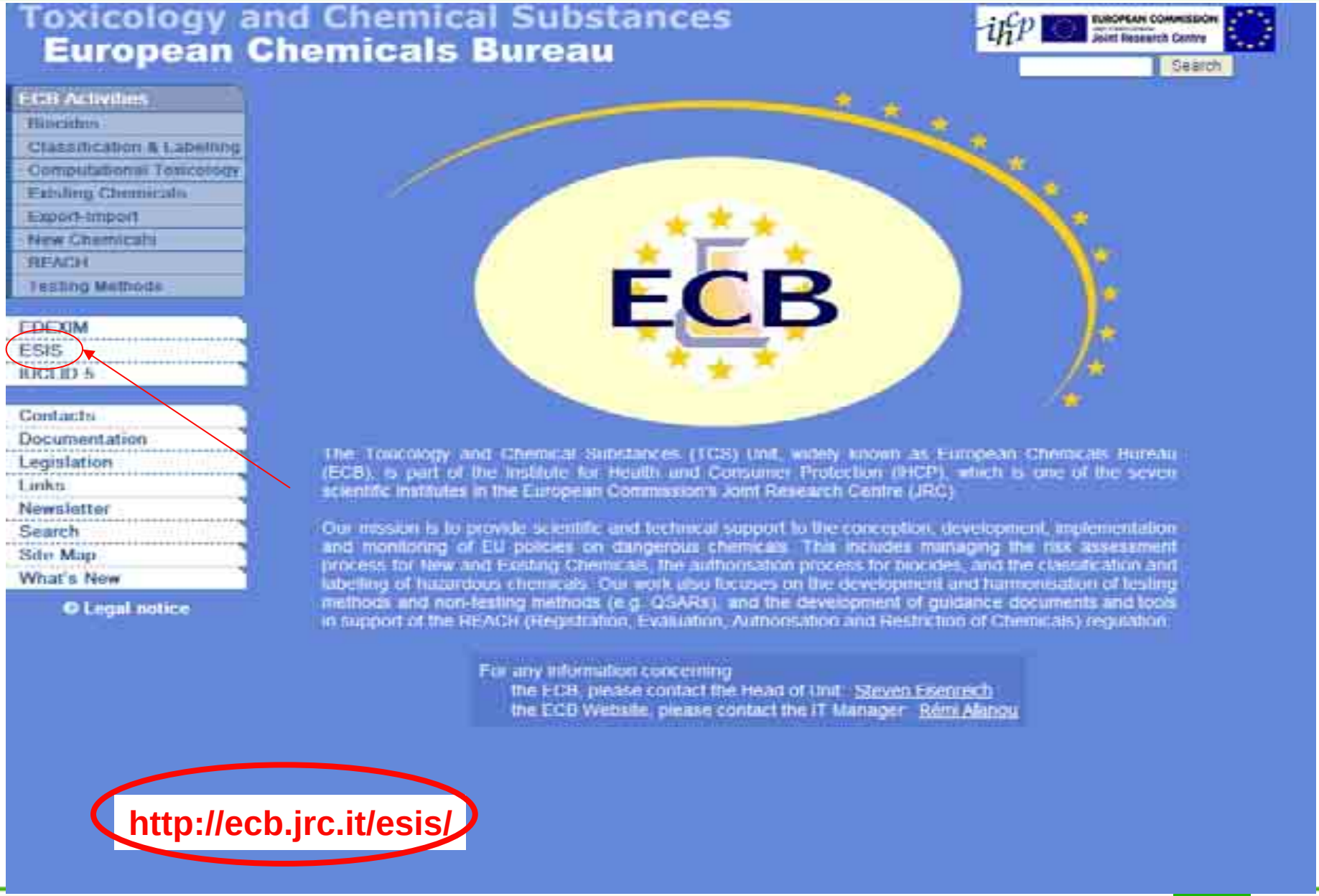
Banche dati per tossicita’ chimica


TOXNET Windows Internet Explorer
http://toxnet.nlm.nih.gov/
United States National Library of Medicine
NLM
TOXNET
Toxicology Data Network
TOXNET POA Access
SIS Home
About Us
Site Map & Search
Contact Us
TOXNET - Databases on toxicology, hazardous chemicals, environmental health, and toxic releases
Select Database
ChemIDplus
HSDB
TOXLINE
CCRIS
DART
GENETOX
IRIS
ITER
LactMed
Multi-Database
TRI
Haz-Map
Household Products
TOXMAP
Additional Resource
CPDB
Search All Databases
Enter term(s) to search all databases.
(e.g. asthma air pollution, ibuprofen fever, vinyl chloride)
Search
Clear
Help
TOXNET Search Options
Search all databases: Enter term(s) in box above
Search a specific database: Click database at left
Database description: Click on the
Env. Health & Toxicology
Portal to environmental health and toxicology resources
Support Pages
Help
TOXNET FAQ
TOXNET Update Status
Fact Sheet
Database Description
Training Manuals
News
http://toxnet.nlm.nih.gov/


NCBI
PubChem
PubChem Text Search
PubChem Compound
http://pubchem.ncbi.nlm.nih.gov/
Name, Synonym, CAS
PubChem Compound:
PubChem Substance:
PubChem BioAssay:
Structure Search:


U.S. ENVIRONMENTAL PROTECTION AGENCY
Distributed Structure-Searchable Toxicity (DSSTox) Public Database Network
Search: All EPA This Area Go
About DSSTox
Work in Progress
Frequent Questions
Structure Data Files
Central Field Definition Table
Apps, Tools & More
DSSTox Community
Site Map
Glossary of Terms
Help
DSSTox
http://www.epa.gov/ncct/dsstox/index.html
Distributed Structure-Searchable Toxicity (DSSTox) Database Network is a project of EPA's National Center for Computational Toxicology, helping to build a public data foundation for improved structure-activity and predictive toxicology capabilities. The DSSTox website provides a public forum for publishing downloadable, structure-searchable, standardized chemical structure files associated with toxicity data.
EPA DSSTox Structure-Browser
DSSTox Structure Browser Information Page
Chemical Structures
Toxicity Data
DSSTox SDF Files
Standardized
Documented
Structure-Searchable
Application-independent
DSSTox Graphic Flowchart
DSSTox Project Goals
DSSTox Publications
25 February 2008
***File Updates and Enhancements:
Addition of new DSSTox Standard Chemical Field to all files
STRUCTURE_InChIKey
Additional QA review, structural/CAS modifications, elimination of abbreviations in field entries, etc.
Addition of categorical and ranked activity summary fields in 5 DSSTox Data Files (CPDBAS, DBPCAN, EPAFHM, FDAMDD, NCTRER), corresponding to standard PubChem bioassay activity fields:
PUBCHEM_ACTIVITY_OUTCOME (active/inactive/inconclusive):
ActivityOutcome_CPDBAS_Rat
ActivityOutcome_CPDBAS_Mouse
ActivityOutcome_CPDBAS_Hamster
ActivityOutcome_CPDBAS_Dog_Primates
ActivityOutcome_CPDBAS_Mutagenicity
ActivityOutcome_CPDBAS_SingleCellCall
ActivityOutcome_CPDBAS_MultiCellCall
DSSTox Data Files: Relative "All Updated"


Www.iss.it
Ambiente e connessa prevenzione primaria
http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7
Istituto Superiore di Sanità
Viale Regina Elena 299
00161 - Roma (I)
Telefono:
Fax:
Cancerogeni chimici: strutture e dati sperimentali (ISSCAN)
Documenti relativi
Guida all'uso [PDF - 0.13 MBytes]
Presentation and Guidance for use [PDF - 0.14 MBytes]
Strutture chimiche - Chemical Structures [PDF - 2.22 MBytes]
Dati - Data (file XLS) [ZIP - 0.19 MBytes]
Relazioni struttura-attività - Structure-Activity Relationships (file SDF) [ZIP - 0.32 MBytes]


Toxicology and Chemical Substances
European Chemicals Bureau
ihcp
EUROPEAN COMMISSION
Joint Research Centre
Search
ECB Activities
Biocides
Classification & Labelling
Computational Toxicology
Existing Chemicals
Export-Import
New Chemicals
REACH
Testing Methods
EDEXIM
ESIS
IUCLID 5
Contacts
Documentation
Legislation
Links
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Search
Site Map
What's New
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ECB
The Toxicology and Chemical Substances (TCS) Unit, widely known as European Chemicals Bureau (ECB), is part of the Institute for Health and Consumer Protection (IHCP), which is one of the seven scientific institutes in the European Commission's Joint Research Centre (JRC).
Our mission is to provide scientific and technical support to the conception, development, implementation and monitoring of EU policies on dangerous chemicals. This includes managing the risk assessment process for New and Existing Chemicals, the authorisation process for biocides, and the classification and labelling of hazardous chemicals. Our work also focuses on the development and harmonisation of testing methods and non-testing methods (e.g. QSARs), and the development of guidance documents and tools in support of the REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulation.
For any information concerning
the ECB, please contact the Head of Unit: Steven Eisenreich
the ECB Website, please contact the IT Manager: Rémi Allanou
http://ecb.jrc.it/esis/

Banche dati: referenze

Benigni,R., Bossa,C., Richard,A.M., and Yang,C. (2008): A novel approach: chemical relational databases, and the role of the ISSCAN database on assessing chemical carcinogenicity. *Ann.Ist.Super.Sanità*, 44:48-56.

Yang,C., Richard,A.M., and Cross,K.P. (2006): The Art of Data Mining the Minefields of Toxicity Databases to Link Chemistry to Biology. *Curr.Comput.-Aid.Drug Des.*, 2:135-150.

Richard,A.M., Gold,L.S., and Nicklaus,M.C. (2006): Chemical structure indexing of toxicity data on the Internet: Moving toward a flat world. *Current Opinion in Drug Discovery & Development*, 9:314-325.