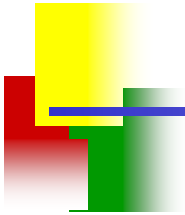



# Physical/Chemical Properties



## EPISuite™ Estimation Methods

# Physical/Chemical Properties

 Provides characteristics used throughout the risk assessment process

- Physical state
- Environmental fate
- Toxicity
- Routes of exposure
  - Human and environmental

# Important Properties

## Common Properties

- Melting point (MP)
- Boiling point (BP)
- Vapor Pressure (VP)
- Water Solubility (WSol)

## Less Common Properties

- Octanol/water partition coefficient ( $K_{ow}$  or P)
- Henry's Law Constant (HLC)
- Dissociation constant ( $pK_A$  or  $pK_B$ )

# Overview of Presentation

- Introduction to EPI Suite™ estimation methods
- Discussion of each physical property
  - What it is
  - What it can tell the assessor
  - How it is estimated
  - Interpreting the results
- EPI demonstration for example chemical
- Hands on session for three sample chemicals

# EPISuite™ - Introduction

- ✚ P2 Framework tool developed over the past 20 years to screen new chemicals lacking experimental data
- ✚ Provides 3 types of results
  - Physical/chemical (P/Chem) properties
  - Environmental fate properties
  - Environmental fate models
- ✚ Free
  - [www.epa.gov/oppt/exposure/docs/episuitedi.htm](http://www.epa.gov/oppt/exposure/docs/episuitedi.htm)

# EPI Suite™ P/Chem Modules

## EPI – Estimation Programs Interface

- **MPBPVP©** - Melting point, boiling point, and vapor pressure
- **LOGKOW©** - Octanol/water partition coefficient
- **WS/KOW©** - Water solubility from Kow
- **Henry's Law Constant Program©** - Air/water partition coefficient

# Experimental Data

- ✚ Reliable experimental data are always preferred over estimated data**
- ✚ EPI Suite can use experimental data to improve the estimations of the other properties**
- ✚ A list of sources for experimental data is provided in the P2 Framework Manual, Appendix B**

# EPI Suite™ - Built in Databases

## EPI Interface is linked to SRC's PHYSPROP Database

- Contains >25,000 chemicals with experimental data:

• MP	10,800	• VP	2,837
• BP	6,629	• pK <sub>A</sub>	1,652
• WS	6,340	• HLC	1,713
• K <sub>ow</sub>	13,500		

## Experimental values are automatically retrieved if available

## Experimental values must be manually entered

- For liquids with unknown MP, enter an MP of 20 °C

# Physical/Chemical Properties

## Provides

- **Basic information on the nature and characteristics of a chemical substance**

## Which gives insight into:

- **Partitioning in the environment**
- **Potential for environmental exposure**
- **Potential routes of human exposure**
- **Toxicity and biological effects**

# Octanol/Water Partition Coefficient

 Provides partitioning between octanol and water

- Concentration in octanol / concentration in water
- Covers a wide range of values
  - Typically reported in log units (i.e.,  $\log K_{ow}$ )

 Indicates

- Partitioning in biological systems
- Absorption through membranes

# $K_{ow}$ (cont.)

 **Important parameter used to by EPI to estimate numerous other properties**

- **Water solubility**
- **Bioconcentration**
- **Soil adsorption**
- **Aquatic toxicity**

 **QSAR Methodology**

- **Uses an atom/fragment contribution method combined with correction factors**

# Log K<sub>ow</sub> Rules of Thumb

Log K <sub>ow</sub>	Indicates to the Assessor:
<1	Highly soluble in water (hydrophilic)
>4	Not very soluble in water (hydrophobic)
>8	Not readily bioavailable
>10	Difficult to measure experimentally. Essentially insoluble in water. Not bioavailable.

# Interpreting $K_{ow}$ Results

- ✚  $K_{ow}$  affects partitioning across biological membranes
  - Octanol is used to mimic fat in biological organisms
  - The higher the  $K_{ow}$ , the more likely a chemical will partition to octanol and, therefore, be present in fat
  - The lower the  $K_{ow}$ , the more likely a chemical will partition to water and, therefore, be present in the body tissues
- ✚  $K_{ow}$  affects absorption through biological membranes
  - Liquids with a  $\log K_{ow}$  of 2-4 tend to absorb well through the skin
  - Chemicals with a  $\log K_{ow} > 4$  tend to not absorb well
  - Chemicals with a  $\log K_{ow}$  of 5-6 tend to bioconcentrate

# MP, BP, and VP

## Provides physical state

- **MP**
  - > 25 °C – solid
  - < 25 °C – liquid
- **BP**
  - < 25 °C – gas

## Indicates

- **Environmental partitioning**
- **Environmental fate**
- **Worker and general population exposure**

# MPBPWIN v1.40, MP & BP

## Melting Point

- EPI provides a weighted average of the results of two methods
  - Method of Joback (group contribution)
  - Gold and Ogle method  $MP = 0.5839 * BP$  (in °K)

## Boiling Point

- Adapted from Stein and Brown Method (group contribution)

# MPBPWIN v1.40, VP

## Vapor Pressure

### ■ Three Estimation Methods

- Antoine
- Modified Grain method
- Mackay method (generally not that applicable)

### ■ Solids

- The preferred method is the Modified Grain method
- The method will use an experimental MP if entered
  - The melting point is used to adjust the vapor pressure from a super-cooled liquid to a solid

### ■ Liquids

- Mean of the Grain and Antoine methods is used

# MP, BP Interpreting Results

## ✚ Environmental partitioning

- Gases are volatilized in the atmosphere
- Solids are present in the atmosphere as particulates (dusts)
- Liquids tend to dissolve more rapidly and have higher water solubility than high melting organic solids

## ✚ Worker and general population exposure

- Gases through inhalation
- Liquids through dermal contact
  - Lower MP tends to increase absorption through the skin, digestive tract, and lungs
- Solids through dermal contact and inhalation of dust
- Liquids and solids through ingestion

# VP – Interpreting Results

## ✚ Environmental Partitioning

- High VP means more likely to be present in the atmosphere as vapor
- VP determines the phase in the atmosphere
  - $> 10^{-4}$  mm Hg - vapor phase
  - $10^{-4} - 10^{-8}$  mm Hg – vapor/particulate mixture
  - $< 10^{-8}$  mm Hg – particulate
- Can be used to gauge the rate of volatilization from soil, plants, and other *dry* surfaces (see HLC for wet surfaces)

## ✚ Exposure

- $< 10^{-6}$  mm Hg – lower limit of concern for human inhalation exposure for vapors ( $\approx$  BP of 400 °C)

# Water Solubility

## Provides

- Degree to which a chemical will dissolve in 1 liter of water

## Indicates to the assessor

- Distribution between environmental compartments
- Potential for environmental exposure through release to aquatic compartment
- Human exposure through ingestion of drinking water

# WSKOW v1.40

## ✚ QSAR based on $\log K_{ow}$

- $\log S \text{ (mol/L)} = 0.796 - 0.854 \log K_{ow} - 0.00728 \text{ MW} + \text{Correction Factors (CF)}$
- $\log S \text{ (mol/L)} = 0.693 - 0.96 \log K_{ow} - 0.0092 (\text{MP } ^\circ\text{K} - 25) - 0.00314 \text{ MW} + \text{CF}$ 
  - Uses 235 correction factors

## ✚ Accepts experimental $K_{ow}$ and MP values

## ✚ Accuracy greatly improved if an experimental MP is provided!

# WS Rules of Thumb

<b>Water solubility (mg/L)</b>	<b>Classification</b>
<b>&gt;10,000</b>	<b>Very soluble</b>
<b>&gt;1,000 – 10,000</b>	<b>Soluble</b>
<b>&gt;100 – 1,000</b>	<b>Moderately soluble</b>
<b>&gt;0.1 – 100</b>	<b>Slightly soluble</b>
<b>&lt;0.1</b>	<b>Insoluble</b>

# Interpreting WS Results

## Chemicals with high WS

- Greater possibility of human and aquatic exposure
- More likely to be absorbed through GI tract or lungs

## Chemicals with low WS

- Less likely to be absorbed into tissues
- Higher potential to bioconcentrate

## Distribution between environmental compartments

- Higher water solubility indicates partitioning to water
  - Possible removal from soil into ground water by rain run-off
  - Possible removal from atmospheric into ground water by rain washout

# WS – Additional Influences

## Potential for exposure

- Environmental exposure due to presence in surface water
- Human exposure through ingestion of drinking water
- $<10^{-6}$  g/L – lower limit of concern for adverse effects, aquatic exposure, and general population exposure

## Degradation potential

- Water insoluble chemicals may not degrade in the environment
  - Microorganisms may be unable to absorb them

# Henry's Law Constant

 The ratio of a chemical's concentration in the gas phase to that in the aqueous phase (at equilibrium)

- **Units**

- atm-m<sup>3</sup>/mole (EPI)
- Pa-m<sup>3</sup>/mole
- Dimensionless (1/40.9 \* atm-m<sup>3</sup>/mole)

# Henry's Law Constant

## Provides

- An indication of a chemical's volatility from water

## Indicates to the assessor

- Environmental partitioning
- Amount removed by stripping in a sewage treatment plant
- Environmental exposure

# HENRYWIN v3.10

## Three different estimations provided:

- Vapor pressure / water solubility estimate
  - Best method, but only using experimental VP and WS
- Group method estimate
  - Preferred method, but not always provided
  - Smaller set of fragments, no estimates for many structure types
- Bond contribution method estimate
  - Larger set of fragments, estimates for more structure types

## Based on methodology originally described by Hine and Mookerjee

- Updated with additional fragments and correction factors
- Updated to allow estimation at different temperatures

# Interpreting HLC Results

  $>10^{-3}$  atm-m<sup>3</sup>/mol

- **Rapid volatilization from water to air**
  - Stripped from sewage treatment plants
  - Volatilizes readily from environmental waters

  $10^{-7}$  atm-m<sup>3</sup>/mol is the HLC of water

- **Values  $<10^{-7}$  indicate negligible volatilization from water to air**
  - Not stripped from sewage treatment plants
  - Does not volatilize from environmental waters

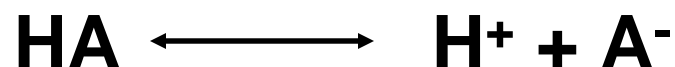
# HLC Rules of Thumb

<b>HLC</b>	<b>Classification</b> (Volatility from Water)
$\geq 10^{-1}$	<b>Very volatile</b>
$10^{-1} - 10^{-3}$	<b>Volatile</b>
$10^{-3} - 10^{-5}$	<b>Moderately volatile</b>
$10^{-5} - 10^{-7}$	<b>Slightly volatile</b>
$< 10^{-7}$	<b>Nonvolatile</b>

# Dissociation Constants – pKa/pKb

## ✚ Provides

- The concentration of the dissociated (ionized) and undissociated (neutral) forms of an acid, base, or organic salt in water.



## ✚ Indicates to the assessor

- WS, VP, log  $K_{ow}$  and HLC trends as a function of pH
- Ionization radically affects partitioning in the environmental

# Interpreting Results

 **As the percent ionization increases:**

- **Water solubility increases**
  - Ions are more soluble
- **Vapor pressure decreases**
  - Ions are less volatile
- **Henry's Law constant decreases**
- **Log  $K_{ow}$  decreases**

# Sources of Experimental Data

## Most useful for analogs

- **IUPAC Compilations**
  - **Dissociation Constants of Organic Acids in Aqueous Solution**
  - **Dissociation Constants of Organic Bases in Aqueous Solution**
- **Other compilations**
  - **Techniques of Chemistry. Vol II. Organic Solvents**
- **Primary Literature**
- **Handbooks**
- **Internet**

# Common Organic Acids

<b>Compound</b>	<b>pK<sub>A</sub> Range</b>
<b>Carboxylic Acids</b>	<b>1 – 5</b>
<b>Benzoic Acids</b>	<b>1 – 5</b>
<b>Phenols</b>	<b>4 – 10</b>
<b>Alcohols</b>	<b>9 – 15</b>
<b>Thiols</b>	<b>8 – 12</b>
<b>Thiophenols</b>	<b>2 – 7</b>
<b>Sulfonic acids</b>	<b>4 – -4</b>
<b>Phosphoric acids</b>	<b>3 – -4</b>

# Running EPI Suite™

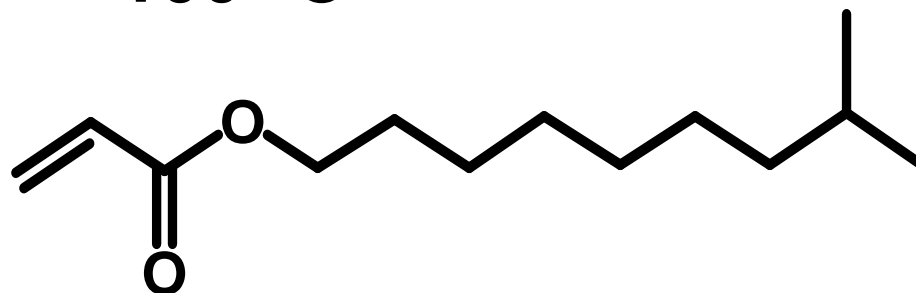


EPI Suite v3.12

**CAS # 1330-61-6**

**2-Propenoic acid, isodecyl ester**

**MP = -100 °C**



# EPI Suite™ – Input Screen

**EPI v3.12**

File Edit Functions BatchMode ShowStructure Output Fugacity STP Other Help

PhysProp Previous Get User Save User CAS Input CALCULATE ClearInputField What's New

Enter SMILES:

Chem NAME:

NameLookup

Henry LC (atm-m<sup>3</sup>/mole):  Wat Sol (mg/L):  MP:

Vap Pr (mm Hg):  BP:

River:  Lake:  Log Kow :

Water Depth (meters):  1


Wind Velocity (m/sec):  5

Current Velocity(m/sec):  1

Output

Summary

Full



The EPI (Estimation Programs Interface) Suite™ was developed by the EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). Important information on the application of the individual models contained within the EPI Suite™ is included in the EPI Suite™ User's Guide.

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# EPI Suite™ – Chemical Entry

The screenshot displays the EPI Suite v3.12 software interface. The main window has a menu bar (File, Edit, Functions, BatchMode, ShowStructure, Output, Fugacity, STP, Other, Help) and a toolbar with buttons: PhysProp, Previous, Get User, Save User, CAS Input, CALCULATE, ClearInputField, and What's New. The main form contains several input fields: 'Enter SMILES:', 'Chem NAME:', 'NameLookup', 'Henry LC (atm-m3/mole):', 'River:' (with a dropdown menu), 'Water Depth (meters):', 'Wind Velocity (m/sec):', and 'Current Velocity(m/sec):'. A modal dialog box titled 'SMILECAS Database Retrieval' is open, prompting the user to 'Enter CAS Number (with or without hyphens):'. The text '1330-61-6' is entered in the dialog's input field. Below the input field are 'OK' and 'Cancel' buttons. A blue arrow points from the 'River' dropdown menu to the 'OK' button. In the bottom left corner, there is the EPA logo and a text box containing the following information:

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# EPI Suite™ – Calculations

EPI v3.12

File Edit Functions BatchMode ShowStructure Output Fugacity STP Other Help

PhysProp Previous Get User Save User CAS Input **CALCULATE** 3 Field What's New

Enter SMILES: O=C(C=C)OCCCCCCCCC(C)C  
001330-61-6


Chem NAME: 2-Propenoic acid, isodecyl ester  
NameLookup

Henry LC (atm-m3/mole):  Wat Sol (mg/L):  MP: -100 1  
Vap Pr (mm Hg):  BP:

River: Lake: Log Kow :

Water Depth (meters): 1  
Wind Velocity (m/sec): 5  
Current Velocity(m/sec): 1

Output  
 Summary 2  
 Full



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# EPI Suite™ – Output

SMILES : O=C(C=C)OCCCCCCCCC(C)C

CHEM : 2-Propenoic acid, isodecyl ester

CAS NUM: 001330-61-6

MOL FOR: C13 H24 O2

MOL WT : 212.34

----- EPI SUMMARY (v3.10) -----

## Physical Property Inputs:

Water Solubility (mg/L): -----

Vapor Pressure (mm Hg) : -----

Henry LC (atm-m<sup>3</sup>/mole) : -----

Log Kow (octanol-water): -----

Boiling Point (deg C) : -----

Melting Point (deg C) : -100.00

# Octanol Water Partition Coefficient

## Summary output

Log Octanol-Water Partition Coef (SRC):  
Log Kow (KOWWIN v1.66 estimate) = 5.07

## Full Output

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	-CH3 [aliphatic carbon]		1.0946
Frag	7	-CH2- [aliphatic carbon]		3.4377
Frag	1	-CH [aliphatic carbon]		0.3614
Frag	1	=CH2 [olefinic carbon]	0.5473	0.5184
Frag	1	=CH- or =C< [olefinic carbon]	0.4911	0.3836
Frag	1	-C(=O)O [ester, aliphatic attach]	0.5184	-0.9505
Const		Equation Constant	0.3614	0.2290
			0.3836	
			0.9505	
			Log Kow =	5.0742

# BP, MP, and VP

## Summary output

**Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.40):**

**Boiling Pt (deg C): 253.36 (Adapted Stein & Brown method)**

**Melting Pt (deg C): 11.48 (Mean or Weighted MP)**

**VP(mm Hg,25 deg C): 0.0227 (Mean VP of Antoine & Grain methods)**

**MP (exp database): -100 deg C** ←

**BP (exp database): 158 @ 50 mm Hg deg C** ←

# Water Solubility

## Summary output

Water Solubility Estimate from Log Kow (WSKOW v1.40):  
Water Solubility at 25 deg C (mg/L): 3.034  
log Kow used: 5.07 (estimated)  
melt pt used: -100.00 deg C

## Full Output

Log Kow (estimated) : 5.07  
Log Kow (experimental): not available from database  
Log Kow used by Water solubility estimates: 5.07

Equation Used to Make Water Sol estimate:

Log S (mol/L) = 0.693-0.96 log Kow-0.0092(Tm-25)-0.00314 MW + Correction

Melting Pt (Tm) = -100.00 deg C (Use Tm = 25 for all liquids)

Correction(s):

-----

No Applicable Correction Factors

Log Water Solubility Value (moles/L) : -4.845

Water Solubility at 25 deg C (mg/L): 3.034

# Henry's Law Constant

## Summary Output

Henry's Law Constant (25 deg C) [HENRYWIN v3.10]:

Bond Method : 1.18E-003 atm-m<sup>3</sup>/mole

Group Method: 1.20E-003 atm-m<sup>3</sup>/mole

Henry's LC [VP/WSol estimate using EPI values]: 2.090E-003 atm-m<sup>3</sup>/mole

# Hands On Session

- ✚ **Run the example chemicals through EPI**
  - **Sample 1**
  - **Sample 2**
  - **Sample 3**
- ✚ **Identify the physical/chemical property estimates**
- ✚ **Enter results into the Sustainable Futures Assessment Summary for each chemical**