Interpretive Assistance

for

Sustainable Futures Summary

Assessment

Updated January 22, 2007

This document was developed to help compile estimation results from U.S. EPA's Sustainable Futures (SF) / P2 Framework methods and is used during SF hands-on training in the proper use of the methods.

Participants in the voluntary Sustainable Futures Initiative are asked to submit the information contained in this worksheet along with their SF PMNs in the submitter's choice of format.

NOTE: Due to the dynamic nature of the Internet, the URLs listed in this document may have changed. A search using any of the publicly available search engines should locate the new URL.

Interpretive Assistance
for
Sustainable Futures Summary Assessments

This document was developed to help interpret estimations from the Sustainable Futures / P2 Framework models. Information is also included here which helps assign concern levels to estimations based on U.S. EPA OPPT's New Chemicals Program criteria http://www.epa.gov/opptintr/newchems/index.htm. Information contained in this document is presented in greater detail in the P2 Framework Manual. For more information on the models, estimations provided, and interpretation of results, please check the manual at http://www.epa.gov/opptintr/newchems/pubs/sustainablefutures.htm.

PLEASE NOTE: It is strongly suggested that any Sustainable Futures Summary Assessment provide an interpretation of model estimations relative to potential risk for the chemical being evaluated.

Topic Page

Sustainable Futures / P2 Framework Models

EPISuite™ download at no cost from: www.epa.gov/oppt/exposure/docs/episuitedl.htm

ECOSAR download at no cost from: http://www.epa.gov/oppt/newchems/21ecosar.htm

OncoLogic download at no cost from:
http://www.epa.gov/oppt/newchems/tools/oncologic.htm

E-FAST download at no cost from: http://www.epa.gov/opptintr/exposure/docs/efast.htm

ChemSTEER download at no cost from:
http://www.epa.gov/oppt/exposure/docs/chemsteer.htm

Access PBT Profiler at: www.pbtprofiler.net

Analog Identification Methodology (AIM): Contact EPA for access

PHYSICAL/CHEMICAL PROPERTIES AND ENVIRONMENTAL FATE ESTIMATIONS

EPISuite™ - Running the models

The modules in EPISuite can be used by either running the EPI platform which automatically initiates a run of all models, or by running each individual module as a stand alone program. Please note, when running the programs individually as stand alone models, the user has the ability to change many default parameters that would otherwise be unavailable through the larger EPI platform.

EPISuite™ - Entering Data

The chemical structure can be entered using SMILES notation - or - if the chemical has a CAS Registry Number, the CAS numbers may be entered and the structure will be retrieved from the EPISuite™ built-in database if available. The newest version of EPISuite™ (3.12) also has a name look-up function. If any experimental data are available for the chemical, then all data should be entered into the input screen for EPISuite™. Experimental data can be retrieved from the built-in PHYSPROP database in EPISuite™ by entering the chemical identifier, and choosing the PhysProp button in the upper left corner. For chemicals that are known liquids with no experimental MP data, enter 20 deg C as an experimental MP into the input screen for all EPISuite™ predictions.

EPISuite™ - Output Screen

The program can be run in 2 modes, and the option window to select a mode is located in the bottom right portion of the data entry screen. When the program is run in **"summary" mode**, the user will only be provided the quantitative/qualitative results for each endpoint with no supplemental information on how the endpoint was predicted. However, in **"full" mode**, the user will be given additional information regarding derivation of the prediction such as the fragments identified which are relevant to the endpoint, coefficient values, corrections factors, etc.

Interpreting Results from EPISuite™

Melting Point and Boiling Point - Estimated by MPBPWIN

MP < 25 deg C	Chemical is assessed as a liquid
MP > 25 deg C	Chemical is assessed as a solid
BP < 25 deg C	Chemical is assessed as a gas

Vapor Pressure - Estimated by MPBPWIN

$\geq 10^{-4}$	Chemical mostly in the vapor (gas) phase
$10^{-5} - 10^{-7}$	Chemical in the vapor and particulate phase
$\leq 10^{-8}$	Chemical mostly in the solid phase

For chemicals with a VP < 10^{-6}, there is low concern for inhalation exposure.

Water Solubility (mg/L) - Estimated by WSKOWWIN

> 10,000	Very soluble
> 1,000 - 10,000	Soluble
> 100 - 1,000	Moderate solubility
> 0.1 - 100	Slightly soluble
< 0.1	Negligible solubility

Log K_{ow} (Log P) - Estimated by KOWWIN

< 1	Highly soluble in water (hydrophilic)
> 4	Not very soluble in water (hydrophobic)
> 8	Not readily bioavailable
> 10	Not bioavailable - difficult to measure experimentally

Henry's Law Constant (atm-m^3/mole) - Estimated by HENRYWIN

$\geq 10^{-1}$	Very volatile from water
10^{-1} - 10^{-3}	Volatile from water
10^{-3} - 10^{-5}	Moderately volatile from water
10^{-5} - 10^{-7}	Slightly volatile from water
$< 10^{-7}$	Nonvolatile

If experimental vapor pressure ***and*** water solubility data are available and entered as input data into EPISuite™, then the VP/Wsol estimate (instead of the bond or group estimation method) should be used.

Atmospheric Oxidation Half-life - Estimated by AOPWIN

≤ 2 hours	Rapid
2 hrs - ≤ 1 day	Moderate
> 1 day - ≤ 10 days	Slow
>10 days	Negligible
>2 days	Has potential for long range transport in air

Hydrolysis Rates - Estimated by HYDROWIN

- Only Esters, Carbamates, Epoxides, Halomethanes, and certain Alkyl Halides are estimated in HYDROWIN.

Biodegradation - Estimated by BIOWIN: 6 Models available in EPISuite™

1. Probability of Rapid Biodegradation (BIOWIN):

BIOWIN Linear and BIOWIN Nonlinear

> 0.50	Likely to biodegrade fast
< 0.50	*Not* likely to biodegrade fast

2. Expert Survey Biodegradation (Primary and Ultimate):

Predicted Rating	Time Required for Biodegradation	Predicted Rating	Time Required for Biodegradation
5.0	Hours	3.0	Weeks
4.5	Hours - days	2.5	Weeks - months
4.0	Days	2.0	Months
3.5	Days - weeks	1.0	Longer

3. Biodegradability in the MITI-1 (OECD 301C) test: (MITI): MITI Linear and MITI Nonlinear

> 0.50	Ready Biodegradable
< 0.50	Not Ready Biodegradable

4. Ready biodegradability prediction based on a Bayesian battery approach:

Yes = Ready biodegradable
No = Not ready biodegradable

Soil Adsorption Coefficient (Log K_{oc}) - Estimated by PCKOCWIN

≥ 4.5	Very strong sorption to soil and sediment, *negligible migration potential to groundwater*
3.5 - 4.4	Strong sorption to soil and sediment, *negligible to slow migration potential to groundwater*
2.5 - 3.4	Moderate sorption to soil and sediment, *slow migration potential to groundwater*
1.5 - 2.4	Low sorption to soil and sediment, *moderate migration potential to groundwater*
< 1.5	Negligible sorption to soil and sediment, *rapid migration potential to groundwater*

Bioconcentration Factors - Estimated by BCFWIN

> 5000	High bioconcentration potential
1000 - 5000	Moderate bioconcentration potential
< 1000	Low bioconcentration potential

STPWIN - Percent Removal in Sewage Treatment Plants

–Gives an indication of the percent removed from biodegradation (Bio P), sludge adsorption (Bio S), and aeration (Bio A) in a POTW or Sewage Treatment Plant.

Old Method: Negligible biodegradation. (half-life = 10,000 hours) is the default value for the primary clarifier (P), aeration vessel (A), and final settling tank (S) unless otherwise specified in the input screen for EPISuite™.

Draft Method: Biodegradation accounted for in calculation of STP removal, in addition to P,A, and S tanks.

**Unless experimental data indicate otherwise, the EPA will not use a value greater than 90% when determining rate of removal from STP.*

LEV3EPI - Fugacity Model

–Provides overall persistence derived from a level III multimedia model. Gives an indication of which environmental compartment the chemical is expected to partition to and calculates an approximate overall environmental persistence time. The level III model considers degradation (unlike level I and II models) and can be run for a variety of release scenarios.

WVOL - Volatilization from Water

–Uses molecular weight, Henry's Law Constant, and water solubility to estimate an ***upper*** limit for volatilization from a body of water. The model ***does not*** take into account potential adsorption to sediment and suspended organic matter when the K_{oc} is high, which can increase the volatilization half-life significantly. Therefore, if the K_{oc} for a given chemical is high, the volatilization half-lives for a model river and model lake are expected to be significantly lower than predicted in WVOL.

PERSISTENCE

U.S. EPA describes Persistence criteria in the PBT category for Premanufacture Notices in the Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances at http://www.epa.gov/tri/pbt-final_rule.pdfhttp://www.epa.gov/fedrgstr/EPA-TOX/1999/November/Day-04/t28888.htm and in the final rule for TRI reporting of PBT Chemicals http://www.epa.gov/tri/pbt-final_rule.pdf. The criteria below are for compartmental half-lives and are used by the PBT Profiler (described in this document) to estimate environmental persistence potential of chemicals based on the predominant compartment. These Persistence criteria are:

PERSISTENCE (compartmental half-life)	Not Persistent	Persistent	
Water, Soil, Sediment*	< 60 d	≥ 60 d	> 180 d
Air**	≤ 2 d	> 2 d	

* New Chemical Program Criteria
** TRI Reporting Criteria

HAZARD ESTIMATIONS

Aquatic Toxicity Hazard - ECOSAR

Develop Full Standard Aquatic Toxicity Profile

The standard aquatic toxicity profile consists of 3 acute values (fish LC_{50}, daphnid LC_{50}, and algae EC_{50}), 3 chronic values (fish ChV, daphnid ChV, and algae ChV), and determination of a chronic COC which will be used as input into E-FAST to determine aquatic exposure levels. Examples of toxicity values that are generally used to fulfill the standard aquatic toxicity profile are provided below.

Organism	Acute Toxicity Values	Chronic Toxicity Values
Fish	96-hour LC_{50}	30-day ChV*
Daphnid (Aquatic Invertebrate)	48-hour LC_{50}	ChV* or 16-day EC_{50}
Algae	72- or 96-hour EC_{50}	ChV*
Chronic Concentration of Concern (COC)	Lowest ChV* value/10	

* A ChV value is defined as the geometric mean of the NOEC and the LOEC

Chronic COC for Aquatic Toxicity Profile:
Chronic COC = Lowest ChV / (10)
If a NOEC value is available from a chronic study for any species, that value can be used directly as the chronic COC. (No assessment factor needed)

A full standard profile for each chemical should be created using predicted data or experimental data. If no predicted or experimental data are available for the chemical of interest, then analog data may be used. If a single measured or predicted toxicity value is available for a species but the corresponding acute or chronic value is not, then a ratio (derived from experimental data sets) can be used to estimate the corresponding acute or chronic toxicity value:

Chronic toxicity estimate = (acute toxicity value) / (ratio)
Acute toxicity estimate = (chronic toxicity value) x (ratio)

A ratio of 10 is commonly applied to fish and daphnids and a ratio of 4 is commonly applied to algae for most chemical classes. Example calculations are provided below.

Fish LC_{50} = 0.10 mg/L → extrapolated fish ChV = (0.10 mg/L)/10 = **0.01 mg/L (ppm)**
Algae ChV = 0.02 mg/L → extrapolated algae EC_{50} = (0.02 mg/L) x 4 = **0.08 mg/L (ppm)**

Specific chemical classes with their own ratios:
polycationic polymers: a ratio for fish = 18, ratio for daphnids = 14, ratio for green algae = 4
nonionic surfactants: a ratio for fish = 5, ratio for daphnids = 5, ratio for green algae = 4
anionic surfactants: a ratio for fish = 6.5, ratio for daphnids = 6.5, ratio for green algae = 4

A full toxicity profile needs to be developed to perform an aquatic toxicity assessment. If an acute or chronic toxicity endpoint cannot be determined for one or more species from measured data on the chemical or analog or from predicted data, then category data can be used to fulfill the endpoint. For example, a fish or daphnid toxicity value can be estimated using the fish-to-daphnid toxicity ratio of chemicals within the same category (e.g., acrylates). Use data from multiple chemicals if possible. All assumptions and toxicity data used for the estimation need to be documented in the Sustainable Futures Summary Assessment.

The following criteria can be used to assign aquatic toxicity concern levels:

SF Concern	ECOSAR Results
Low	All 3 acute values are >100 mg/L, AND all three chronic values are >10.0 mg/L, or there are "No Effects at Saturation" (or NES). **NES occurs when a chemical is not soluble enough to reach the effect concentration, i.e., the water solubility is lower than an effect concentration, or, for liquids, when K_{ow} criteria are exceeded for an endpoint. For solids, NES is expected if K_{ow} exceeds the specific SAR K_{ow} cutoffs, or the effect concentration is more than one order of magnitude (≥10 X) less than water solubility.*
Moderate	Any of the 3 acute values are >1.0 mg/L and <100 mg/L, OR any of the chronic values are >0.1 mg/L and <10.0 mg/L
High	Any of the 3 acute values are <1.0 mg/L, OR any of the chronic values are <0.1 mg/L

NOTE: K_{ow} cutoffs are specific to each SAR used in ECOSAR. The criteria can be found on the bottom of the results screen for ECOSAR or in the ECOSAR User's Manual available for download at http://www.epa.gov/oppt/newchems/sarman.pdf.

NOTE: A chemical's half-life in the environment (e.g., hydrolysis half-life) can determine the type of risk assessment performed. If the half-life is *less than one hour*, then only the degradation products are assessed. If the half-life is *greater than one hour, but less than 14 days*, then both the intact chemical and its products are assessed. If the half-life is *greater than 14 days*, then only the parent chemical is generally assessed.

NOTE: Guidance on the evaluation of polymers can be found in:
Boethling R.S. and J. V. Nabholz. 1997. "Environmental assessment of polymers under the U.S. Toxic Substances Control Act". *In:* Hamilton, J.D. and R. Sutcliffe, eds. Ecological assessment of polymers: Strategies for product stewardship and regulatory programs. New York, NY: Van Nostrand Reinhold, 187-234. ISBN 0-442-02328-6

Human Health Hazard - Cancer

Interpretation of OncoLogic Results:

SF Concern	OncoLogic Results	Definition - OncoLogic Result
Low	Low	Unlikely to be a carcinogen
Further Research Needed	Marginal	Likely to have equivocal carcinogenic activity
Moderate	Low-Moderate	Likely to be weakly carcinogenic
	Moderate	Likely to be moderately active carcinogen
High	Moderate-High	Highly likely to be a moderately active carcinogen
	High	Highly likely to be a potent carcinogen

Interpretation of Experimental Data:

SF Concern	Definition - Experimental Data
Low	Negative experimental data
Moderate	Positive cancer bioassay in experimental animals ***or*** chemical class known to produce carcinogenic effects
High	Positive experimental data in humans (e.g. epidemiology study)

NOTE: Measured data from a properly conducted study on the SF chemical or a relevant analog always takes precedence over predicted data.

Human Health Hazard - Non-Cancer

Criteria for Assigning Non-Cancer Hazard Concern Levels:

SF Concern	Definition - Experimental Data
Low	No basis for concern identified ***or*** systemic toxicity with NOAEL ≥ 1000 mg/kg/day; only minor clinical signs of toxicity; liver and/or kidney weight increase or clinical chemistry changes with LOAEL ≥ 500 mg/kg/day
Moderate	Suggestive animal studies for chemical or analog(s) ***or*** chemical class known to produce toxicity ***or*** organ pathology (gross and/or microscopic) with LOAEL ≤ 500 mg/kg/day; clinical chemistry changes and organ weight changes at ≤ 500 mg/kg/day; NOAEL ≤ 1000 mg/kg/day
High	Evidence of adverse effects in humans ***or*** conclusive evidence of severe effects in animal studies. Death, organ pathology (microscopic) at LOAEL ≤ 100 mg/kg/day; multiple organ toxicity; NOAEL ≤ 10 mg/kg/day.

NOTE: Most often, regulatory decisions will be made based on the following human health effects: reproductive; immune; developmental; neurotoxicity; and systemic. If analog data are used, absorption considerations should be made for the chemical of interest.

NOTE: Assistance on the evaluation of non-cancer human health concerns of polymers can be found in: P2 Framework Manual, Oct 2003 version, edited Jan 2004, pg. 169-170 at http://www.epa.gov/oppt/p2framework/docs/p2manua.htm

PBT POTENTIAL ESTIMATIONS

PBT Profiler - U.S. EPA describes Persistence, Bioaccumulative, and Toxicity (PBT) criteria in the PBT category for Premanufacture Notices in the Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances at http://www.epa.gov/tri/pbt-final_rule.pdfhttp://www.epa.gov/fedrgstr/EPA-TOX/1999/November/Day-04/t28888.htm and in the final rule for TRI reporting of PBT Chemicals http://www.epa.gov/tri/pbt-final_rule.pdf. These criteria are used by the PBT Profiler to estimate PBT potential of chemicals.

These PBT criteria are:

PERSISTENCE	Not Persistent	Persistent	
Water, Soil, Sediment*	< 60 d	≥ 60 d	> 180 d
Air**	≤ 2 d	> 2 d	
BIOACCUMULATION	Not Bioaccumulative	Bioaccumulative	
Fish BCF*	< 1000	≥ 1000	≥ 5000
TOXICITY	Not Toxic	Toxic	
Fish ChV*	> 10 mg/L *or* No Effects at Saturation	0.1-10 mg/L	< 0.1 mg/L

NOTE: The PBT Profiler is not appropriate for certain types of chemicals, such as metals. Before using the PBT Profiler determine if the chemical being evaluated is appropriate for running in the PBT Profiler. Extensive information is provided within the on-line model at www.pbtprofiler.net
* New Chemical Program Criteria
** TRI Reporting Criteria

Also, ***the EPA DOES NOT use the PBT Profiler to regulate chemicals***. The toxicity assessment performed by the PBT Profiler only considers potential hazards due to chronic exposure to the aquatic environment and does not perform a quantitative human health hazard assessment. When the Agency reviews a chemical for its PBT characteristics, they also consider potential human health effects due to environmental exposure in addition to aquatic toxicity. ***In the U.S. EPA New Chemical Program, EPA maintains a "no release to the environment" policy for all PBT chemicals.***

IMPORTANT NOTE:
Evaluate exposure if a moderate or high hazard concern has been identified for *any* endpoint.

EXPOSURE ESTIMATIONS

Aquatic Exposure - E-FAST

Predicted Environmental Concentration (PEC):
Amount expected to be found in surface water after release from industrial processes; also called surface water concentration (SWC).

Estimated values can be determined using E-FAST and found under the "General SIC Code Information" tab in the results screen. The **10% percentile, 7Q10 stream concentrations (μg/L)** are used for an SF Assessment.

To run E-FAST you will need to determine a chronic **Concentration of Concern (COC)** based on the toxicity values derived in the Aquatic Toxicity section. The COC is one of the inputs for the E-FAST program and an explanation for the determination of a chronic COC can be found on the following page of this document.

Human Exposure - ChemSTEER and E-FAST

For Occupational Exposure Doses:
LADD, ADD, and APDR values will be estimated by **ChemSTEER**

For General Population Exposure Doses:
LADDpot, ADDpot, and ADRpot values will be estimated by **E-FAST.** The **10% percentile values (mg/kg/day)** are used for an SF Assessment.

Lifetime Average Daily Dose (LADD or LADDpot):
The predicted lifetime exposure used to determine cancer risk usually based on an average lifetime of 70 - 75 years and a working lifetime of 30 - 40 years.

Potential Average Daily Dose (ADD or ADDpot):
The predicted dose that represents potential chronic exposure based on duration of repeated exposure usually approximating an average of 30 years.

Potential Acute Dose Rate (APDR or ADRpot):
The predicted acute dose rate that represents acute exposure usually based on single 8 hour working day exposure duration.

NOTE: For the purposes of an SF Assessment, the defaults for average lifetime, body weight, exposure duration, and ingestion rate are pre-set in both ChemSTEER and E-FAST and should not be changed unless accurate data for these inputs are available.

RISK ESTIMATIONS

Reminder: RISK = HAZARD x EXPOSURE

For chemicals with an identified hazard concern, the potential exposure must be determined to make an assessment of risk. If a low concern for hazard is identified (hazard approx. = 0) or very low exposure is identified (exposure approx. = 0), then there is an inherently low concern for risk because of the mathematical relationship between hazard and exposure.

Estimating Aquatic Risk

Determine an Acute and Chronic Concentration of Concern (COC):
Concentration at which potential acute or chronic aquatic toxicity may be of concern for aquatic species. Calculate a COC for every species in the full profile.

Acute COC:
Acute COC for fish = LC_{50} / (5)
Acute COC for daphnia = EC_{50} / (5)
Acute COC for algae = EC_{50} / (4) **-OR-** If an **algae ChV** value exists, use that value as the acute COC and do not estimate the COC using an EC_{50} value divided by a factor.
If a NOEC value is available from an acute study for any species, that value can be used directly as the acute COC. (No assessment factor needed)

Chronic COC:
Chronic COC for fish = ChV / (10)
Chronic COC for daphnia = ChV / (10)
Chronic COC for algae = ChV / (10)
For experimental data, if EC_{10} > NOEC, use EC_{10} = ChV. If EC_{10} < NOEC, use NOEC = ChV

Example calculations are provided below:

Fish LC_{50} = 0.10 mg/L → calculated Acute COC = (0.10 mg/L) /5 = **0.02 mg/L (ppm)**
Daphnid ChV = 0.02 mg/L → calculated Chronic COC = (0.02 mg/L) /10 = **0.002 mg/L (ppm)**

NOTE: COCs are rounded up to 1 significant digit (e.g., a COC of 1.75 ppb is rounded up to 2 ppb). Most COC values less than 1 ppb are rounded up to 1 ppb for the assessment due to limitations in reliable analytical methods to test below 1 ppb, should verification be needed.

No values less than 1 ppb (traditional lower detection limit) should be reported; unless SAR, analogs, or experimental data analysis support a COC < 1 ppb.

Estimating Acute Aquatic Risk

The potential for acute risk to aquatic organisms exists if the predicted environmental concentration (PEC) is greater than the acute concentration of concern (COC).

If Acute COC > PEC Low concern for risk
If Acute COC < PEC Potential for risk

Estimating Chronic Aquatic Risk

The potential for chronic risk to aquatic organisms may exist if the PEC exceeds the chronic COC, AND the exceedance occurs for 20 days or more per year. This is because although there is a potential for the concentration of the chemical in the water to reach levels exceeding the hazardous level, the levels are not exceeded for a sufficient duration of time to induce any chronic effects. The 20-day criterion is derived from partial life-cycle tests (daphnid chronic and fish early life- stage tests) that typically range from 21 to 28 days in duration. Low concern for chronic risk exists if the COC is exceeded on fewer than 20 days per year, or the PEC is less than the chronic COC.

E-FAST will predict how many days per year the PEC exceeds the COC. The number of days the COC is exceeded can be found on the "PDM SIC" tab in the output screen of E-FAST.

EXAMPLE Worksheet for Identification of Acute and Chronic Risk to Aquatic Organisms:

Acute Endpoint	Value	Factor	Acute COC	PEC	Risk?
Fish LC50	0.079 ppm	5	0.02 ppm	0.055 ppm	**Yes**
Daphnid LC50	0.11 ppm	5	0.02 ppm	0.055 ppm	**Yes**
Algae EC50	0.083 ppm	4	0.07* ppm	0.055 ppm	No

* Since an algae ChV value was available (see below), the ChV value was used as the algae acute COC.

Chronic Endpoint	Value	Factor	Chronic COC	PEC	Risk?
Fish ChV	0.018 ppm	10	0.002 ppm	0.055 ppm	**Yes***
Daphnid ChV	0.027 ppm	10	0.003 ppm	0.055 ppm	**Yes***
Algae ChV	0.067 ppm	10	0.007 ppm	0.055 ppm	**Yes***

*However, E-FAST indicated that the PEC exceeds the COC for only 9.4 days per year. Since that is below the 20 day criterion, there is no potential for chronic risk to the aquatic environment.

Example Summary of Aquatic Risk : There is potential for acute risk to the aquatic environment because the PEC is greater than the acute COC (for fish and daphnids). There is low concern for chronic risk because even though the PEC exceeds the chronic COC for fish, it is only exceeded for 9.4 days according to E-FAST and under EPA guidelines, this is not sufficiently long enough duration to induce chronic effects.

Estimating Human Health Non-Cancer Risk

For the determination of risk to the human population from non-cancer human health effects, a quantitative value called the Margin of Exposure (MOE) is calculated. This "margin" is essentially the established "safety buffer" between the hazardous effects level (dose) and the predicted exposure dose. The EPA OPPT office utilizes margins of exposure that they believe are sufficiently protective of human health when assessing new chemicals. The calculated MOEs for each chemical are compared to the MOE criteria used by the OPPT office and the results are evaluated to determine the potential for risk. When referring to non-cancer effects, these margins of exposure or "safety buffers" must be at least 100X or 1000X protective of human health depending on the type of non-cancer data identified in the hazard assessment.

If hazard data for ANY of the non-cancer health effect endpoints have indicated a moderate or high hazard concern, then an MOE for EACH moderate/high concern endpoint should be determined! The lowest MOE value calculated from that group should be recorded for assessment purposes and will be used as the quantitative value to determine the potential overall risk to human health from non-cancer effects.

The lowest MOE will represent the "worst-case" scenario for the chemical and therefore, if the lowest MOE does not indicate a risk, then there is an assumed "low potential for risk" for all other endpoints which had mathematically larger MOE values.

However, if even one of the endpoints has a calculated MOE indicating the potential for risk, then overall the chemical should be flagged as having potential risks to human health. The subsequent pages give more in-depth assistance on the determination of MOE for acute and chronic risk from occupational exposure and from exposures to the general population.

The following table shows the human health non-cancer endpoints and the corresponding acute/chronic exposure values to use for calculation of an MOE:

Endpoint	Exposure dose used for MOE calc.
Single Dose Studies	
Acute Toxicity	ADRpot (acute) *Acute risk is ONLY assessed for chemicals with an LD_{50} value < 50 mg/kg.
Repeated Dose Studies	
Irritation	Can not be used to determine MOE
Skin Sensitizer	Can not be used to determine MOE
Reproductive Effects	ADDpot (chronic)
Immune System Effect	ADDpot (chronic)
Developmental Toxicity	ADRpot (acute)
Genotoxicity	Can not be used to determine MOE
Mutagenicity	Can not be used to determine MOE
Neurotoxicity	ADDpot (chronic)
Systemic Effects	ADDpot (chronic)

Estimating Acute Risk to the General Population using an MOE:

NOTE: When the acute toxicity studies indicate LD_{50} values > 50 mg/kg for a chemical, there is no need to calculate a Margin of Exposure (MOE) for acute exposure and a low concern for acute risk is assumed.

There is a potential acute hazard concern for chemicals with an LD_{50} < 50 mg/kg. An MOE needs to be calculated and the potential for acute risk to the general population needs to be assessed when acute toxicity studies with LD_{50} values < 50 mg/kg have been identified.

Margin of Exposure (MOE) based on Acute Exposure:
Ratio of the identified effect level (LD_{50} value determined in health hazard section) to the estimated acute dose rate (predicted from E-FAST).
MOE_{acute} = LD_{50} (mg/kg) / ADRpot (from E-FAST)
MOE < 1000 indicates potential for risk
MOE > 1000 indicates low concern for risk

Estimating Chronic Risk to General Population or to Workers using an MOE:

NOTE: Regulatory decisions are most often based on the following human health effects: reproductive; immune; developmental; neurotoxicity; and systemic.

Margin of Exposure (MOE) based on Chronic Exposure: An MOE is the ratio of the No-Observed Adverse-Effect-Level (NOAEL) or the Lowest-Observed Adverse-Effect-Level (LOAEL) for the effect (determined in health hazard section) to the estimated exposure value (predicted from exposure models). If both a NOAEL and LOAEL are available, then the NOAEL value is used for calculation of the MOE.

$MOE_{chronic}$, Occupational = NOAEL or LOAEL (Non-Cancer) / APDR or ADD (from ChemSTEER)
$MOE_{chronic}$, General Population = NOAEL or LOAEL (Non-Cancer) /ADRpot or ADDpot (from E-FAST)

Risk Determination : There is a potential risk concern for chemicals with an MOE < 100 based on studies with NOAEL values and for chemicals with an MOE < 1000 based on studies with only LOAEL values. The preference is to identify a NOAEL value and use that value for your MOE calculations. The average daily dose (ADD or ADDpot) is used to determine an MOE with one exception; an MOE for developmental toxicity is based on the acute dose rate (APDR or ADRpot).

For Calculation based on NOAEL:
MOE < 100 indicates potential for risk
MOE > 100 indicates low concern for risk

For Calculation based on LOAEL:
MOE < 1000 indicates potential for risk
MOE > 1000 indicates low concern for risk

For MOE values based on ***developmental toxicity data*** a body weight of 60 kg should be used as input when determining the exposure values (ADD, ADR, and LADD) instead of the default of 70 kg because that particular endpoint is only assessed in females.

Example Worksheet for Identification of the Potential for Acute and Chronic Risk to Human Health based on a Non-Cancer MOE:

Population	Effect	NOAEL	LOAEL	Exposure	MOE
Occupational	Systemic	40 mg/kg-d	200 mg/kg-d	1.8×10^{-2} mg/kg-d ChemSTEER ADD	2222
	Neurotox	40 mg/kg-d	200 mg/kg-d	1.8×10^{-2} mg/kg-d ChemSTEER ADD	2222
General Population	Systemic	40 mg/kg-d	200 mg/kg-d	2.1×10^{-6} mg/kg-d E-FAST ADDpot	1.9×10^{7}
	Neurotox	40 mg/kg-d	200 mg/kg-d	2.1×10^{-6} mg/kg-d E-FAST ADDpot	1.9×10^{7}

The MOE used to evaluate Risk from Occupational Exposure = 2222
The MOE used to evaluate Risk from General Population Exposure = 1.9×10^{7}

Example Summary of Human Health Risk : There is low concern for risk from occupational exposure or exposures to the general population because the MOEs are greater than 100 (based on studies with a NOAEL).

Estimating Human Health Cancer Risk

General Overview for a Cancer Risk Assessment:

NOTE: For the purposes of a Sustainable Futures P2 Assessment, a human health cancer risk assessment will not be required, but a cancer health hazard assessment should be completed for the chemical.

For Occupational Exposure Doses: LADD will be calculated by **ChemSTEER**

For General Population Exposure Doses: LADDpot will be calculated by **E-FAST**.

Slope Factor $(q1^*)(mg/kg\text{-}day)^{-1}$ (Calculated) = A measure of individual's extra risk (increased likelihood) of developing cancer for each incremental increase in exposure to a chemical. It approximates the upper bound of the slope of the dose-response curve using the linearized multistage procedure at low doses. The calculation of a slope factor requires tools that are not provided in the P2 Framework but can downloaded from the web for free. The software package is called "The Benchmark Dose Software (BMDS)", and can be found at: http://cfpub.epa.gov/ncea/

Cancer Risk = LADD or LADDpot (mg/kg-day) x Slope Factor $(q1^*)$ $(mg/kg\text{-}day)^{-1}$

Generally, a cancer risk of $> 1 \times 10^{-6}$ (1 in 1,000,000) for the general population and $> 1 \times 10^{-5}$ (1 in 100,000) for worker exposure indicates the potential for risk.

REFERENCES CITED

Boethling R.S. and J. V. Nabholz. 1997. Environmental assessment of polymers under the U.S. Toxic Substances Control Act. In: Hamilton, J.D. and R. Sutcliffe, eds. Ecological assessment of polymers: Strategies for product stewardship and regulatory programs. New York, NY: Van Nostrand Reinhold, 187-234. ISBN 0-442-02328-6.

Ecological Assessment of Polymers: Strategies for Product Stewardship and Regulatory Programs. John D. Hamilton (Editor), Roger Sutcliffe (Editor) ISBN: 0-471-28782-2.

U.S. EPA. 1996. ECOSAR User's Manual. "Estimating Toxicity of Industrial Chemicals to Aquatic Organisms Using Structure-Activity Relationships". R.G.Clements (Editor), Contributors: R.G. Clements, J.V. Nabholz, M. Zeeman. Office of Pollution Prevention and Toxics 7403M, U.S. Environmental Protection Agency, Washington, DC. 20460. Available in PDF at: http://www.epa.gov/oppt/newchems/sarman.pdf.

U.S. EPA. 1999a. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances, Federal Register: November 4, 1999 (Volume 64, Number 213), pages 60194-60204 Available at: http://www.epa.gov/fedrgstr/EPA-TOX/1999/November/Day-04/t28888.htm

U.S. EPA. 1999b. Persistent Bioaccumulative Toxic (PBT) Chemicals; Lowering of Reporting Thresholds for Certain PBT Chemicals; Addition of Certain PBT Chemicals; Community Right-to-Know Toxic Chemical Reporting: Final rule, Federal Register: October 29, 1999 (Volume 64, Number 209), 58666-58753 Available in PDF at: http://www.epa.gov/tri/pbt-final_rule.pdf

U.S. EPA. 2004. The Pollution Prevention (P2) Framework, EPA-748-B-03-001. Office of Pollution Prevention and Toxics 7403M, U.S. Environmental Protection Agency, Washington, DC. 20460. October 2003 version updated in January 2004. Available at: http://www.epa.gov/opptintr/p2framework/docs/p2manua.htm

NOTE: Assistance on the evaluation of polymers can be found in :

Boethling R.S. and J. V. Nabholz. 1997. "Environmental assessment of polymers under the U.S. Toxic Substances Control Act". *In:* Hamilton, J.D. and R. Sutcliffe, eds. Ecological assessment of polymers: Strategies for product stewardship and regulatory programs. New York, NY: Van Nostrand Reinhold, 187-234. ISBN 0-442-02328-6