Appendix B – Evaluation of Toxic Degradates of Concern

Structural activity relationship models such as ECOSAR are used to characterize major degradates and identify toxic degradates of concern by comparing degradate modeled toxicities to MITC, which is the stressor of concern in this risk assessment. ECOSAR, a utility under EPISuite 4, estimates the toxicity of chemicals discharged to water. ECOSAR predicts toxicity to fish, aquatic invertebrates and algae using an extensive set of structure-activity relationships (SARs). The program estimates a chemical's acute (short-term) toxicity and, when available, and chronic (long-term or delayed) toxicity (USEPA, 2010[2]). **Table B-1** shows that ECOSAR estimated MITC toxicities are underpredicted with the exception of freshwater, which is slightly overpredicted. However, **Table B-2** shows that the margins of the underprediction are generally surpassed by the margin that ECOSAR predicts higher toxicity for parent MITC as compared to all of the major degradates as shown in Table C-2. The only exception to this is DMU toxicity for green algae, which ECOSAR predicts is lower than the measured toxicity for MITC. However, inclusion of DMU as a degradate of concern based on green algae toxicity is not expected to significantly impact the existing risk determinations. The ECOSAR RUNS for MITC, methylamine, DMTU, DMU, and syn-methylthioformamide/anti-methylformamide are shown in **Figures B-1, B-2, B-3, B-4, and B-5**, respectively.

Table B-1. MITC measured versus ECOSAR predicted toxicity.

Taxa	Endpoint	MITC Measured Toxicity (ppm)	MITC ECOSAR Toxicity (ppm)	ECOSAR Departure Factor [2]
Freshwater Fish[1]	96-hr LC_{50} (Acute)	0.0512	0.079	0.556
Daphnid	48-hr LC_{50} (Acute)	0.055	1.207	21.945
Green Algae	96-hr EC_{50} (Acute)	0.254	1.412	5.559

1. The lowest toxicity value between rainbow trout and bluegill sunfish shown in the table.
2. ECOSAR Departure Factor = MITC ECOSAR Toxicity/MITC Measured Toxicity.

Table B-2. MITC versus ECOSAR predicted toxicity for methylamine (deg. 1), DMTU (deg. 2), DMU (deg. 3), syn-N-methylthioformamide (deg. 4), and anti-N-methylthioformamide (deg. 5) (departure factors in parenthesis).

Taxa	Endpoint	MITC ECOSAR Toxicity (ppm)	Deg. 1 ECOSAR Toxicity (ppm)	Deg. 2 ECOSAR Toxicity (ppm)	Deg. 3 ECOSAR Toxicity (ppm)	Deg. 4 ECOSAR Toxicity (ppm)	Deg. 5 ECOSAR Toxicity (ppm)
Freshwater Fish[1]	96-hr LC_{50} (Acute)	0.079	210.956 (2,670.3)	56,266.277 (712,231.2)	306.85 (3,884.2)	17,844.49 (225,879.6)	17,844.49 (225,879.6)
Daphnid	48-hr LC_{50} (Acute)	1.207	12.337 (10.2)	6.720 (5.6)	6,171.71 (5,113.3)	6,623.911 (5,487.9)	6,623.911 (5,487.9)
Green Algae	96-hr LC_{50} (Acute)	1.412	2.247 (1.6)	4.617 (3.27)	0.075 (0.05)	920.575 (652.0)	920.575 (652.0)

1. The lowest toxicity value between rainbow trout and bluegill sunfish shown in the table.
2. ECOSAR Departure Factor = Degradate ECOSAR Toxicity/MITC Measured Toxicity.

Figure B-1. MITC ECOSAR run.

SMILES : N(=C=S)C
CHEM : Methane, isothiocyanato-
CAS Num:
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C2 H3 N1 S1
MOL WT : 73.11
Log Kow: 1.30 (KowWin estimate)
Melt Pt:
Wat Sol: 7600 mg/L (experimental database)

ECOSAR v1.00 Class(es) Found

Thiocyanates

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Thiocyanates	: Fish	96-hr	LC50	0.079
Thiocyanates	: Daphnid	48-hr	LC50	1.207
Thiocyanates	: Green Algae	96-hr	EC50	1.412
Thiocyanates	: Fish	ChV		0.013 !
Thiocyanates	: Daphnid	ChV		0.180 !
Thiocyanates	: Green Algae	ChV		0.333
Neutral Organic SAR	: Fish	96-hr	LC50	220.353
(Baseline Toxicity)	: Daphnid	48-hr	LC50	116.832
	: Green Algae	96-hr	EC50	37.792
	: Fish	ChV		21.244
	: Daphnid	ChV		9.534
	: Green Algae	ChV		12.036

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect.

Note: ! = exclamation designates: The toxicity value was determined from a predicted SAR using established acute-to-chronic ratios and ECOSAR regression techniques which are documented in the supporting Technical Reference Manual. When possible, this toxicity value should be considered in a weight of evidence approach.

Thiocyanates:

For All Acute and Chronic Toxicity Values: If the log Kow of the chemical is greater than the value listed below, or if the compound is solid and the LC50, EC50 or ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: 6.0 (Fish 96-hr LC50)
Maximum LogKow: 5.0 (Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Figure B-2. Methylamine ECOSAR run.

SMILES : NC
CHEM : Methanamine
CAS Num:
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C1 H5 N1
MOL WT : 31.06
Log Kow: -0.64 (KowWin estimate)
Melt Pt:
Wat Sol: 1.08E+006 mg/L (experimental database)

ECOSAR v1.00 Class(es) Found

Aliphatic Amines

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Aliphatic Amines	: Fish	96-hr	LC50	210.956
Aliphatic Amines	: Daphnid	48-hr	LC50	12.337
Aliphatic Amines	: Green Algae	96-hr	EC50	2.247
Aliphatic Amines	: Fish		ChV	2.907
Aliphatic Amines	: Daphnid		ChV	0.007
Aliphatic Amines	: Green Algae		ChV	1.794
Aliphatic Amines	: Fish (SW)	96-hr	LC50	219.921
Aliphatic Amines	: Mysid Shrimp (SW)	96-hr	LC50	12.503
Aliphatic Amines	: Green Algae (SW)	96-hr	EC50	2.224
Aliphatic Amines	: Fish (SW)		ChV	2.907
Aliphatic Amines	: Mysid Shrimp (SW)		ChV	0.007
Aliphatic Amines	: Green Algae (SW)		ChV	1.575

Neutral Organic SAR	: Fish	96-hr	LC50	4088.551
(Baseline Toxicity)	: Daphnid	48-hr	LC50	1714.937
	: Green Algae	96-hr	EC50	250.419
	: Fish		ChV	411.433
	: Daphnid		ChV	99.337
	: Green Algae		ChV	55.980

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect.

Aliphatic Amines:

For Fish 96-hr LC50: For aliphatic amines with log Kow greater than 7.0, a test duration of greater than 96 hrs may be required for proper expression of toxicity. Also, if the toxicity value obtained by the use of this equation exceeds the water solubility (measured or estimated), mortalities greater than 50% would not be expected in a saturated solution during an exposure period of 96 hrs.

For Daphnid 48-hr LC50: For aliphatic amines with log Kow greater than 5.0, a test duration of greater than 48 hrs may be required for proper expression of toxicity. Also, if the toxicity value obtained by the use of this equation exceeds the water solubility (measured or estimated), significant mortalities would not be expected in a saturated solution during an exposure period of 48 hrs.

For Green Algae Acute Toxicity Values: If the log Kow of the chemical is greater than 7, or if the compound is solid and the EC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For Mysid Shrimp Acute Toxicity Values: If the log Kow of the chemical is greater than 6, or if the compound is solid and the EC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For Fish and Daphnid Chronic Toxicity Values: If the log Kow of the chemical is greater than 8.0, or if the compound is solid and the ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For Green Algae Chronic Toxicity Values: If the log Kow of the chemical is greater than 7.0, or if the compound is solid and the ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: 6.0 (Fish, Mysid LC50)
Maximum LogKow: 5.0 (Daphnid LC50)
Maximum LogKow: 7.0 (Green Algae EC50)
Maximum LogKow: 8.0 (Fish, Daphnid ChV)
Maximum LogKow: 7.0 (Green Algae ChV)
Maximum Mol Wt: 1000

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Figure B-3. DMTU ECOSAR run.

SMILES : N(C(=S)NC)C
CHEM : Thiourea, N,N'-dimethyl-
CAS Num: 000534-13-4
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C3 H8 N2 S1
MOL WT : 104.17
Log Kow: -0.38 (KowWin estimate)
Melt Pt:
Wat Sol: 1E+006 mg/L (experimental database)

ECOSAR v1.00 Class(es) Found

Thioureas

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Thioureas	: Fish	96-hr	LC50	56266.277
Thioureas	: Daphnid	48-hr	LC50	6.720
Thioureas	: Green Algae	96-hr	EC50	4.617
Thioureas	: Fish		ChV	4731.437 !
Thioureas	: Daphnid		ChV	0.523 !
Thioureas	: Green Algae		ChV	0.338
Neutral Organic SAR	: Fish	96-hr	LC50	8259.677
(Baseline Toxicity)	: Daphnid	48-hr	LC50	3575.216
	: Green Algae	96-hr	EC50	580.884
	: Fish		ChV	826.408
	: Daphnid		ChV	216.845
	: Green Algae		ChV	136.173

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect.

Note: ! = exclamation designates: The toxicity value was determined from a predicted SAR using established acute-to-chronic ratios and ECOSAR regression techniques which are documented in the supporting Technical Reference Manual. When possible, this toxicity value should be considered in a weight of evidence approach.

Thioureas :

For Fish and Daphnid Acute Toxicity Values: If the log Kow of the chemical is greater than 5.0, or if the compound is solid and the LC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For Green Algae Acute Toxicity Values: If the log Kow of the chemical is greater than 6.4, or if the compound is solid and the EC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For All Chronic Toxicity Values: If the log Kow of the chemical is greater than 8.0, or if the compound is solid and the ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: 5.0 (LC50)
Maximum LogKow: 6.4 (EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Figure B-4. DMU ECOSAR run.

SMILES : O=C(NC)NC
CHEM : Urea, N,N -dimethyl-
CAS Num: 000096-31-1
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C3 H8 N2 O1
MOL WT : 88.11
Log Kow: -0.62 (KowWin estimate)
Melt Pt:
Wat Sol: 1.615E+004 mg/L (WskowWin estimate)

ECOSAR v1.00 Class(es) Found

Substituted Ureas
Amides

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Substituted Ureas	: Fish	96-hr	LC50	2055.694
Substituted Ureas	: Daphnid	48-hr	LC50	6171.706
Substituted Ureas	: Green Algae	96-hr	EC50	0.075
Substituted Ureas	: Fish		ChV	24.377
Substituted Ureas	: Daphnid		ChV	308.215
Substituted Ureas	: Green Algae		ChV	0.026 !
Amides	: Fish	96-hr	LC50	1348.192
Amides	: Daphnid	48-hr	LC50	306.850
Amides	: Green Algae	96-hr	EC50	1.042
Amides	: Fish		ChV	7.970
Amides	: Daphnid		ChV	4.048 !
Amides	: Green Algae		ChV	0.147
Neutral Organic SAR (Baseline Toxicity)	: Fish	96-hr	LC50	11265.005
	: Daphnid	48-hr	LC50	4733.666
	: Green Algae	96-hr	EC50	695.488
	: Fish		ChV	1133.227
	: Daphnid		ChV	274.924
	: Green Algae		ChV	155.900

Note: * = asterisk designates: Chemical may not be soluble

enough to measure this predicted effect.

Note: ! = exclamation designates: The toxicity value was determined from a predicted SAR using established acute-to-chronic ratios and ECOSAR regression techniques which are documented in the supporting Technical Reference Manual. When possible, this toxicity value should be considered in a weight of evidence approach.

Substituted Ureas:

For Fish and Daphnid Acute Toxicity Values: If the log Kow of the chemical is greater than 5.0, or if the compound is solid and the LC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For Green Algae Acute Toxicity Values: If the log Kow of the chemical is greater than 6.4, or if the compound is solid and the EC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For All Chronic Toxicity Values: If the log Kow of the chemical is greater than 8.0, or if the compound is solid and the ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: 5.0 (LC50)
Maximum LogKow: 6.4 (EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Amides :

No limitations known at this time.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: >8.5 (LC50)
Maximum LogKow: >8.0 (EC50,ChV)
Maximum Mol Wt: 1000

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Figure B-5. syn-N-methylthioformamide (deg. 4), and anti-N-methylthioformamide ECOSAR run.

SMILES : NC(=S)C
CHEM : Ethanethioamide
CAS Num: 000062-55-5
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C2 H5 N1 S1
MOL WT : 75.13
Log Kow: -0.83 (KowWin estimate)
Melt Pt:
Wat Sol: 1.63E+005 mg/L (experimental database)

ECOSAR v1.00 Class(es) Found

Neutral Organics

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organics	: Fish	96-hr	LC50	17844.490
Neutral Organics	: Fish	14-day	LC50	17238.707
Neutral Organics	: Daphnid	48-hr	LC50	6623.911
Neutral Organics	: Green Algae	96-hr	EC50	920.575
Neutral Organics	: Fish	30-day	ChV	1538.136
Neutral Organics	: Daphnid		ChV	490.584
Neutral Organics	: Green Algae		ChV	219.521
Neutral Organics	: Fish (SW)	96-hr	LC50	30757.049
Neutral Organics	: Mysid Shrimp	96-hr	LC50	1.34e+005
Neutral Organics	: Fish (SW)		ChV	511.459
Neutral Organics	: Mysid Shrimp (SW)		ChV	26748.623
Neutral Organics	: Earthworm	14-day	LC50	256.639

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect.

Neutral Organics:

For Fish LC50 (96-h), Daphnid LC50, Mysid: If the log Kow is greater than 5.0, or if the compound is solid and the LC50 exceeds the water solubility by 10X, no effects at saturation are predicted.

For Fish LC50 (14-day) and Earthworm LC50: If the log Kow is greater than 6.0, or if the compound is solid and the LC50 exceeds the water

solubility by 10X, no effects at saturation are predicted.

For Green Algae Acute Toxicity Values: If the log Kow of the chemical is greater than 6.4, or if the compound is solid and the EC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For All Chronic Toxicity Values: If the log Kow of the chemical is greater than 8.0, or if the compound is solid and the ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50, Mysid LC50)
Maximum LogKow: 6.0 (Fish 14-day LC50; Earthworm LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000