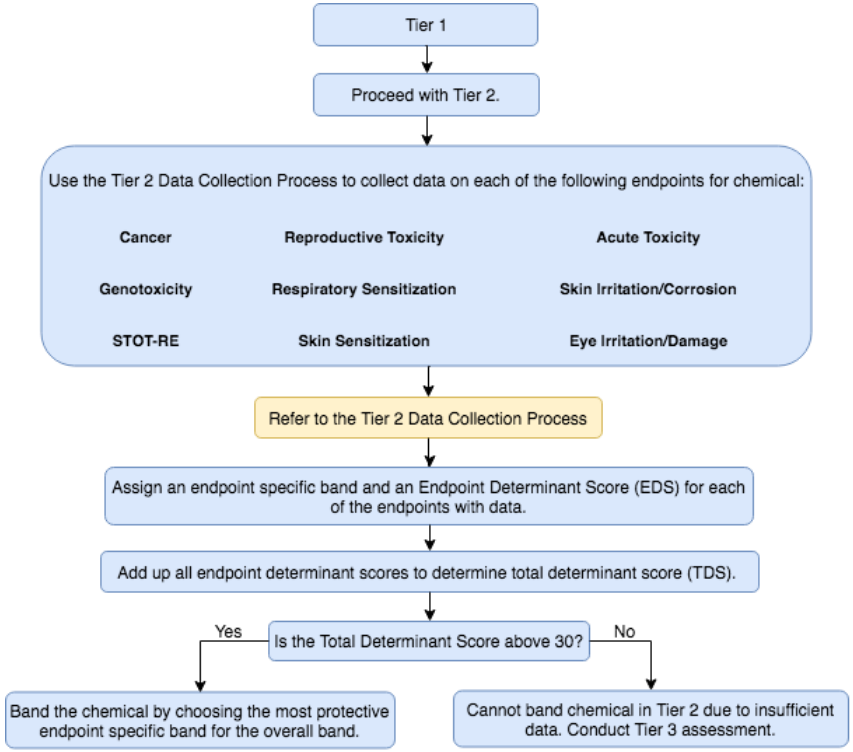
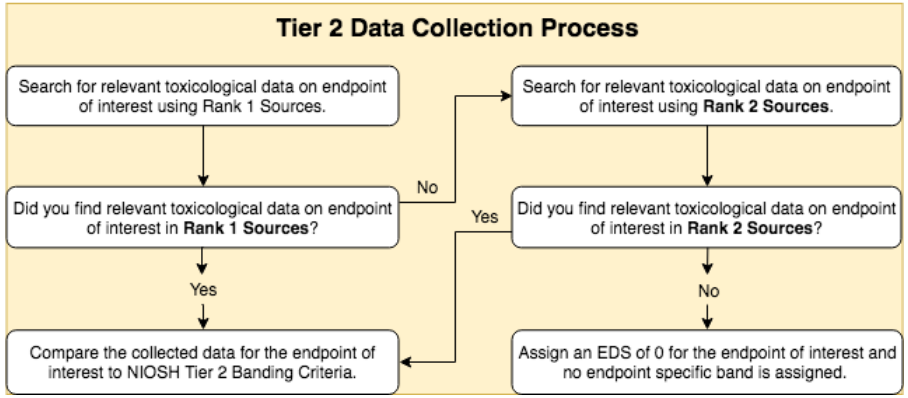
Tier 2 Resources

Detailed overview of the Tier 2 Process





List of Information Sources for Banding in Tier 2

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Carcinogenicity	1	U.S. National Toxicology Program Report on Carcinogens [NTP-ROC 2016]	NTP-RoC
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
		International Agency for Research on Cancer [IARC 2015]	IARC
		Health Canada [Health-Canada 1996]	HC
		State of California Office of Environmental Health Hazard Assessment [CAL/EPA 2010]	Cal OEHHA
Reproductive toxicity	1	U.S. National Toxicology Program [NTP 2016]	NTP
		Health Canada [Health-Canada 1996]	HC
		California Environmental Protection Agency [CAL/EPA 2016]	CalEPA
		Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
	2	Organization for Economic Co-operation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
		U.S. EPA Office of Pesticides: Reregistration Eligibility Decision Documents [EPA 2016a]	U.S. EPA RED
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	ECHA; REACH
Specific Target Organ Toxicity (STOT-RE)	1	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
		California Environmental Protection Agency [CAL/EPA 2016]	CalEPA
		U.S. National Toxicology Program [NTP 2016]	NTP
		Health Canada [Health-Canada 1996]	HC

	2	European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		Organization for Economic Co-operation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
Genotoxicity	1	U.S. National Toxicology Program [NTP 2016]	NTP
		Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. National Toxicology Program Report on Carcinogens [NTP-ROC 2016]	NTP-RoC
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Hazardous Substance Data Bank [HSDB 2016]	HSDB
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
Respiratory sensitization	1	Organization for Economic Co-operation and Development [OECD 2016]	OECD
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
		Association of Occupational and Environmental Clinics [AOEC 2016]	AOEC
Skin sensitization	1	NIOSH Skin Notation Profiles [NIOSH 2009b]	SK Profiles
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		Organization for Economic Co-operation and Development [OECD 2016]	OECD

		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Hazardous Substance Data Bank [HSDB 2016]	HSDB
Acute Toxicity	1	National Library of Medicine ChemID Plus [ChemID 2016]	ChemID Plus
		U.S. EPA Superfund Chemical Data Matrix [EPA 2016b]	U.S. SCDM
		Pesticide Properties Database [PPDB 2007]	PPDB
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Hazardous Substance Data Bank [HSDB 2016]	HSDB
		Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
Skin Irritation/Skin Corrosion	1	NIOSH Skin Notation Profiles [NIOSH 2009b]	SK Profiles
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		Organization for Economic Co-operation and Development [OECD 2016]	OECD
	2	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
Serious Eye Damage/Eye Irritation	1	Organization for Economic Cooperation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
	2	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS

Recommended Sources for Tier 2 Banding by Endpoint

Sources	OEB Endpoint								
	Cancer	Reproductive Toxicity	STOT. RE	Genotoxicity	Respiratory Sensitization	Skin Sensitization	Acute Toxicity	Skin Corrosion /Irritation	Eye Corrosion/ Irritation
NTP-ROC	Rank 1			Rank 1					
NTP	Rank 1	Rank 1	Rank 1	Rank 1					
IRIS	Rank 1		Rank 1		Rank 2			Rank 2	Rank 2
IARC	Rank 1								
HC	Rank 1	Rank 1	Rank 1						
Cal OEHHA	Rank 1								
ATSDR		Rank 1	Rank 1	Rank 1	Rank 2		Rank 2	Rank 2	Rank 2
Cal EPA		Rank 1	Rank 1						
OECD		Rank 2	Rank 2		Rank 1	Rank 1		Rank 1	Rank 1
Chem ID plus							Rank 1		
US SCDM							Rank 1		
PPDB							Rank 1		
NIOSH SKN						Rank 1		Rank 1	
HSDB				Rank 2		Rank 2	Rank 2		
AOEC					Rank 2				
WHO-IPCS		Rank 2	Rank 2	Rank 1	Rank 1	Rank 1	Rank 1	Rank 1	Rank 1
REACH		Rank 2		Rank 2	Rank 1	Rank 1		Rank 1	Rank 1
EPA RED		Rank 2	Rank 2						

Assigned Scores for the Presence of Toxicological Endpoints Encountered in the Tier 2 Evaluation*

Toxicological Endpoint	Endpoint Determinant Score (EDS)
Cancer	Qualitative (WOE) = 20 or 30 Quantitative = 30
Reproductive and Developmental Toxicity	30
Systemic Target Organ Toxicity (STOT-RE)	30
Genotoxicity	5
Respiratory Sensitization	5
Skin Sensitization	10
Acute Toxicity/Lethality (LD_{50} or LC_{50})	5
Skin Irritation/Corrosion	5
Eye Irritation/Corrosion	5
Data Sufficiency/Total Determinant Score (TDS)	30/125

**Total Determinant Score (TDS) must be above 30 to band a specific chemical. A TDS below 30 signifies that there is not enough information to band the chemical in Tier 2 and user must proceed with Tier 3. The only exception is if the final Tier 2 band is determined to be E, then the TDS rule does not apply.*

Endpoint Specific Criteria for Banding

Cancer

Criteria for Carcinogenicity Toxicity (Quantitative Analysis)

NIOSH Banding Criteria for **Cancer**			
Exposure/ Dosing Route	**Band**		
	C	**D**	**E**
Slope factor	< 0.01 (mg/kg-day)$^{-1}$	≥ 0.01 to < 10 (mg/kg-day)$^{-1}$	≥ 10 (mg/kg-day)$^{-1}$
Inhalation unit risk	$< 3 \times 10^{-6}$ (µg/m^3)$^{-1}$	$\geq 3 \times 10^{-6}$ to < 0.01 (µg/m^3)$^{-1}$	≥ 0.01 (µg/m^3)$^{-1}$
TD_{05}	> 5 mg/kg-day	> 0.005 to ≤ 5 mg/kg-day	≤ 0.005 mg/kg-day
TC_{05}	> 16700 µg/m^3	> 5 to ≤ 16700 µg/m^3	≤ 5 µg/m^3

Criteria for Carcinogenicity Toxicity (Qualitative Analysis)

Classification	***Band***	***Determinant Score***
National Toxicology Program Report on Carcinogens		
Known to be human carcinogen	**E**	**30**
Reasonably anticipated to be human carcinogen	**E**	**30**
Environmental Protection Agency Integrated Risk Information System		
Group A (human carcinogen)	**E**	**30**
Carcinogenic to humans	**E**	**30**
Group B1 (probable human carcinogen)	**E**	**30**
Group B2 (probable human carcinogen)	**E**	**30**
Likely to be carcinogenic to humans	**E**	**30**
Group C (possible human carcinogen)	**D**	**20**
Suggestive evidence of carcinogenic potential	**D**	**20**
Group D (not classifiable as to human carcinogenicity)	***No band***	***No score***
Data are inadequate for an assessment of carcinogenic potential	***No band***	***No score***
Group E (evidence of non-carcinogenicity for humans)	**A**	**30**
Not likely to be carcinogenic to humans	**A**	**30**
International Agency for Research on Cancer		
Group 1 (carcinogenic to humans)	**E**	**30**
Group 2A (probably carcinogenic to humans)	**E**	**30**
Group 2B (possibly carcinogenic to humans)	**E**	**30**
Group 3 (not classifiable as to its carcinogenicity to humans)	***No band***	***No score***
Group 4 (probably not carcinogenic to humans)	**A**	**30**
State of California Office of Environmental Health Hazard Assessment		
Type of toxicity = cancer	**E**	**30**

Worksheet for Cancer

Carcinogenicity (20 or 30 points possible)				
	Band A	**Band C**	**Band D**	**Band E**
NTP/EPA/IARC/Canada/California (QUALITATIVE)				
EPA IRIS Slope Factor				
EPA IRIS Inhalation Unit Risk				
Health Canada TD05				
Health Canada TC05				
California Slope Factor				
California Inhalation Unit Risk				

Reproductive Toxicity

Criteria for Reproductive Toxicity Endpoint

NIOSH Banding Criteria for **Reproductive Toxicity** (NOAEL/BMDL/BMCL)					
Exposure/ Dosing Route	**Band**				
	A	**B**	**C**	**D**	**E**
Oral, dermal	> 300 mg/kg-day	> 30 to ≤300 mg/kg-day	> 3 to ≤30 mg/kg-day	> 0.3 to ≤3 mg/kg-day	≤0.3 mg/kg-day
Inhalation (gases and vapors)	> 10,000 ppm	> 1,000 to ≤10,000 ppm	> 100 to ≤1,000 ppm	> 10 to ≤100 ppm	≤10 ppm
Inhalation (dusts and mists)	> 10,000 µg/m^3	> 1,000 to ≤10,000 µg/m^3	> 100 to ≤1,000 µg/m^3	> 10 to ≤100 µg/m^3	≤10 µg/m^3

Worksheet for Reproductive Toxicity

Reproductive Toxicity (30 points possible)					
Data supports:	**Band A**	**Band B**	**Band C**	**Band D**	**Band E**
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.					
Source, Rank 1 or 2:					

Specific Target Organ Toxicity (STOT-RE)

Criteria for Specific Target Organ Toxicity (STOT-RE) Endpoint

NIOSH Banding Criteria for **Specific Target Organ Toxicity** (NOAEL/BMDL)					
Exposure/ Dosing Route	**Band**				
	A	**B**	**C**	**D**	**E**
Oral, dermal	>1,000 mg/kg-day	>100 to ≤1,000 mg/kg-day	>10 to ≤100 mg/kg-day	>1 to ≤10 mg/kg-day	≤1 mg/kg-day
Inhalation (dusts and mists)	>30,000 µg/m^3	>3,000 to ≤30,000 µg/m^3	>300 to ≤3,000 µg/m^3	>30 to ≤300 µg/m^3	≤30 µg/m^3
Inhalation (gases and vapors)	>30,000 ppm	>3,000 to ≤30,000 ppm	>300 to ≤3,000 ppm	>30 to ≤300 ppm	≤30 ppm

** Multiple NOAELs for one chemical substance may be available. The NOAEL selected for banding should be the NOAEL used by the agency as the basis for the reference dose/concentration.*

Worksheet for Specific Target Organ Toxicity – Repeated Exposure (STOT-RE) Endpoint

Specific Target Organ Toxicity (STOT-RE) (30 points possible)					
Data supports:	**Band A**	**Band B**	**Band C**	**Band D**	**Band E**
If data available, put data, notes, etc. in this row corresponding to the correct band criteria; otherwise leave blank.					
Source, Rank 1 or 2:					

Genotoxicity

Criteria for Genotoxicity Endpoint

NIOSH Banding Criteria for **Genotoxicity**		
Band		
A	**C**	**E**
Negative Results	Mixed results	Positive Results

Worksheet for Genotoxicity

Genotoxicity (5 points possible)			
Data supports:	**Negative Results (Band A)**	**Mixed Results (Band C)**	**Positive Results (Band E)**
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.			
Source, Rank 1 or 2:			

Respiratory Sensitization

Criteria for Respiratory Sensitization Endpoint

NIOSH Banding Criteria for **Respiratory Sensitization**		
Band		
A	**C**	**E**
No evidence of respiratory sensitization	Mixed results	Positive evidence of respiratory sensitization

Worksheet for Respiratory Sensitization Endpoint

Respiratory sensitization (10 points possible)			
Data supports:	**No evidence of respiratory sensitization (Band A)**	**Mixed results (Band C)**	**Respiratory sensitization based on totality of evidence (Band E)**
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.			
Source, Rank 1 or 2:			

Skin Sensitization

Criteria for Skin Sensitization Endpoint

NIOSH Banding Criteria for **Skin Sensitization**			
Test Type	**Band**		
	A	**C**	**E**
EC3 (%) (based on LLNA)	Non-skin sensitizer	EC3 (%) ≥2.0 ≤ 100 (weak to moderate skin sensitizer)	EC3 (%) ≤2.0 (strong to extreme skin sensitizer)
GPMT	No positive response or low incidence data	30% to 60% responding at > 0.1% intradermal induction concentration OR ≥ 30% responding at > 1% intradermal induction concentration	≥ 30% responding at ≤0.1% intradermal induction concentration OR ≥ 60 % responding at >0.1% to ≤1% intradermal induction concentration
Beuhler	No positive response or low incidence data	≥ 60% responding at > 0.2 to ≤ 20% topical induction dose OR ≥15% responding at > 20% topical induction dose	≥15% responding at ≤0.2% topical induction concentration OR ≥ 60% responding at any topical induction concentration
Qualitative	Negative results	Mixed results	Positive results OR NIOSH SK-SEN notation

Worksheet for Skin Sensitization

Skin sensitization (5 points possible)			
Data supports:	**Non-sensitizer (Band A)**	**Moderate sensitizer (Band C)**	**Extreme sensitizer (Band E)**
IF data available, put data, calculations, notes, etc. in this row corresponding to the correct band criteria; otherwise leave blank.			
Source, Rank 1 or 2:			

Acute Toxicity

Criteria for Acute Toxicity Endpoint

NIOSH banding criteria for **Acute Toxicity**					
Exposure/Dosing Route	**Band**				
	A	**B**	**C**	**D**	**E**
Oral toxicity (LD_{50})	>2,000 mg/kg-bodyweight	>300 to ≤ 2,000 mg/kg-bodyweight	>50 to ≤ 300 mg/kg-bodyweight	>5 to ≤ 50 mg/kg-bodyweight	≤ 5 mg/kg-bodyweight
Dermal toxicity (LD_{50})	> 2,000 mg/kg-bodyweight	>1,000 to ≤ 2,000 mg/kg-bodyweight	>200 to ≤ 1,000 mg/kg-bodyweight	>50 to ≤ 200 mg/kg-bodyweight	≤ 50 mg/kg-bodyweight
Inhalation gases (LC_{50})	> 20,000 ppmV/4h	>2,500 to ≤ 20,000 ppmV/4h	>500 to ≤ 2,500 ppmV/4h	>100 to ≤ 500 ppmV/4h	≤ 100 ppmV/4h
Inhalation vapors (LC_{50})	> 20.0 mg/liter/4h	>10.0 to ≤ 20.0 mg/liter/4h	>2.0 to ≤ 10.0 mg/liter/4h	>0.5 to ≤ 2.0 mg/liter/4h	≤ 0.5 mg/liter/4h
Inhalation dusts and mists (LC_{50})	> 5.0 mg/liter/4h	>1.0 to ≤ 5.0 mg/liter/4h	>0.5 to ≤ 1.0 mg/liter/4h	>0.05 to ≤ 0.5 mg/liter/4h	≤ 0.05 mg/liter/4h

Worksheet for Acute Toxicity

Acute Toxicity (5 points possible)						
Data Supports:		**A**	**B**	**C**	**D**	**E**
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.	**Oral toxicity (LD_{50})**					
	Dermal toxicity (LD_{50})					
	Inhalation gases (LC_{50})					
	Inhalation vapors (LC_{50})					
	Inhalation dusts and mists (LC_{50})					
Source, Rank 1 or 2:						

***If multiple LD50 or LC50 values are found for each route of exposure/chemical state, record only the lowest value in this chart.*

Skin Corrosion/Irritation

Criteria for Skin Corrosion/Irritation Endpoint

NIOSH Banding Criteria for **Skin Irritation/Skin Corrosion**			
Band			
A	**B**	**C**	**E**
Non-irritating	Mild to moderate irritation	Moderate to severe irritation; reversible direct effects OR If results are mixed or indicate irritant potential with severity unspecified	Skin corrosion; irreversible effects pH value of ≤2.0 or >*11*.5

Worksheet for Skin Corrosion/Irritation Endpoint

Skin irritation/corrosion (5 points possible)				
Data supports:	**Non-irritating (Band A)**	**Mild to moderate irritation; reversible direct effects (Band B)**	**Moderate to severe irritation; reversible effects OR if results are mixed or indicate irritant potential with severity unspecified (Band C)**	**Skin Corrosion; irreversible effects OR pH value ≤2.0 or >11.5 (Band E)**
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.				
Source, Rank 1 or 2:				

Eye Damage/Eye Irritation

Criteria for Eye Damage/Eye Irritation Endpoint

NIOSH Banding Criteria for **Serious Eye Damage/Eye Irritation**			
Band			
A	**B**	**C**	**E**
Non-irritating	Mild to moderate irritation	Severe irritation; moderate to severe irritation OR Irritant with unspecified severity, no conclusion, or mixed results	Irreversible eye damage

Worksheet for Eye Damage/Eye Irritation

Eye damage/Eye irritation (5 points possible)				
Data supports:	**Non-irritating (A)**	**Mild to moderate irritation (B)**	**Severe irritation; moderate to severe irritation; OR no classification system, no conclusion, or mixed results (C)**	**Irreversible eye damage (E)**
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.				
Source, Rank 1 or 2:				

Checklist for Tier 2 Hazard Banding

Chemical Name: **CAS:**			
Endpoint	**Data**	**EDS**	**Endpoint Band**
Carcinogenicity	Source:		
Reproductive Toxicity	Source:		
Specific Target Organ Toxicity (STOT-RE)	Source:		
Genotoxicity	Source:		
Respiratory Sensitization	Source:		
Skin Sensitization	Source:		
Acute Toxicity	Source:		
Skin Corrosion/Irritation	Source:		
Eye Damage/Irritation	Source:		
OVERALL Tier 2 BAND		**TDS=**	