OSHA ATE Calculator Users Guide

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Overview

This User Guide is designed to help manufactures and importers of chemicals use the Acute Toxicity Estimate (ATE) Calculator when the classification of a mixture is based on ingredients of the mixture via application of the additivity formula. This guide provides guidance in Section 2 on how to enter data into the calculator and in Section 3 by providing examples of how data should be entered into the calculator using the Mixtures Examples #1 – 4 presented in document Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016).

1. Approach to Calculating the Acute Toxicity Estimate of a mixture

The approach to estimating an untested mixture's acute toxicity is to calculate an Acute Toxicity Estimate for the mixture ($ATE_{mixture}$) which represents the Oral or Dermal LD_{50} or Inhalation LC_{50} of the mixture. This is accomplished by collecting the LD_{50}/LC_{50} for each ingredient if it is known or a point estimate of an ingredient's LD_{50}/LC_{50}. An ingredient's point estimate is based on either an acute toxicity range from a known limit dose test or a classification. The ATE calculation uses one of two additivity formulas depending on the percentage of ingredient(s) with unknown toxicity. Detailed guidance on the application of the additivity approach to determine the classification of an untested mixture is provided in document Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016).

2. Data Entry into the ATE Calculator

The basic steps to enter data and calculate the mixture ATE are illustrated below:

Step 1: Select the checkbox(es) for all relevant Exposure Route(s).

Data Input Section

1. Choose Exposure Route(s):

☑Oral   ☐Dermal   ☐Inhalation – Gases   ☐Inhalation – Vapors   ☐Inhalation – Dusts/Mists

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Step 2: Enter the Ingredient Name, Wt%, and either a LD_{50}/LC_{50} **or** Limit Dose Data **or** Classification for the default Ingredient row.

Data Input Section

1. Choose Exposure Route(s):

☑ Oral ☐ Dermal ☐ Inhalation – Gases ☐ Inhalation – Vapors ☐ Inhalation – Dusts/Mists

2.1 Enter Ingredients: Oral

Ingredient	WT%	LD_{50} (mg/kg)	Limit Dose Data (mg/kg)	Classification
Ingredient 1	10	50	Select Limit Dose Data ⬍	Select Classification ⬍

Sum Unknown Toxicity ⓘ Enter weight (%)

[Add Ingredient] [Reset] [Calculate]

Step 3: To add another ingredient, select the Add Ingredient button.

Data Input Section

1. Choose Exposure Route(s):

☑ Oral ☐ Dermal ☐ Inhalation – Gases ☐ Inhalation – Vapors ☐ Inhalation – Dusts/Mists

2.1 Enter Ingredients: Oral

Ingredient	WT%	LD_{50} (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Ingredient 1	10	50	Select Limit Dose Data ⬍	Select Classification ⬍	
Enter ingredient	Enter weight (%)	Enter LD50 (mg/kg)	Select Limit Dose Data ⬍	Select Classification ⬍	Remove

Sum Unknown Toxicity ⓘ Enter weight (%)

[Add Ingredient] [Reset] [Calculate]

Step 4: Enter the Ingredient Name, Wt%, and either LD_{50}/LC_{50} **or** Limit Dose Data **or** Classification for the newly inserted Ingredient row.

Step 5: Repeat steps 3 and 4 for each Ingredient until all "relevant ingredient"[1] rows are entered. If necessary, a row can be deleted by selecting the Remove button at the end of a row.

Step 6: If the sum of "relevant ingredients" without any information on acute toxicity[2] for the selected route of entry is > 10% then enter the sum of the ingredient's weight percent in the Sum Unknown Toxicity field.

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[1] See "Relevant Ingredient" Concept on page 42 in Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016).

[2] See "Data are not available for one or more ingredients of the mixture" on page 45 in Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016).

Data Input Section
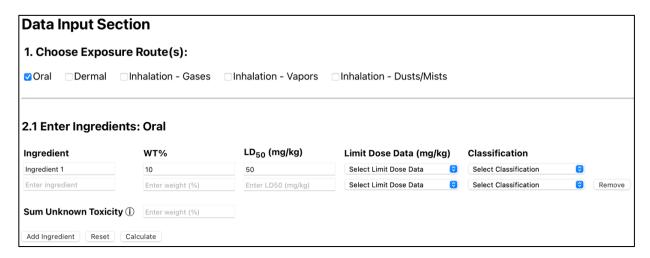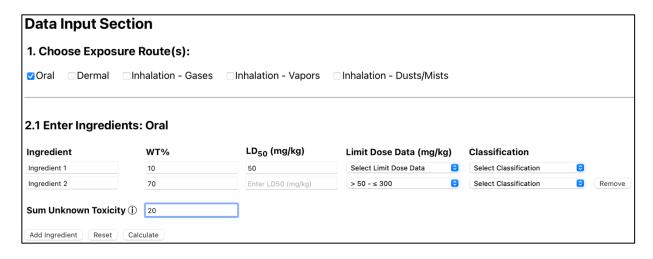
1. Choose Exposure Route(s):

☑Oral ☐Dermal ☐Inhalation – Gases ☐Inhalation – Vapors ☐Inhalation – Dusts/Mists

2.1 Enter Ingredients: Oral

Ingredient	WT%	LD$_{50}$ (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Ingredient 1	10	50	Select Limit Dose Data	Select Classification	
Ingredient 2	70	Enter LD50 (mg/kg)	> 50 - ≤ 300	Select Classification	Remove

Sum Unknown Toxicity ⓘ 20

Add Ingredient | Reset | Calculate

Step 4: Select the Calculate button.

Data Input Section

1. Choose Exposure Route(s):

☑Oral ☐Dermal ☐Inhalation – Gases ☐Inhalation – Vapors ☐Inhalation – Dusts/Mists

2.1 Enter Ingredients: Oral

Ingredient	WT%	LD$_{50}$ (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Ingredient 1	10	50	Select Limit Dose Data	Select Classification	
Ingredient 2	70	Enter LD50 (mg/kg)	> 50 - ≤ 300	Select Classification	Remove

Sum Unknown Toxicity ⓘ 20

Add Ingredient | Reset | Calculate

Oral Exposure Route Result

Oral ATE mix = 89 mg/kg (Oral Category 3)

If desired, a user my select the Reset button within a given route of entry to clear all ingredient information and re-start the ingredient data entry at Step 2.

2. Example ATE Calculations

The following 4 mixture examples are taken directly from OSHA's Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016). These 4 examples provide the basis for illustrating how to enter various types of data into the calculator[3].

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[3] See "Consistent application of the additivity formula" on page 41 in Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016).
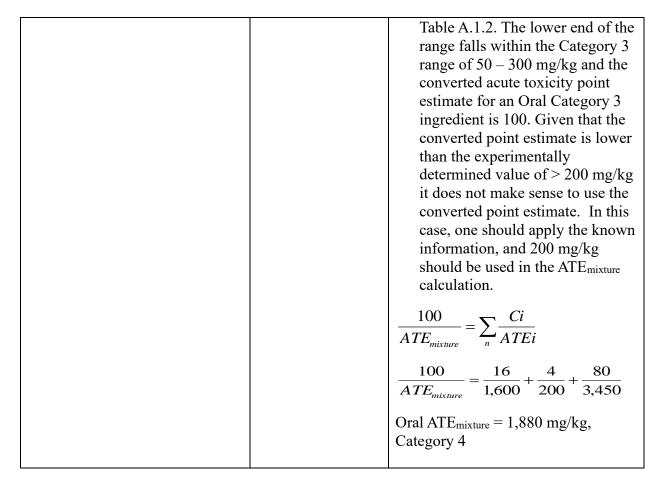
2.1 Example #1

<table>
<tr>
<td colspan="3" align="center">Mixture Example #1
Acute Toxicity – Dermal</td>
</tr>
<tr>
<td>Data</td>
<td>HCS 2012
Classification</td>
<td>Rationale</td>
</tr>
<tr>
<td>Component data:

Component 1:5%, Dermal LD_{50} = 40 mg/kg
Component 2: 44%, Dermal LD_{50} > 200 < 1,000
Component 3: 48%, Dermal LD_{50} = 190 mg/kg
Component 4: 3%, Acute Dermal Toxicity Category 4</td>
<td>Acute Toxicity Dermal Category 2</td>
<td>The LD_{50} data for Components 1 and 3 are used in the $ATE_{mixture}$ calculation since data are available.

Apply the guidance in Note (b) to Table A.1.1 of HCS 2012
– The Dermal LD_{50} > 200 < 1,000 range estimate for Component 2 is converted to the acute toxicity point estimate of 300 mg/kg using Table A.1.2. of HCS 2012
– The classification category for Component 4 is converted to the acute toxicity point estimate of 1,100 using Table A.1.2.

Equation 1

$$\frac{100}{ATE_{mixture}} = \sum_n \frac{Ci}{ATEi}$$

$$\frac{100}{ATE_{mixture}} = \frac{5}{40} + \frac{44}{300} + \frac{48}{90} + \frac{3}{1,100}$$

Dermal $ATE_{mixture}$ = 124 mg/kg, Category 2</td>
</tr>
</table>

The screen shot below illustrates how the data from Example 1 should be entered into the ATE Calculator along with the calculated result.
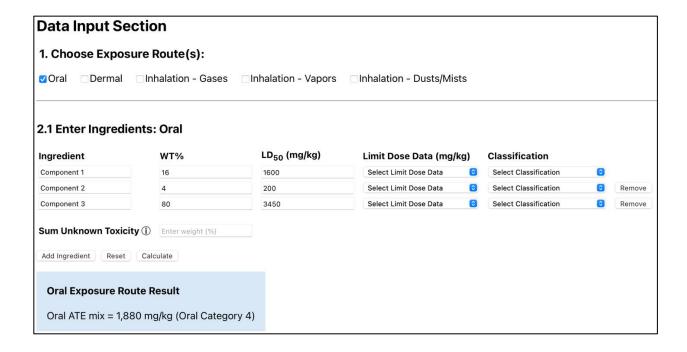
Data Input Section

1. Choose Exposure Route(s):

☐ Oral ☑ Dermal ☐ Inhalation – Gases ☐ Inhalation – Vapors ☐ Inhalation – Dusts/Mists

2.2 Enter Ingredients: Dermal

Ingredient	WT%	LD_{50} (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Component 1	5	40	Select Limit Dose Data ⇕	Select Classification ⇕	
Component 2	44	Enter LD50 (mg/kg)	> 200 - ≤ 1,000 ⇕	Select Classification ⇕	Remove
Component 3	48	90	Select Limit Dose Data ⇕	Select Classification ⇕	Remove
Component 4	3	Enter LD50 (mg/kg)	Select Limit Dose Data ⇕	Category 4 ⇕	Remove

Sum Unknown Toxicity ⓘ   Enter weight (%)

[Add Ingredient] [Reset] [Calculate]

Dermal Exposure Route Result

Dermal ATE mix = 124 mg/kg (Dermal Category 2)

2.2 Example #2

Mixture Example #2 Acute Toxicity – Oral		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 16%, oral LD_{50} = 1,600 mg/kg Component 2: 4%, oral LD_{50} > 200 < 2,000 Component 3: 80%, oral LD_{50} = 3,450 mg/kg	Acute Oral Toxicity Category 4	Per A.1.3.6.1 (a) include ingredients with a known acute toxicity, which fall into any of the acute toxicity categories, or have an oral LD_{50} > 2000 ≤5000 mg/kg body weight The LD_{50} data for Components 1 and 3 are used in the $ATE_{mixture}$ calculation since data are available. Apply the guidance in Note (b) to Table A.1.1 – The use of expert judgment is needed to determine what value to use in the $ATE_{mixture}$ calculation for Component 2. The oral LD_{50} > 200 < 2,000 range for Component 2 does not match up with the ranges provided in

		Table A.1.2. The lower end of the range falls within the Category 3 range of 50 – 300 mg/kg and the converted acute toxicity point estimate for an Oral Category 3 ingredient is 100. Given that the converted point estimate is lower than the experimentally determined value of > 200 mg/kg it does not make sense to use the converted point estimate. In this case, one should apply the known information, and 200 mg/kg should be used in the ATE$_{mixture}$ calculation. $$\frac{100}{ATE_{mixture}} = \sum_{n} \frac{Ci}{ATEi}$$ $$\frac{100}{ATE_{mixture}} = \frac{16}{1,600} + \frac{4}{200} + \frac{80}{3,450}$$ Oral ATE$_{mixture}$ = 1,880 mg/kg, Category 4

The screen shot below illustrates how the data from Example 2 should be entered into the ATE Calculator along with the calculated result.
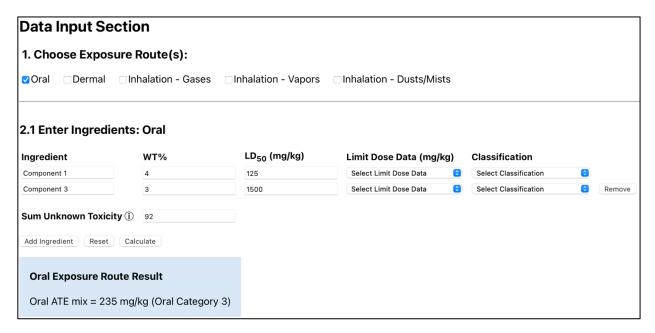
Data Input Section

1. Choose Exposure Route(s):

☑ Oral   ☐ Dermal   ☐ Inhalation – Gases   ☐ Inhalation – Vapors   ☐ Inhalation – Dusts/Mists

2.1 Enter Ingredients: Oral

Ingredient	WT%	LD$_{50}$ (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Component 1	16	1600	Select Limit Dose Data	Select Classification	
Component 2	4	200	Select Limit Dose Data	Select Classification	Remove
Component 3	80	3450	Select Limit Dose Data	Select Classification	Remove

Sum Unknown Toxicity ⓘ   Enter weight (%)

Add Ingredient   Reset   Calculate

Oral Exposure Route Result

Oral ATE mix = 1,880 mg/kg (Oral Category 4)

2.3 Example #3

Mixture Example #3 Acute Toxicity – Oral		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 4%, oral LD_{50} = 125 mg/kg Component 2: 92%, No data available Component 3: 80%, oral LD_{50} = 1500 mg/kg Component 4: 0.9%, No data available Component 5: 0.1%, oral LD50 = 10 mg/kg, Oral Category 2	Acute Oral Toxicity Category 3	Components 1 and 3 are included in the $ATE_{mixture}$ calculation because they have data that fall within an acute toxicity category. The total concentration of ingredients with unknown acute toxicity (i.e. Component 2) is 92%. Therefore, the $ATE_{mixture}$ equation that corrects for ingredients with unknown acute toxicity above 10% of the mixture must be used. Component 2 does not have any useable information for the oral route $ATE_{mixture}$ calculation and is in the mixture at a concentration $\geq 1\%$ so an additional statement is included. Apply the "relevant ingredients" concept means that ingredient 4 could be excluded from both the $ATE_{mixture}$ calculations. This same reasoning could also apply to ingredient 5, as it is below the "relevant ingredients" threshold; however, the use of expert judgment is necessary to make this decision for ingredient 5 as it is classified in Category 2. For this example, it was decided that since the percentage of this ingredient is well below the threshold (i.e. 0.1%) and the ingredient is classified in Category 2, it would be excluded from the ATE calculation. $$\frac{100 - \left(\sum C_{unknown} if > 10\%\right)}{ATE_{mixture}} = \sum_{n} \frac{C_i}{ATE_i}$$

| | | $$\frac{100-(92)}{ATE_{mixture}} = \frac{4}{125} + \frac{3}{1500}$$ $ATE_{mixture} = 235$ mg/kg, Category 3 "92% of the mixture consists of an ingredient of unknown acute oral toxicity." |

The screen shot below illustrates how the data from Example 3 should be entered into the ATE Calculator along with the calculated result. Note that the Component 4 and Component 5 are not "relevant ingredients" and thus are not included in the data entry into the ATE Calculator.

Data Input Section

1. Choose Exposure Route(s):

☑ Oral   ☐ Dermal   ☐ Inhalation - Gases   ☐ Inhalation - Vapors   ☐ Inhalation - Dusts/Mists

2.1 Enter Ingredients: Oral

Ingredient	WT%	LD$_{50}$ (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Component 1	4	125	Select Limit Dose Data	Select Classification	
Component 3	3	1500	Select Limit Dose Data	Select Classification	Remove

Sum Unknown Toxicity ⓘ   92

[Add Ingredient] [Reset] [Calculate]

Oral Exposure Route Result

Oral ATE mix = 235 mg/kg (Oral Category 3)

2.4 Example #4

Mixture Example #4 Acute Toxicity – Multiple Routes				
Components	**Wt%**	**Acute toxicity test data**		
		Oral	**Dermal**	**Inhalation Vapors**
Component 1	26	LD$_{50}$: 2,737 mg/kg	LD$_{50}$: 6,480 mg/kg	LC$_{50}$: 11 mg/l
Component 2	23	LD$_{50}$: 4,500 mg/kg	LD$_{50}$:> 6,000 mg/kg	LC$_{50}$: 19 mg/l
Component 3	11	LD$_{50:}$ > 5,000 mg/kg	No data available	No data available
Component 4	40	LD$_{50}$: 400 mg/kg	Dermal limit dose > 2,000 mg/kg (No signs of toxicity)	LC$_{50}$: 4 mg/l

Oral route

$$\frac{100}{ATE_{mixture}} = \sum_n \frac{Ci}{ATEi}$$

$$\frac{100}{ATE_{mixture}} = \frac{26}{2,737} + \frac{23}{4,500} + \frac{40}{400}$$

$ATE_{mixture}$ = 873 mg/kg, Acute Oral Toxicity Category 4

Inhalation route

$$\frac{100 - \left(\sum C_{unknown} \text{ if } > 10\%\right)}{ATE_{mixture}} = \sum_n \frac{C_i}{ATE_i}$$

$$\frac{100 - (11)}{ATE_{mixture}} = \frac{26}{11} + \frac{23}{19} + \frac{40}{4}$$

$ATE_{mixture}$ = 6.6 mg/l, Acute inhalation toxicity Category 3 and "11% of the mixture consists of an ingredient of unknown acute inhalation toxicity"

Mixture Example #4 Acute Toxicity	
HCS 2012 Classification	**Rationale**
Acute Oral Toxicity Category 4 Acute Inhalation toxicity Category 3	Review of the component test data show there is relevant evidence to suggest acute toxicity via the oral and inhalation routes so the $ATE_{mixture}$ calculation was applied to the oral and inhalation routes **Oral route** – Data is available for all ingredients via the oral route – Components 1 and 4 are included in the $ATE_{mixture}$ calculation because they have data that fall within a acute toxicity category – Component 2: per A.1.3.6.1 (a) include ingredients with a known acute toxicity, which fall into any of the acute toxicity categories, or have an oral $LD_{50} > 2000 \leqslant 5000$ mg/kg body weight – Apply the guidance in Note (a) to Table A.1.1 for Components 1, 2 and 4 in the $ATE_{mixture}$ calculation since LD_{50} data is available **Inhalation route**

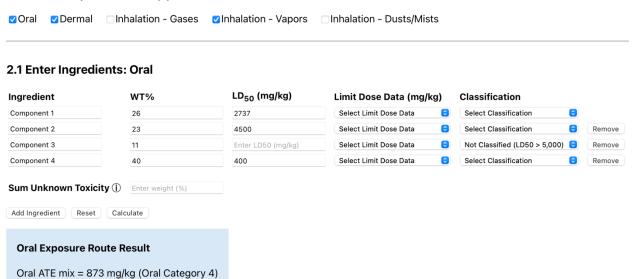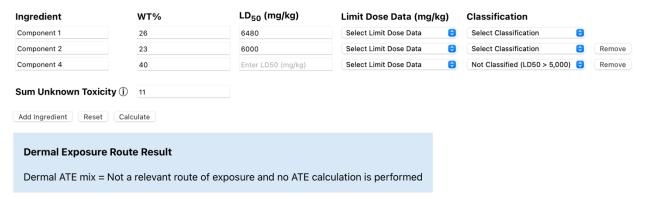|	
	– The total concentration of ingredients with unknown inhalation acute toxicity (i.e., Component 3) is 11%. Therefore, the $ATE_{mixture}$ equation that corrects for ingredients with unknown acute toxicity above 10% of the mixture. must be used for the inhalation route – Components 1, 2 and 4 are included in the $ATE_{mixture}$ calculation because they have data that fall within an acute toxicity category – Apply the guidance in Note (a) to Table A.1.1 for Components 1, 2 and 4 in the $ATE_{mixture}$ calculation since LD_{50} data is available – Component 3 does not have any useable information for the inhalation route $ATE_{mixture}$ calculation and is in the mixture at a concentration $\geq 1\%$ so an additional statement is included **Dermal route** Review of the ingredient test data via the dermal route show that the data are not applicable to the dermal $ATE_{mixture}$ calculation

The screen shot below illustrates how the data from Example 4 should be entered into the ATE Calculator along with the calculated results.

Data Input Section

1. Choose Exposure Route(s):

☑ Oral ☑ Dermal ☐ Inhalation – Gases ☑ Inhalation – Vapors ☐ Inhalation – Dusts/Mists

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2.1 Enter Ingredients: Oral

Ingredient	WT%	LD$_{50}$ (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Component 1	26	2737	Select Limit Dose Data	Select Classification	
Component 2	23	4500	Select Limit Dose Data	Select Classification	Remove
Component 3	11	Enter LD50 (mg/kg)	Select Limit Dose Data	Not Classified (LD50 > 5,000)	Remove
Component 4	40	400	Select Limit Dose Data	Select Classification	Remove

Sum Unknown Toxicity ⓘ Enter weight (%)

[Add Ingredient] [Reset] [Calculate]

> **Oral Exposure Route Result**
>
> Oral ATE mix = 873 mg/kg (Oral Category 4)

2.2 Enter Ingredients: Dermal

Ingredient	WT%	LD$_{50}$ (mg/kg)	Limit Dose Data (mg/kg)	Classification	
Component 1	26	6480	Select Limit Dose Data	Select Classification	
Component 2	23	6000	Select Limit Dose Data	Select Classification	Remove
Component 4	40	Enter LD50 (mg/kg)	Select Limit Dose Data	Not Classified (LD50 > 5,000)	Remove

Sum Unknown Toxicity ⓘ 11

[Add Ingredient] [Reset] [Calculate]

> **Dermal Exposure Route Result**
>
> Dermal ATE mix = Not a relevant route of exposure and no ATE calculation is performed

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2.4 Enter Ingredients: Inhalation - Vapors

Ingredient	WT%	LC$_{50}$ (mg/l)	Limit Dose Data (mg/kg)	Classification	
Component 1	26	11	Select Limit Dose Data	Select Classification	
Component 2	23	19	Select Limit Dose Data	Select Classification	Remove
Component 4	40	4	Select Limit Dose Data	Select Classification	Remove

Sum Unknown Toxicity ⓘ 11

[Add Ingredient] [Reset] [Calculate]

> **Inhalation - Vapors Exposure Route Result**
>
> Inhalation - Vapors ATE mix = 6.6 mg/l (Inhalation - Vapors Category 3)