OSHA ATE Calculator Users Guide

Definitions

Ingredient – the specific substance contained within the mixture or a mixture within another mixture.

WT – percent by weight of the ingredient within the mixture.

LD₅₀ mg/kg – Dose (expressed in milligrams per kilogram) of a substance or mixture that kills 50 percent (after single exposure) of animals in an oral or dermal study. Oral studies are usually performed in rats or mice while dermal studies often used rabbits. However, other animal species may be used in the tests.

LC₅₀ ppm – Concentration of a gas (expressed in parts per million) of a substance or mixture that kills 50 percent (single exposure for 1-4 hours) of animals in an inhalation study. Inhalation studies are usually performed in rats, however, other animal species (e.g., mice, rabbits, pigeons) may be used in the tests. The HCS and GHS use a 4-hour time point to calculate lethality so any value other than 4 hours would need to be converted to the 4-hour value (GHS, Rev.10, paragraph 3.1.5.3).

LC₅₀ mg/l - Concentration of a vapor (expressed in milligrams per liter air) of a substance or mixture that kills 50 percent (single exposure for 1-4 hours) of animals in an inhalation study. Inhalation studies are usually performed in rats, however, other animal species (e.g., mice, rabbits, pigeons) may be used in the tests. The HCS and GHS use a 4-hour time point to calculate lethality so any value other than 4 hours would need to be converted to the 4-hour value (GHS, Rev.10, paragraph 3.1.5.3).

LC₅₀ mg/l – Concentration of a mist, dusts, or particles (expressed in milligrams per liter air) of a substance or mixture that kills 50 percent (single exposure for 1-4 hours) of animals in an inhalation study. Inhalation studies are usually performed in rats, however, other animal species (e.g., mice, rabbits, pigeons) may be used in the tests. Sometimes this information will be expressed as mg/m³. This information is easily converted to mg/l by dividing the concentration in mg/m³ by 1000 to get the mg/l value. The HCS and GHS use a 4-hour time point to calculate lethality so any value other than 4 hours would need to be converted to the 4-hour value (GHS, Rev.10, paragraph 3.1.5.3).

Limit dose data – this value is used if the only data available for an individual ingredient is a range estimate.

Classification – this value is used if the only data available for an individual ingredient is the hazard category for this specific endpoint.

Table of Contents

TABLE OF CONTENTS	
OVERVIEW	
1. APPROACH TO CALCULATING THE ACUTE TOXICITY ESTIMATE OF A MIXTURE	
2. APPROACH TO ENTERING DATA INTO THE ATE CALCULATOR	
2. Example ATE Calculations	6
2.1 EXAMPLE #1	
2.2 Example #2	
2.3 EXAMPLE #3	10
2.4 FXAMPLE #4	11

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 LD₅₀ or Inhalation LC₅₀ of the mixture. This is accomplished by collecting the LD₅₀/LC₅₀ for each ingredient if it is known or a point estimate of an ingredient's LD₅₀/LC₅₀. 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).

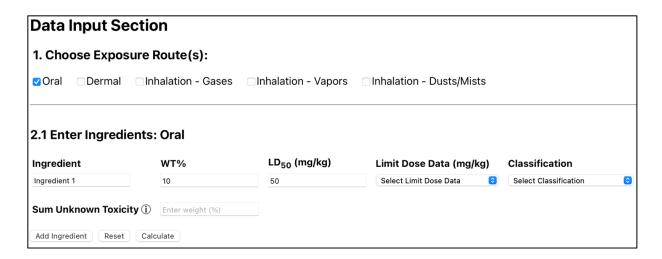
2. Data Entry into the ATE Calculator

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

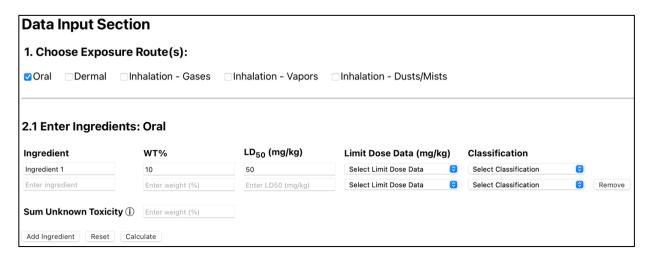
Step 1: Select the checkbox(es) for all relevant Exposure Route(s).

Data Input Section				
1. Cho	ose Expos	sure Route(s):		
✓Oral	□ Dermal	□Inhalation - Gases	□Inhalation - Vapors	☐ Inhalation - Dusts/Mists

Step 2: Enter the Ingredient Name, Wt%, and either a LD₅₀/LC₅₀ **or** Limit Dose Data **or** Classification for the default Ingredient row.



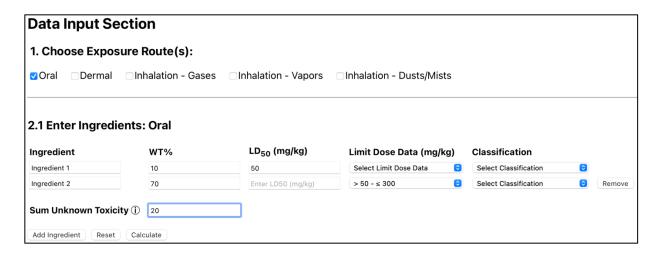
Step 3: To add another ingredient, select the Add Ingredient button.



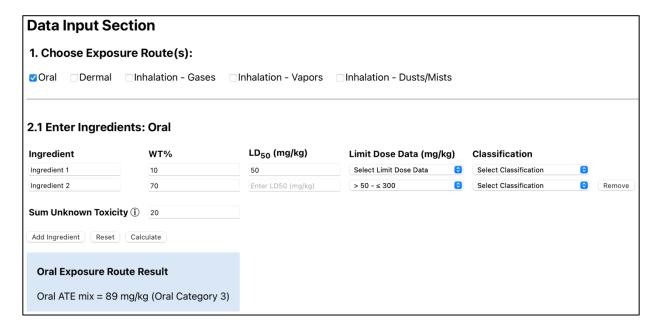
- Step 4: Enter the Ingredient Name, Wt%, and either LD₅₀/LC₅₀ **or** Limit Dose Data **or** Classification for the newly inserted Ingredient row.
- Step 5: Repeat steps 3 and 4 for each Ingredient until all "relevant ingredient" rows are entered. If necessary, a row can be deleted by selecting the Remove button at the end of a row.
- Step 6: If the sum of "relevant ingredients" without any information on acute toxicity² for the selected route of entry is > 10% then enter the sum of the ingredient's weight percent in the Sum Unknown Toxicity field.

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).



Step 4: Select the Calculate button.



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

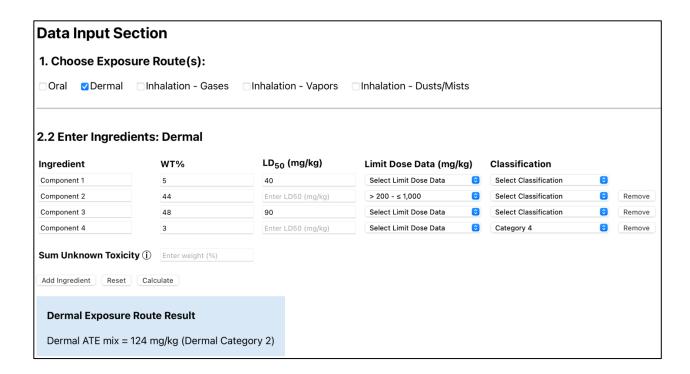
The following 4 mixture examples are taken directly from OSHA's Hazard Classification Guidance for Manufactures, Importers, and Employers (OSHA 3844-02 2016). These 4 examples provide the basis for illustrating how to enter various types of data into the calculator³.

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

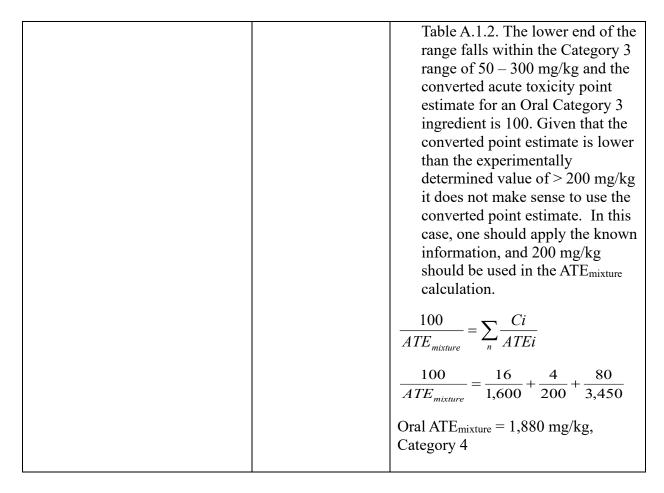
Mixture Example #1 Acute Toxicity — Dermal		
Data	HCS 2012	Rationale
	Classification	
Component data: Component 1:5%, Dermal LD ₅₀ = 40 mg/kg Component 2: 44%, Dermal LD ₅₀ > 200 < 1,000 Component 3: 48%, Dermal LD ₅₀ = 190 mg/kg Component 4: 3%, Acute Dermal Toxicity Category 4	Acute Toxicity Dermal Category 2	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

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

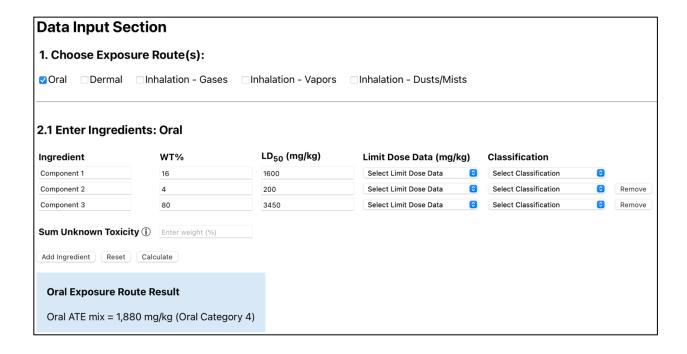


2.2 Example #2

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 =	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 $LD_{50} > 2000 \le 5000$ mg/kg body weight The LD_{50} data for Components 1 and	
3,450 mg/kg		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	



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

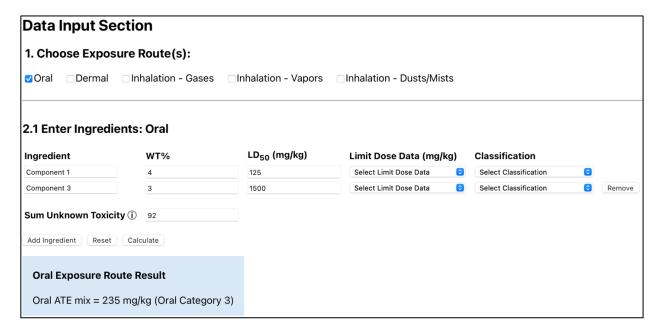


2.3 Example #3

$$\frac{100 - (92)}{ATE_{mixture}} = \frac{4}{125} + \frac{3}{1500}$$

$$ATE_{mixture} = 235 \text{ mg/kg, Category 3}$$
"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.



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	$LD_{50:} > 5,000 \text{ mg/kg}$	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

$$\frac{100}{\text{ATE}_{\text{mixture}}} = \sum_{n} \frac{\text{Ci}}{\text{ATEi}}$$

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

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

Inhalation route

$$\frac{100 - \left(\sum C_{\text{unknown}} \text{ if } > 10\%\right)}{\text{ATE}_{\text{mixture}}} = \sum_{n} \frac{C_{\text{i}}}{\text{ATE}_{\text{i}}}$$

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

 $ATE_{mixture} = 6.6 \, \text{mg/l}$, 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	on Rationale		
Acute Oral Toxicity	Review of the component test data show there is		
Category 4	relevant evidence to suggest acute toxicity via the oral		
	and inhalation routes so the ATE _{mixture} calculation was		
Acute Inhalation toxicity	applied to the oral and inhalation routes		
Category 3	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 LD₅₀ > 2000 ≤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 LD₅₀ 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 LD₅₀ 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 ≥ 1% so an additional statement is included

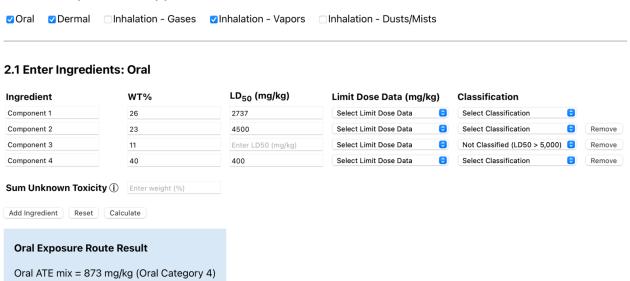
Dermal route

Review of the ingredient test data via the dermal route show that the data are not applicable to the dermal $ATE_{mixture}$ calculation

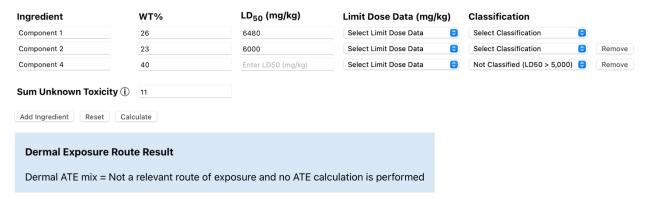
The screen shot below illustrates how the data from Example 4 should be entered into the ATE Calculator along with the calculated results.

Data Input Section

1. Choose Exposure Route(s):



2.2 Enter Ingredients: Dermal



2.4 Enter Ingredients: Inhalation - Vapors

