

Read-Across Techniques for Chemical Classification

A short primer for non-toxicologists.

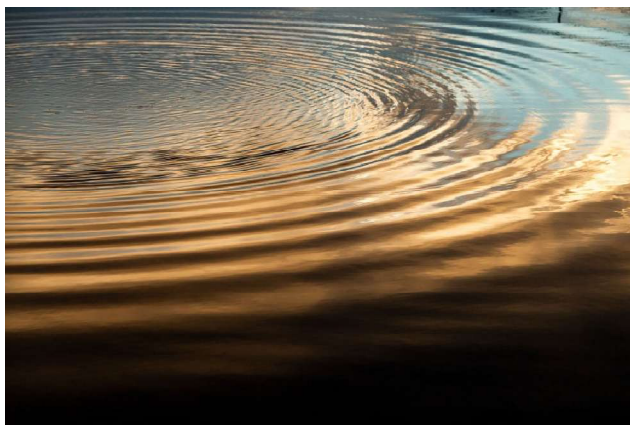
Presenter: Lee Boulineau, Senior Toxicologist, VelocityEHS

What are read-across techniques?

Using known data from similar substances to evaluate novel substances.....



Fire Response



Spill Response



Spice Response

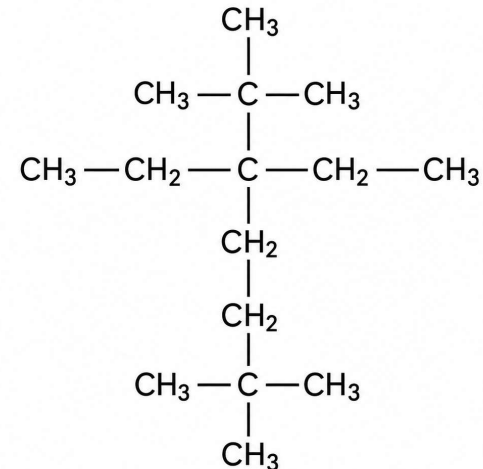
... leading to reasonable assumptions concerning novel substances. In all three cases, we are **leveraging available data from similar substances** and products **to evaluate an unknown substance** and assess its potential toxicological profile.

Read-across is a repeatable reasoning process



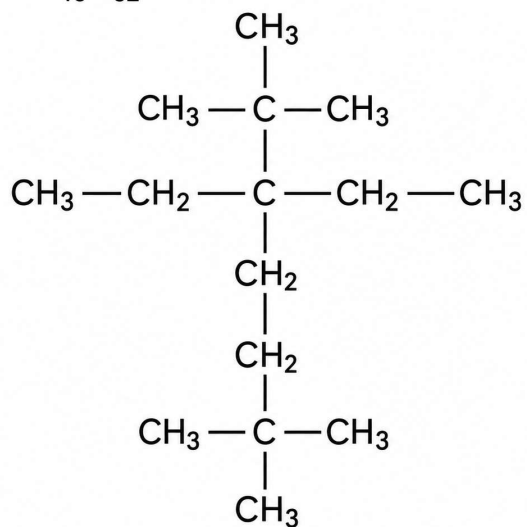
Let's walk-through the method across several endpoints using a single substance.

Planane – C₁₅H₃₂



Read-across Technique: Flammability

Planane – C₁₅H₃₂



Formula: C₁₅H₃₂

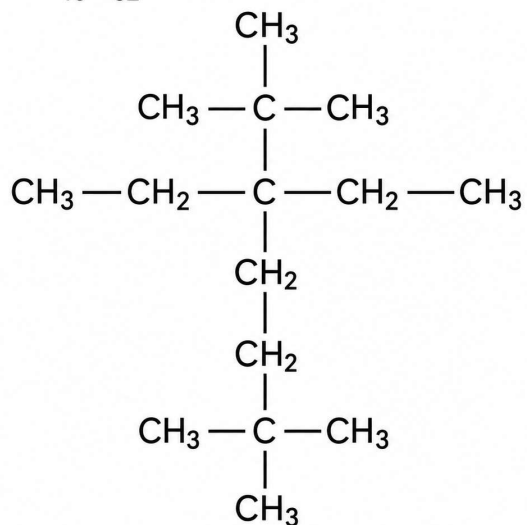
IUPAC Name: 3,3'-Diethyl-2,2',6,6'-tetramethylheptane

Flashpoint: *close cup flashpoint test* **Not Available**
Testing scheduled for ?!?!?

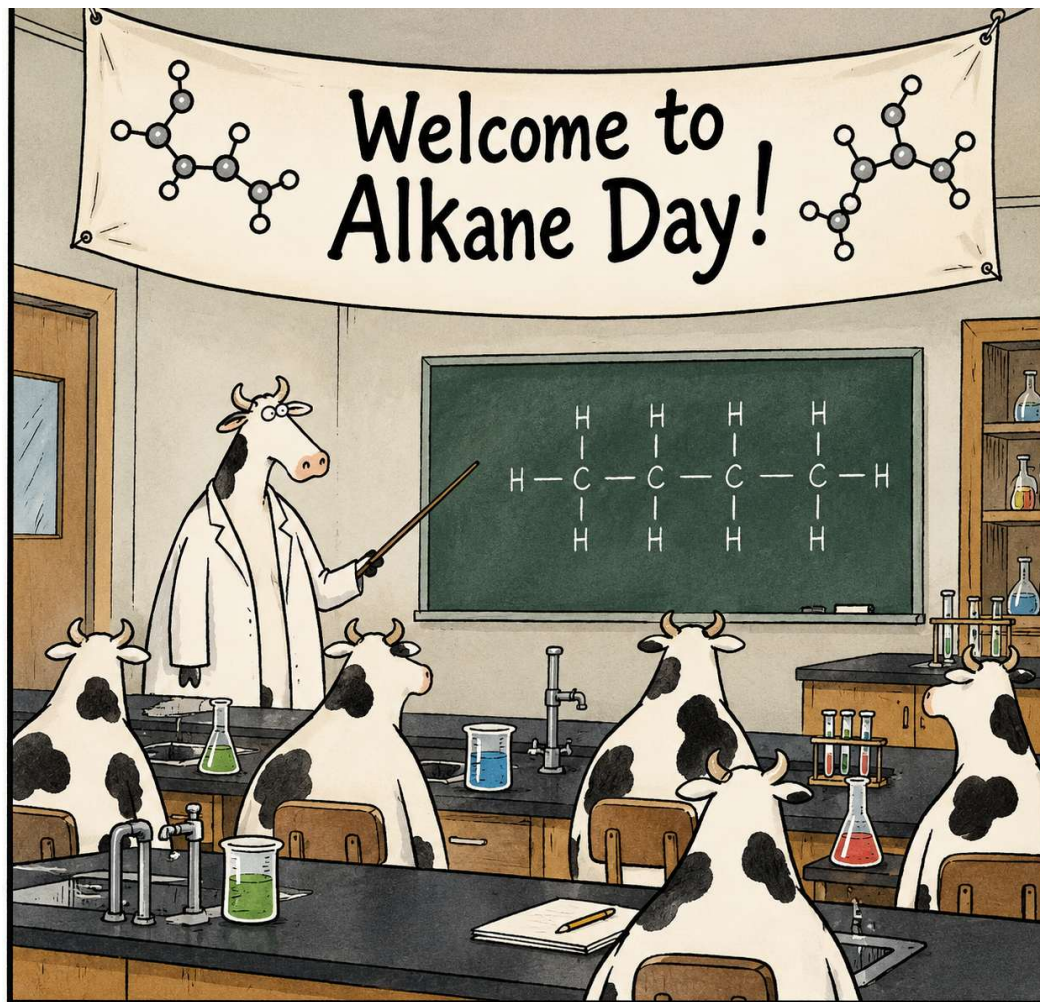
Identify

Read-across Technique: Carbon Number

Planane - C₁₅H₃₂



Compare



Read-across Technique: Flash Point Data

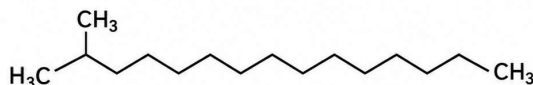
Not flammable

>94 °C Not flammable

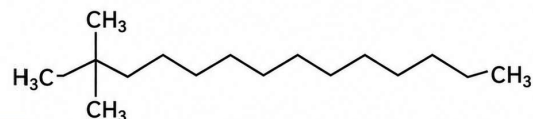
n-Pentadecane



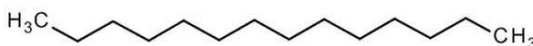
2-Methyltetradecane



2,2-Dimethyltridecane



n-Tetradecane



Combustible

100 °C Not flammable

Weigh
Evidence

Option 1

Non-Flammable based on majority of values obtained

3 of the 4 read-across substances have Flash Points $>93.4^{\circ}\text{C}$ (200°F).

Based upon preponderance of evidence. Logical conclusion!

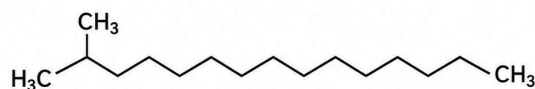


Classify

Option 2

Combustible based on lowest known read-across value

2-Methyltetradecane



Formula: C₁₅H₃₂

IUPAC Name: 2-methyltetradecane.

CAS # 1560-95-8

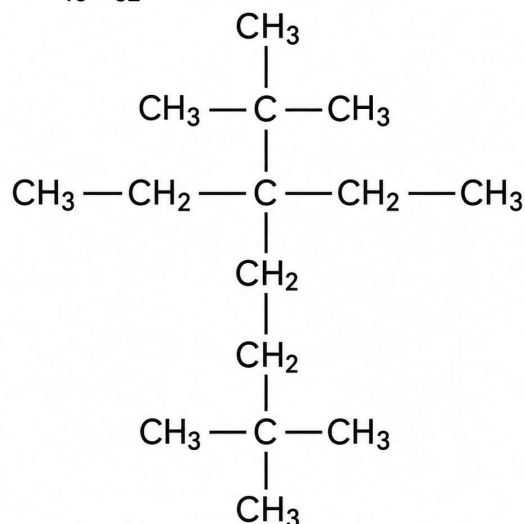
Flashpoint: **87.7 °C (2-Methyl-tetradecane)**

**Conservative approach -
certainly reasonable!**

Classify

Read-across Technique: Aspiration

Planane – C₁₅H₃₂



Formula: C₁₅H₃₂

IUPAC Name: 3,3'-Diethyl-2,2',6,6'-tetramethylheptane

Viscosity: *Not Available*

The same molecule can be assessed for a different endpoint

Identify

Read Across Technique: Aspiration

n-Hexadecane



n-Octadecane



n-Eicosane (n-Icosane)



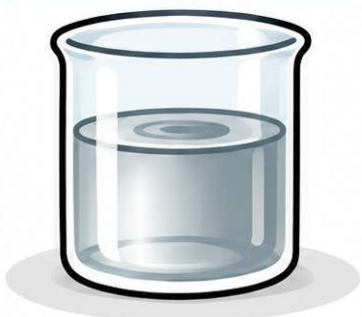
Compare

Again, multiple references reduce the risk of a misleading comparison

Read-across Technique: Viscosity

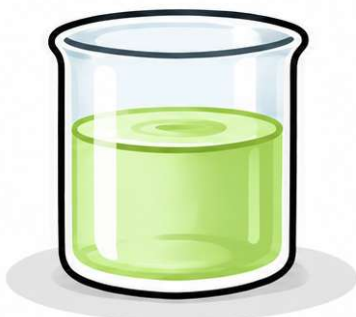
n-Pentadecane

2.86 mPa·s
@ 20 °C
(dynamic)



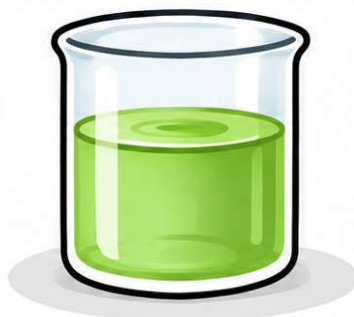
n-Hexadecane

4.51 mm²/s
@ 20 °C



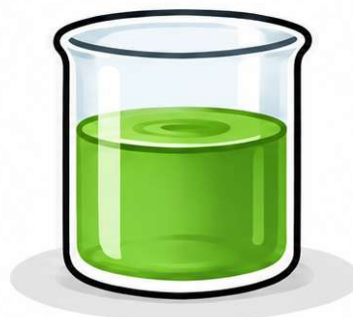
n-Octadecane

4.03 mm²/s
@ 20 °C



n-Octadecane

3.35 mm²/s
@ 50 °C



n-Eicosane

5.36 mm²/s
@ 40 °C



**Weigh
Evidence**

Reliable data determine the best read-across substances.

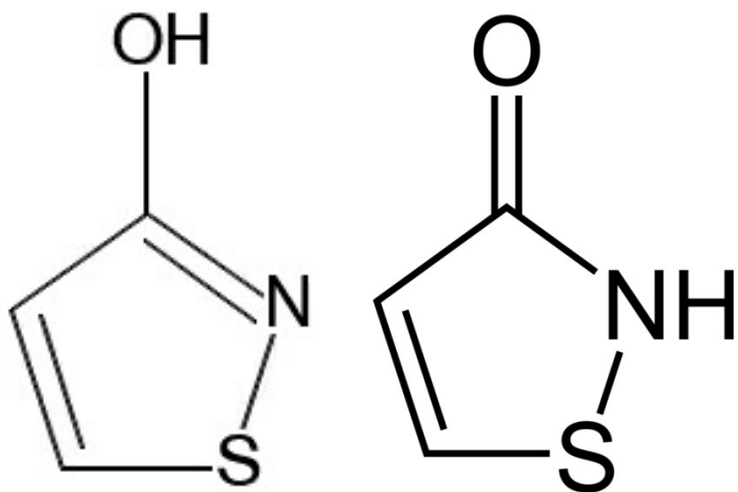
Viscosity evidence consistently
points toward aspiration potential



Classify

Read-across Technique: Functional groups

Functional groups provide an efficient first step to an initial hazard hypothesis



IUPAC Name: 1,2-thiazol-3-ol / 1,2-thiazol-3-one

CAS #: 1003-07-2

Hazard Hypothesis: Skin Sensitization

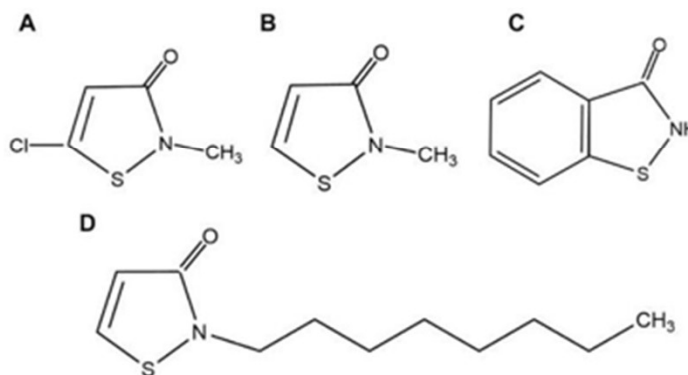
Base functional group: NOT A SENSITIZER (ECHA)

Identify

Read-across Technique: Functional groups

Known sensitizers such as CMIT, MIT, BIT, and OIT establish a strong class-based concern.

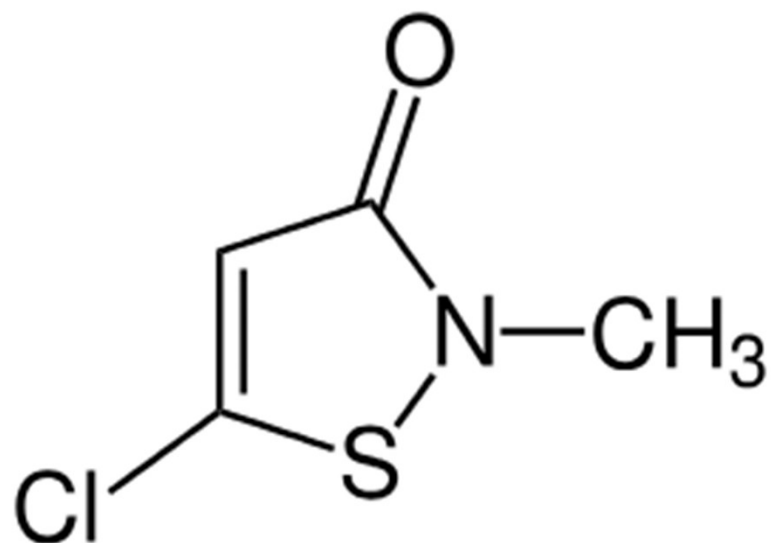
A – CMIT; B – MIT; C – BIT; D – OIT



Compare

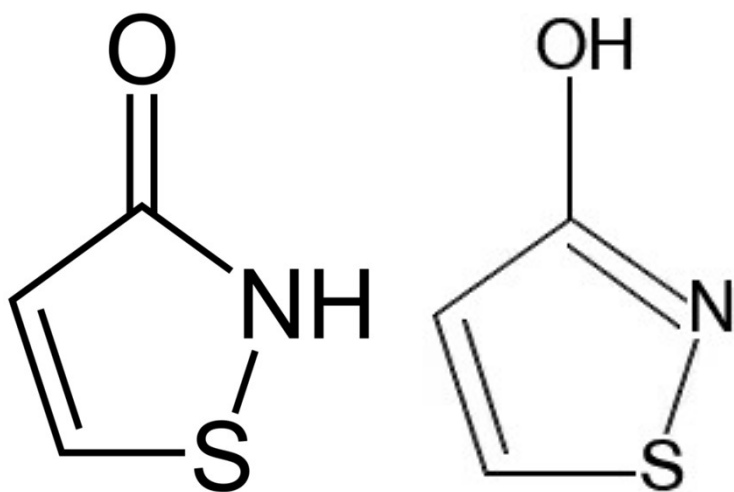
Read Across Technique: Functional groups

CMIT has a classification limit of 0.0015% or 15 ppm under ECHA.



Weigh
Evidence

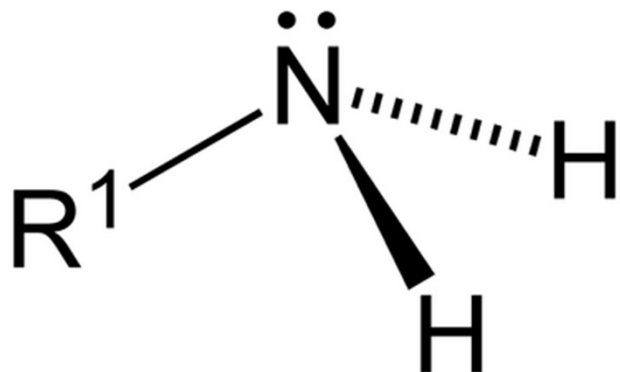
Read Across Technique: Functional groups



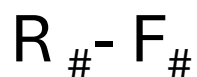
Any compound with these base structures and any substitution, whether on the nitrogen, sulfur, or carbon atoms in the rings, should be considered a skin (and potentially respiratory) sensitizer ***unless testing (animal or human) indicates otherwise.***

Classify

Read Across Technique: Functional groups



This technique may be also used to evaluate to potential for hazards such as skin corrosion/irritation, eye damage/irritation (primary amines), and in certain cases Specific Target Organ Toxicity (soluble fluorides).



(Soluble fluorides)

Identify

Classify

Trust *but* Verify

Key Take-Aways from Our Walk-Through

1

Evaluate more than one substance as a read-across.

Three or more would be ideal.



Substance
A



Substance
B



Substance
C



2

Use read-across to advocate for needed testing.

These techniques while useful, are not a substitute for testing.



FLASH POINT TEST



☒ Supports conclusion

☒ Rules out conclusion