

Substantially similar mixtures bridging principle example

While this specific example uses skin sensitization data, the reader is reminded that the substantially similar mixtures bridging principle can be applied to other hazard classes as prescribed in the purple book.

Substantially similar mixtures

Given the following:

- (a) Two mixtures: (i) A + B;
 (ii) C + B;
- (b) The concentration of ingredient B is essentially the same in both mixtures;
- (c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);
- (d) Ingredient B is a sensitizer and ingredients A and C are not sensitizers;
- (e) A and C are not expected to affect the sensitizing properties of B.

If mixture (i) or (ii) is already classified based on test data, then the other mixture can be assigned the same hazard category.

Background information:

1. Existing animal test data on ingredient 1 indicates that it is a Category 1 skin sensitizer.
2. Ingredient 1 has been used in products ranging from 1.2 to 6.0 weight percent for years with lack of evidence of skin sensitizing properties (see table below “tested mixture information”).
3. Ingredients 2(a) and 2(b) are analogous lubricant materials with slightly different viscosities. Ingredients 2(a) and 2(b) have both been tested in animal studies and are not skin sensitizers. They are not expected to affect the sensitization potential of ingredient 1.
4. There are no data to suggest that the other ingredients are skin sensitizers or that they will affect the sensitization potential of ingredient 1.
5. Products containing ingredient 1 were then tested in animal studies, which were all negative. Subsequently, clinical study data were gathered and are summarized below:

Tested mixture information:

Product name	Wt% of ingredient 1 in product	Repeated insult patch tests # of positive cases/# Tested
Product 1	5.0	0/298
Product 2	6.0	0/198
Product 3	6.0	0/307
Product 4	5.0	0/197
Product 5	2.5	0/103

Total: 0/1103

Detailed composition of tested mixture and substantially similar untested mixture:

Tested Mixture (Product 1)	
Ingredient	Wt%
Ingredient 1	5.0
Ingredient 2(a)	91.0
Ingredient 3	3.0
Ingredient 4	0.9
Ingredient 5	0.1

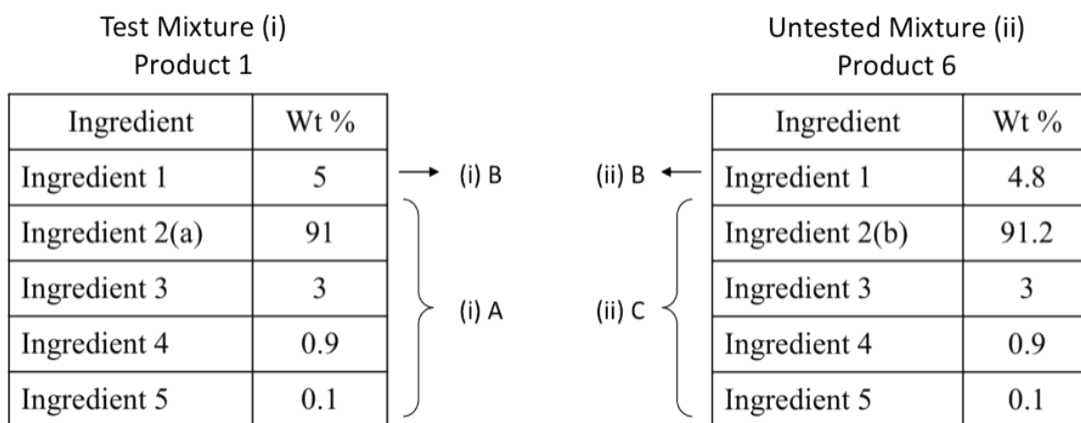
Untested Mixture (Product 6)	
Ingredient	Wt%
Ingredient 1	4.8
Ingredient 2(b)	91.2
Ingredient 3	3.0
Ingredient 4	0.9
Ingredient 5	0.1

Answer:

The untested mixture (Product 6) is not classified for skin sensitization based on the test data available for the similar tested mixture (Product 1).

Rationale:

- (a) Classification via application of substance criteria is not possible since skin sensitization test data was not provided for the untested mixture;
- (b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture;
- (c) Classification of the mixture based on ingredient information should be considered if the classifier chooses not to apply the bridging principle or sufficient data had not been available to apply the bridging principle;
- (d) As illustrated using the figure below, the substantially similar mixtures bridging principle can be applied because:
 - (i) The concentration of ingredient B (i.e., ingredient 1 in both mixtures) is essentially the same in both mixtures



- (ii) Ingredient B is a sensitizer and ingredients A (i.e., ingredients 2(a), 3, 4, 5) in mixture (i) and C (i.e., ingredients 2(b), 3, 4, 5) in mixture (ii) are not sensitizers
- (iii) Ingredients A and C are not expected to affect the sensitizing properties of ingredient B.
- (iv) Since product 1 was already not classified based on test data, then product 6 is also not classified based on the test data.

(Ref.Doc: ST/SG/AC.10/C.4/2010/15 as amended by INF.40(20th session), annex 2)