

## **Batching bridging principle example (specific target organ toxicity – single dose data)**

While this specific example uses specific target organ toxicity – single dose data, the reader is reminded that the batching bridging principle can be applied to other hazard classes as prescribed in the purple book.

### **Batching**

The toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary.

### **Background**

1. Ingredient A is a complex substance that in commercial batches contains a mixture of isomers. Specific target organ toxicity – single exposure effects have been well documented for the ortho-isomers contained in ingredient A.
2. Accidental ingestion of mixtures containing ingredient A in humans due to contamination of drink and food has been reported which resulted in paralysis of the lower extremities.
3. Mixtures containing various concentrations of ingredient A have been tested over the course of many years in animal studies. The results of these studies show a direct correlation of Ingredient A's ortho-isomers concentration in the mixture to statistically significant effects in the animal studies. Based on all available data a specific concentration limit is established that any mixture containing greater than or equal to 0.5% of the ortho-isomers of ingredient A must be classified as Specific target organ toxicity – single exposure; Category 2. Mixtures containing less than 0.5% of the ortho-isomers of ingredient A are not classified.

### **Untested mixture information:**

<b>Manufacturing batch</b>	<b>Wt% of ortho-isomer of ingredient A</b>
Batch 1	0.42
Batch 2	0.52

### **Answer:**

- (a) Batch 1: Applying the batching bridging principle the Untested Batch 1 mixture does not require classification.
- (b) Batch 2: Applying the batching bridging principle the Untested Batch 2 mixture is classified as Specific target organ toxicity – single exposure; Category 2.

### **Rationale:**

- (a) Classification via application of substance criteria is not possible since Specific target organ toxicity – single exposure test data was not provided for each batch of the mixture;
- (b) Classification via the application of bridging principles can be considered since there are sufficient data on both the individual ingredients and similar tested mixtures;

- (c) The batching bridging principle can be applied because the tested product batches of the mixture can be assumed to be substantially equivalent to the untested production batches of the same commercial product. In those cases where there is a reason to believe that a significant variation impacts the toxicity of the batch (i.e. based on the ortho-isomer concentration) then a new classification is necessary (e.g. batch 2).

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