

## Analysis of the *In Vivo* Database Using the GHS Classification System

### RULES FOLLOWED FOR CLASSIFICATION BY NICEATM

#### 1. Animal classification

Each animal is classified into 1 of 4 categories according to the following classification rules.

##### **Category 1:**

Option 1. Effects in the cornea, iris, or conjunctiva that are not expected to reverse or have not fully reversed within the observation period of 21 days (i.e., cornea or iris scores  $\geq 1$  or redness or chemosis scores  $\geq 2$  on Day 21)

OR

Option 2. A corneal opacity score of 4 at any time during the test

OR

Option 3. If the average of the scores on day 1, 2, and 3 for opacity  $\geq 3$  and/or iris  $\geq 1.5$

If an animal is identified under Option 1 or Option 2, then the animal is classified as Cat 1(pos1/3)

If an animal is identified under Option 3, then the animal is classified as Cat 1(pos2/3)

##### **Category 2A:**

If the average of the scores on day 1, 2, and 3 are:

- (a)  $1 \geq \text{opacity} < 3$  or
- (b)  $1 \geq \text{iris} < 1.5$  or
- (c) conjunctival redness  $\geq 2$  or
- (d) chemosis  $\geq 2$

AND

The effect fully reverses within an observation period of normally 21 days (i.e., opacity = 0, and iris = 0, and conjunctival redness  $\leq 1$ , and chemosis  $\leq 1$ )

The animal is then classified as Cat2A

##### **Category 2B:**

If the average of the scores on day 1, 2, and 3 are:

- (a)  $1 \geq \text{opacity} < 3$  or
- (b)  $1 \geq \text{iris} < 1.5$  or
- (c) conjunctival redness  $\geq 2$  or
- (d) chemosis  $\geq 2$

AND

The effect fully reverses within 7 days (i.e., opacity = 0, and iris = 0, and conjunctival redness  $\leq$  1, and chemosis  $\leq$  1)

The animal is then classified as Cat2B

***Nonirritant:***

If the average of the scores on day 1, 2, and 3 for opacity  $<1$ , and iris  $<1$ , and conjunctival redness  $<2$ , and chemosis  $<2$

The animal is then classified as nonirritant

**2. Study Classification**

Each study is then classified based upon the number of animals within each category and based on the following rules.

***Category 1:***

1. At least 1 out of 3 animals or 2 out of 6 animals classified as Cat 1(pos1/3)
2. One out of 6 animals classified as Cat 1(pos1/3) and another animal classified as Cat 1(pos2/3)
2. At least 2 out of 3 animals or 4 out of 6 animals classified as Cat 1(pos2/3)

If neither of the above options are fulfilled, then the following classifications can be applied

***Category 2A:***

At least 2 out of 3 animals or 4 out of 6 animals classified as Cat2A or 2B

***Category 2B:***

At least 2 out of 3 animals or 4 out of 6 animals classified as Cat2B

***Nonirritant:***

At least 2 out of 3 animals or 4 out of 6 animals classified as nonirritant