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Reviewed by: SanYvette Williams, DVM SW 4/2/91
Section IV, Tox. Br. II (HFAS) (H7509C)
Secondary reviewers: Elizabeth Doyle, Ph. D. EDD. 4/5/91,
Section IV, Tox. Branch II (HFAS) (H7509C)

DATA EVALUATION REPORT

CHEMICAL: Silver Copper Zeolite

CHEMICAL NO: 129057 **HED NO.:** 1-0266

STUDY TYPE: Eye Irritation in Rabbits (81-4)

ACCESSION NO.: 416385-01 **SLS STUDY NO.:** 3214.1

STUDY TITLE: Primary Eye Irritation Study In Rabbits With Silver Copper Zeolite

STUDY DIRECTOR: Rusty E. Rush, B.S.

SPONSOR: Kanebo Zeolite, USA, Inc., Empire State Bldg., 350 5th Ave., NY,NY 10118

PERFORMING LAB: Springborn Laboratories, Inc., Mammalian Toxicology Division, Spencerville, OH 45887

GLP COMPLIANCE: Signed statement on page 3.

QUALITY ASSURANCE: Signed statement included on page 4.

CONCLUSIONS: Based on the no rinse group mean irritation scores, Silver Copper Zeolite is considered to be a moderate (Mean irritation scores > 6.0 at 24 hours, but maximum mean irritation score $\leq$ 30.0 and any corneal or iridial changes having been totally reversed by day 14) ocular irritant in the rabbit (Tox. Category III).

CLASSIFICATION: This study satisfies the data requirements for Guideline No. 81-4 and is classified as Core - Guideline.

A. MATERIALS:

Test compound: Silver Copper Zeolite in the form of a blue powder. Purity was not included.

Test animal: Young adult, female New Zealand White rabbits were used in the experiment. Body weights prior to the initiation of the study ranged from 2.1 to 2.4 grams on the day of treatment. They were supplied by Mohican Valley Rabbitry, Loudonville, OH. All were acclimated 5 days prior to initiation of the study.

B. **STUDY DESIGN:**

On the day of study initiation, the eyes of 9 female rabbits were examined macroscopically with and without fluorescein dye. Those animals showing preexisting corneal or conjunctival injury or irritation were not used. A dose of 0.061 g of test article (0.1 ml) was introduced into the lower conjunctival sac of the right eye of each rabbit. The left eyes were used as controls. Both eyes of three rabbits were rinsed after 30 seconds with physiological saline (rinse group). The remaining six did not have their eyes examined (no rinse group).

Both eyes of all nine animals were examined for evidence of eye irritation at approximately 1, 24, 48, and 72 hours, and up to 7 days post-treatment. After the 24 hour scoring interval, the fluorescein examination procedure was repeated on all test and control eyes. The fluorescein exam was conducted on affected eyes at each subsequent interval until a negative response was obtained.

Ocular irritation scores were added for each animal and the group mean irritation score of all animals was calculated for each scoring interval. Then, based on the severity and duration of response, the eye irritation properties were classified according to certain criteria (Text included).

B. **RESULTS:**

In the no rinse group, Silver Copper Zeolite produced moderate ocular irritation. At the 24 hour scoring interval, corneal opacity was observed in 2/6 (33%) of the rabbits. This had resolved by 48 hours, however. Confirmation of corneal injury was made after fluorescein dye was retained. At the 1 hour scoring interval, 6/6 (100%) of the animals displayed iritis. This also had resolved after 48 hours. Conjunctival redness, swelling, and discharge (conjunctivitis) was present in 6/6 (100%) of the test animals at 1 hour post-treatment. The conjunctivitis had resolved in all by day 7 (termination). Group mean irritation scores for the no rinse group are given below:

Group Mean Irritation Scores

1 Hour	- 14.0
24 Hours	- 9.3
48 Hours	- 1.7
72 Hours	- 0.7

Reactions to test article were not as severe in the rinse group as compared to the no rinse group. At the 1 hour interval, iritis was observed in 3/3 (100%) of the test animals, but it resolved by 24 hours post-treatment. There was also a minimal amount of conjunctivitis (swelling and redness) noted in 3/3 (100%) of the animals at 1 hour post-treatment. This resolved after 24 hours.

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There was no effect on the cornea of any of the animals that was related to treatment. Group mean irritation scores for the rinse group are given below:

Group Mean Irritation Scores

1 Hour - 9.0
24 Hours - 2.0
48 Hours - 0.7
72 Hours - 0.0

C. **CONCLUSIONS:**

Based on the no rinse group mean irritation scores, Silver Copper Zeolite is considered to be a moderate (Mean irritation scores > 6.0 at 24 hours, but maximum mean irritation score $\leq$ 30.0 and any corneal or iridial changes having been totally reversed by day 14) ocular irritant in the rabbit (Tox. Category III).

This study satisfies the data requirements for guideline #81-4. It is classified as core - Guideline.

OCULAR EVALUATION CRITERIA

Evaluation Criteria	Irritation Rating
Maximum mean irritation score $\leq$ 1.0	Nonirritant
Mean Irritation score $\leq$ 6.0 at 24 hours and no corneal or iridal irritation. Irritation must be completely reversible by day 7.	Slight Irritant
Mean irritation score > 6.0 at 24 hours, but maximum mean irritation score $\leq$ 30.0 and any corneal or iridal changes are completely reversible by day 14.	Moderate Irritant
Maximum mean irritation score > 30.0, or any corneal or iridal findings persist at 14 or 21 days.	Severe Irritant
Irreversible alteration - gross destruction.	Corrosive

OCULAR IRRITATION GRADING SYSTEM

	Score
CONJUNCTIVAE	
(A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
Blood vessels normal	0
Blood vessels definitely injected (hyperemic) above normal (slight erythema)	1
More diffuse, deeper crimson red, individual vessels not easily discernible (moderate erythema)	2*
Diffuse beefy red (marked erythema)	3*
(B) Chemosis	
No swelling	0
Any swelling above normal (includes nictitating membrane, slightly swollen)	1
Obvious swelling with partial eversion of lids	2*
Swelling with lids about half closed	3*
Swelling with lids more than half closed	4*
(C) Discharge	
No discharge	0
Any amount different from normal (does not include small amounts observed in inner canthus of normal animals)	1
Discharge with moistening of the lids and hairs just adjacent to lids	2
Discharge with moistening of the lids and hairs and considerable area around the eye	3

Score = (A + B + C) x 2 Total Maximum = 20

*Positive response.

Ocular Codes

Fluorescein exam indicates apparent mechanical injury to cornea -	MI
Fluorescein exam indicates stippling on cornea -	ST
Fluorescein exam indicates desquamation of cornea -	DES
Fluorescein dye retention associated with corneal opacity	FAO
Sloughing of corneal epithelium -	SCE
Corneal bulging -	CB
Slight dulling of normal luster of cornea -	SDL
Corneal neovascularization, pannus -	VAS
Iritis -	IR
Iris has sluggish reaction to light -	SRL
Test article present in eye -	TAE

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OCULAR IRRITATION GRADING SYSTEM

	Score
CORNEA	
(A) Opacity--degree of density (area most dense taken for reading)	
No ulceration or opacity	0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	1*
Easily discernible translucent area, details of iris slightly obscured	2*
Opalescent (nacreous) area, no details of iris visible, size of pupil barely discernible	3*
Opaque cornea, iris not discernible through opacity	4*
(B) Area of cornea involved	
One quarter (or less) but not zero	1
Greater than one quarter, but less than half	2
Greater than half, but less than three quarters	3
Greater than three quarters, up to a whole area	4

Score = A x B x 5 Total Maximum = 80

IRIS	
(A) Values	
Normal	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris is still reacting to light (sluggish reaction to positive)	1*
No reaction to light, hemorrhage, gross destruction (any or all of these)	2*

Score = A x 5 Total Maximum = 10

*Positive response.