



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

002318

MEMORANDUM

TO: Franklin Gee, Product Manager #17
Registration Division (TS-767)

THRU: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: (1) Pydrin® 2.4EC, EPA Reg. No. 201-401, General
Revision of Label. Change of Signal Word from
DANGER to WARNING. Amendment. (2) Eye Irritation
Study Rabbit - 21 Days.

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Budd
12/2/82

TOX Chem. No. 77A

The Shell Chemical Company has submitted an eye irritation study in rabbits based upon the Draize method of testing and scoring. The test was however modified to extend the observation period from 14 days to 21 days to coincide with the attached criteria and policy notice (Criteria and Policy Notice 2161.2).

Toxicology Branch agrees that the front panel signal word for this formulation should be WARNING based upon the results of the study and attached criteria and policy notice. Toxicology Branch does not agree however with the attendant front and side panel precautionary statements and side panel signal word. Toxicology Branch is therefore requiring that,

- (1) The side panel signal word DANGER be changed to WARNING.
- (2) The front and side panel precautionary statements; Corrosive. Causes eye damage. be deleted and the following phrase be inserted; Causes substantial but temporary eye injury.

Subject: Eye Irritation of Pydrin® 2.4 EC in the Rabbit
(21-Day Observation Period).

Test Compound: Pydrin® 2.4 EC EPA Reg. No. 201-401

Accession Number: 248697

Testing Facility: Westhollow Research Center
Houston, Texas

Project Number: 61530

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Testing Period: July 6, 1982 - July 27, 1982

Report Submitted to Sponsor: September 3, 1982

Materials and Methods:

Nine New Zealand White rabbits (6 males and 3 females) (Ray Nichols Rabbitry, Lumberton, Texas) were individually housed under environmentally controlled conditions. All animals were veterinary certified to be suitable for testing.

Three males and 3 females were allocated for treatment without subsequent eye washing. Three additional males were selected to have their treated eye flushed with tap water following treatment. No pre-existing eye lesions or defects were present at the time of allocation as determined by an examination using 1% ophthalmic fluorescein.

On treatment day (day zero), one-tenth milliliter of undiluted test material was instilled into the right eye of each rabbit. The left eye was untreated and remained as comparative control. Each rabbit was returned to its cage, except for the 3 males whose eyes were designated to be flushed with approximately 300 ml of tap water (at room temperature) approximately 30 seconds after instillation of the test material.

Observations were made at 1.0 hour and at 1, 2, 3, 7, 14 and 21 days after treatment. At each observation period the cornea, iris and conjunctiva were scored for irritation according to the criteria of Draize.

Results:

All scores at 14 days and beyond 14 days were zero. (This reviewer does note that raw data scores were only recorded up to 14 days.) Mean scores were tabulated as follows:

Mean Total Eye Irritation Scores

Conditions		1 hr	24 hr	48 hr	72 hr	7 day	14 day	21 day
Non-washed	Mean Score	11.3	49.7	38.8	26.8	4.1	0.0	0.0
Washed	Mean Score	15.0	41.3	25.3	17.7	1.3	0.0	0.0

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A maximum mean total irritation score of 49.7/110 was observed for unwashed eyes at 24 hours and 41.3/110 for washed eyes at 24 hours following treatment. Opacities developed in all 9 animals following treatment but were all reversed by 14 days.

Washing the eye with water did not significantly reduce irritation or time to recovery.

Conclusion:

Pydrin® 2.4 EC; EPA Reg. No. 201-401, is moderately irritating under these test conditions.

Category of Toxicity: Category 2 - WARNING. Corneal involvement or irritation clearing in 21 days or less.

Reference: Criteria and Policy Notice 2161.2 (Attached).

Albin B Kocialski

Albin B. Kocialski, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

Attachement

Classification:

Core - Guideline

MBK

*Alf. OSP
12/3/82*

OPP:HED:TOX:A.KOCIALSKI:sb 11/24/82 X77395 Rm 820 #m20



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

002318

SPECIAL

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAR 31 1981

MEMORANDUM

SUBJECT: Criteria & Policy Notice 2161.2

TO: See Below:

Attached is a policy notice which has been approved for use throughout the Division. This Division policy should be inserted into your Criteria and Policy Notebook in the proper place.

Questions, problems or suggestions for improvement on this notice should be directed to Rob Forrest, Policy & Liaison Staff, Room 509-C, X77136.

Douglas D. Camp
Director
Registration Division (TS-767-C)

Attachment

Addressees:

- DAA/OPP (Carrie)
- OPP Division Directors
- Branch Chiefs/RD
- Section Heads/RD
- Product Managers/RD
- Regional Branch Chiefs
- Ed Gray, OGC
- Director, PTSED
- Policy & Liaison Staff
- External Affairs Office, Carol Panasewich
- Douglas Sutherland, BFS

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POLICY AND CRITERIA NOTICE

Number 2161.2

Date: MAR 31 1981

Interim Adoption of NAS 1138 Criteria:

Change in Test of Skin and Eye Irritation

and Change in Method of Categorizing Eye Irritation

PURPOSE: To reaffirm existing policy with respect to use of the toxicity criteria for skin and eye irritation as set forth in NAS Publication 1138. This policy has been enunciated previously by the DAA and thus is already in effect.

SCOPE:

1. This policy applies to all applications for new registration, experimental use permits, and Registration Guidance Packages. Product applications currently under review should also be evaluated according to this policy.
2. This policy also applies to already registered products and will be implemented through Registration Standards, RPAR's, and other Agency actions.

BACKGROUND:

40 CFR 162.10(h) prescribes toxicity categories based on the results of acute toxicity tests. Signal words, precautionary labeling, child-resistant packaging, and classification decisions depend on the toxicity categorization of the product.

Over the past several years, scientific opinion on interpretation of eye and skin irritation has evolved into a consensus that is expressed in the National Academy of Sciences (NAS) Publication 1138. EPA has adopted the NAS criteria in its child-resistant packaging regulations and intends to propose the new criteria as part of Subpart F toxicity data requirements and Subpart H labeling regulations.

Eye irritation test methods and categorization criteria will both be changed. Methods for conducting irritation tests will also be revised; however, the criteria for categorizing skin irritants for purposes of labeling will not be revised.

Because the Agency has previously stated its intention of making these revisions, and because problems have arisen that could be resolved by use of these new criteria, this Notice reaffirms adoption of the NAS recommended criteria. These criteria will be formally implemented through appropriate regulation changes.

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POLICY:

1. The NAS-recommended toxicity criteria for skin and eye irritation (given in the attached Tables) are to be used for registration, reregistration, and EUP's.
2. Eye irritation tests will be evaluated and categories assigned based on a 21-day observation period. Reversibility of effects is to be considered in categorizing products for eye irritation. (Current categorization criteria are based on a 7-day observation period).
3. Dermal irritation testing may be conducted on intact skin only for a period of 4 hours or longer depending on certain conditions of expected patterns of human use and exposure. (Current Guidelines testing requires testing on intact and abraded skin for a period of 24 hours).
4. Child-resistant packaging is required for products in Category I with respect to eye irritation and Categories I and II with respect to dermal irritation.

IMPLEMENTATION:

1. This change affects new products, new EUPs, and reregistration of existing products. Products currently under review should also be evaluated in accordance with this Notice.
 2. Testing previously submitted or begun according to the old criteria is acceptable; however, the data may not be sufficient to permit the registrant to take advantage of the new categorizations. Data submitters and potential submitters should be informed of this fact promptly.
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SKULL AND
CROSSBONES
& "POISON"
REQUIRED

002318

SIGNAL
WORD

PRECAUTIONARY STATEMENTS

STATEMENTS OF
PRACTICAL TREATMENT

<p>I Irreversible injury of ocular tissue, or corneal in- volvement or irritation persisting for more than 21 days.</p>	<p>DANGER</p>	<p>No</p>	<p>Corrosive.* Causes irre- versible eye damage. Harmful if swallowed. Do not get in eyes or on clothing. Wear (goggles, face shield, or safety glasses).** Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.</p>	<p>If in eyes: Flush with plenty of water. Get medical attention. If swallowed: drink promptly a large quan- tity of milk, egg whites, gelatin solu- tion, or, if these are not available, drink large quantities of water. Avoid alcohol. <u>NOTE TO PHYSICIAN:</u> Probable mucosal damage may contraindicate the use of gastric lavage.</p>
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<p>II Corneal involvement or irritation clearing in 2/ days or less.</p>	<p>WARNING</p>	<p>No</p>	<p>Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Wear (goggles, face shield, or safety glasses).** Harmful if swallowed. Wash thoroughly with soap and water after handling. Remove contam- inated clothing and wash before reuse.</p>	<p>Same as above except omit NOTE TO PHYSICIAN statement.</p>
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<p>III Corneal involvement or irritation clearing in 7 days or less.</p>	<p>CAUTION</p>	<p>No</p>	<p>Causes (moderate) eye injury (irritation). Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling.</p>	<p>If in eyes: Flush with with plenty of water. Get medical attention if irritation persists.</p>
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<p>IV Minimal effects clearing in less than 24 hours.</p>	<p>CAUTION</p>	<p>No</p>	<p>None required.</p>	<p>None required.</p>
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BEST AVAILABLE COPY

The term "corrosive" may be omitted if the product is not actually corrosive.

*Choose appropriate term of eye protection. Recommendation for goggles or face shield is more appropriate for industrial, commercial, or non-domestic uses. Safety glasses may be recommended for domestic or residential uses.

** GWP required if labeled for residential uses.

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