

2-11-92

MEMORANDUM:

Subject: EPA File Symbol/EPA Reg. Nos.:
228-181, 228-183, 228-185, 228-189, 228-190, 228-204,
228-206, 228-210, 228-215, 228-216, 228-217, 228-218,
228-224, 228-211, 228-237, 228-239, 228-ETE, 228-ETR

From: Mark Perry, Biologist
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

MAP
~~1-31-92~~

To: Joanne I. Miller, PM 23
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: Thomas C. Ellwanger, Section Head
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

E 2/11/92

Applicant: Riverdale Chemical Co.
425 West 194th Street
Glenwood, IL 60411-3699

FORMULATION FROM LABEL:

The following contain MCPP, MCPA, and 2,4-DP: 228-224 228-204
228-215 228-218
228-217 228-206

The following contain MCPP, 2,4-D, and 2,4-DP: 228-183 228-190
228-189 228-210
228-216 228-237
228-181 228-239
228-185 228-211

BACKGROUND

Riverdale Chemical has requested the removal of eye protection requirements from certain product labels. The Registrant maintains that the unnecessary use of such equipment may have a negative safety effect during application, due to discomfort and reduced visibility, rather than achieve its intended purpose. Several category III/IV product amendments have been requested based on previously submitted acute data which, according to the Registrant, does not substantiate the current eye protection requirements. Also requested is the elimination of protective equipment requirements during the application process for the category I/II products 228-217, 228-239, 228-181, and 228-206, which are diluted significantly prior to use. This request is supported by data from similar products which reflect eye category III/IV hazards at the recommended application dilutions.

The products cited for amendment are herbicides of varying formulation all of which contain either MCPP, MCPA, 2,4-DP and/or 2,4-D as the active ingredients. The labeling recommendations for these products apply only to acute eye irritation hazards. The possibility of long-term effects resulting from ocular exposure has not been considered.

The products listed below were submitted for protective clothing amendments. Since PRS is not responsible for the protective clothing statements on the subject labels, only the eye protection amendments will be addressed by this memorandum.

228-228	228-223	228-225	228-179
228-203	228-184	228-226	228-180
228-186	228-219	228-229	

RECOMMENDATION

PRS accepts the rationale presented as justification for allowing product application without eye protection. However, each study considered for amendment must be supported by acceptable eye irritation data. Also, based on this data, it must be clear that the category I/II product (as diluted for use) will not present an eye irritation hazard. If the amendments are acceptable, category I/II products will still require eye protection during mixing and loading or any other process which may result in exposure to the undiluted material. Category III/IV products supported by acceptable acute eye irritation data will not require eye protection during mixing, loading, or application.

The Registrant has cited eye irritation studies which support specific groups of "similar" products. The cited eye studies for the products 228-181, 228-211, 228-183, and 228-189 were reviewed since the initial reviews could not be obtained. All other studies

cited have been previously reviewed and are currently in the PRS review file. The grouped products, supporting eye irritation study results, and PRS recommendations are as follows:

(1) Category III/IV products which requested removal of eye protection requirements:

- a) 228-183 (4/M, MRID 261901)
228-190

Due to differences in product pH and formulation (i.e. corrosion inhibitors), the cited study does not support 228-190. Since the study is in category four for eye irritation, eye protection is not required for 228-183. An acute eye irritation study should be cited or submitted which supports 228-190.

- b) 228-224 (4/G, MRID 404126-01)

Since the cited study is in category four for eye irritation, eye protection is not required for this product.

- c) 228-189** (4/M, MRID 402212-04)
228-210
228-216
228-237

The cited study supports all four products in regard to the label amendments. Since the study is in category four for eye irritation, eye protection is not required for these products.

- d) 228-204 (3/M, MRID 400085)
228-215
228-218

The cited study supports all three products in regard to the label amendments. Since the study is in category three for eye irritation, eye protection is not required for these products.

- e) 228-211 (3/G, MRID 403673-01)

Since the cited study is in category three for eye irritation, eye protection is not required for this product.

f) 228-185** (3/G, MRID 262436)

Since the cited study is in category three for eye irritation, eye protection is not required for this product.

g) 228-ETR
228-ETE

PRS was unable to obtain the jacket for 228-ETR, therefore, this amendment request will be addressed at a later time.

** The Registrant must provide documentation which confirms that the following studies were performed with the corresponding products, as listed below. If verification is not received, the labeling recommendations for these products, as outlined in this memorandum, will not apply.

MRID 402212-04 (EPA Reg. No. 228-189)
MRID 262436 (EPA Reg. No. 228-185)

(2) Category I/II products which requested removal of eye protection requirement during application:

a) 228-181 (2/M, MRID 259762)
228-239

The cited study is applicable to the listed products, however, this study was performed with the undiluted end-use formulation. Since the appropriately diluted material was not tested, this study does not support the requested label amendment.

b) 228-217 (2/G, MRID 402148-02)

The cited study is applicable to the listed product, however, this study was performed with the undiluted end-use formulation. Since the appropriately diluted material was not tested, this study does not support the requested label amendment.

c) 228-206 (1/G, MRID 400592-05)

The cited study is applicable to the listed product, however, this study was performed with the undiluted end-use formulation. Since the appropriately diluted material was not tested, this study does not support the requested label amendment.

LABELING (Summary)

(1) The (category IV) products listed below do not require eye protection during mixing, loading, or application:

228-183	228-210	228-189
228-224	228-216	228-237

(2) The (category III) products listed below do not require eye protection during mixing, loading, or application.

228-215	228-185	228-185
228-204	228-218	228-211

The precautionary language for these products should include the following:

- a) Precautionary Statements: "Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling."
- b) Statements of Practical Treatment: "If In Eyes: Flush with plenty of water. Call a physician if irritation persists."

(3) Regarding the category I/II products, the Registrant claims to possess data on similar products which indicate that recommended use dilutions reduce the eye hazard to the category III/IV level. According to the Registrant, this eye data confirms that eye protection is not necessary following the dilution of 228-217, 228-239, 228-181, and 228-206. The data mentioned by the Registrant has not been cited nor submitted. Neither has the Registrant indicated which products he believes are substantially similar to the four listed above either before or after dilution. Therefore, the amendments for these products are not acceptable. PRS requires acute eye irritation data on each category I/II product (as diluted for use), or data from "substantially similar" products (also diluted for use) to support these label amendments. Also, all supporting studies must be performed with the most concentrated use dilution recommended on each product label.

NOTE: Supporting acute eye irritation data has not been found for the product 228-190. The Registrant should submit or cite an eye study which supports this registration.

NOTE TO PM: The statement "Do not apply directly to water or wetlands" appears on many of these labels. According to a memo from A. Lindsay [4-25-91], this statement should be replaced with "Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark."

NOTE TO PM: Due to eye irritation, the products 228-217, 228-239, 228-181, and 228-206 meet the criteria for child-resistant packaging.

NOTE TO PM: Due to eye irritation, the products 228-217, 228-239, 228-181, and 228-206 meet the criteria for restricted-use classification. The PM should decide if the label contains sufficient alternative labeling language to offset the need for this classification.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 23
 MRID No.: 259762 (Reg. No. 228-181)
 Testing Laboratory: Hazelton
 Author(s): S. Glaza
 Species: Rabbit
 Sex: --
 Weight: --
 Source: Hazelton

Reviewer: M. Perry
 Report Date: 9-30-85
 Report No.: 50705856

Dosage: 0.1 ml
 Test Material: Weedestroy Triamine Lawn Weed Killer
 Quality Assurance (40 CFR §160.12): No

Summary:

1. Toxicity Category: 2
2. Classification: Minimum

Procedure (Deviations From §81-4): A dose of 0.1 ml was placed into the everted lower lid of one eye (n=6) and the eyelids were held together for approximately one second.

Since a Quality Assurance Statement was not included in this study report and a one hour evaluation was not given, a core minimum grade has been assigned.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	---	6/6	6/6	5/6	5/6	5/6	0/6	0/6
Iris	---	6/6	6/6	5/6	2/6	0/6	0/6	0/6
Conjunctivae								
Redness	---	6/6	6/6	6/6	6/6	2/6	0/6	0/6
Chemosis	---	6/6	6/6	6/6	5/6	1/6	0/6	0/6
Discharge*	---	6/6	4/6	1/6	0/6	0/6	0/6	0/6

* Not considered "positive" reaction

Comments: Since corneal involvement and irritation cleared in 8-21 days, this material has been placed into category two for eye irritation.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 23
 MRID No.: 261901 (Reg. No. 228-183)
 Testing Laboratory: Cosmopolitan
 Author(s): G. Rosenfeld
 Species: Rabbit
 Sex: --
 Weight: --
 Source: Not included

Reviewer: M. Perry
 Report Date: 2-6-86
 Report No.: 1451D

Dosage: 0.1 ml
 Test Material: Triamine Spot Weed Killer
 Quality Assurance (40 CFR §160.12): GLP Statement

Summary:

1. Toxicity Category: 4
2. Classification: Minimum

Procedure (Deviations From §81-4): A dose of 0.1 ml was placed into the everted lower lid of one eye (n=6) and the eyelids were held together for approximately one second. The eyes were evaluated at 1, 24, 48, and 72 hours after test material instillation.

Since the source of the test animals was not included in the study report, a core minimum grade has been assigned.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	0/6	0/6				
Iris	0/6	0/6	0/6	0/6				
Conjunctivae								
Redness	0/6	0/6	0/6	0/6				
Chemosis	0/6	0/6	0/6	0/6				
Discharge								

Comments: No positive reactions were observed in any test eyes, therefore, this material has been placed into category four for eye irritation.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 23
 MRID No.: 264843 (Reg. No. 228-189)
 Testing Laboratory: Cosmopolitan
 Author(s): G. Rosenfeld
 Species: Rabbit
 Sex: --
 Weight: --
 Source: Not included.

Reviewer: M. Perry
 Report Date: 7-12-86
 Report No.: 1550D

Dosage: 0.1 ml
 Test Material: Liquid Weed and Feed
 Quality Assurance (40 CFR §160.12): GLP Statement

Summary:

1. Toxicity Category: 4
2. Classification: Minimum

Procedure (Deviations From §81-4): A dose of 0.1 ml was placed into the everted lower lid of one eye (n=6) and the eyelids were held together for approximately one second. The eyes were evaluated at 1, 24, 48, and 72 hours after test material instillation.

Since the source of the test animals was not included in the study report, a core minimum grade has been assigned.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	0/6	0/6				
Iris	1/6	0/6	0/6	0/6				
Conjunctivae								
Redness	0/6	0/6	0/6	0/6				
Chemosis	0/6	0/6	0/6	0/6				
Discharge								

Comments: Since no positive responses were present after the one hour evaluation period, this material has been placed in category four for eye irritation.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 23
 MRID No.: 403673-01 (228-211)
 Testing Laboratory: Product Safety Labs.
 Author(s): R. Shapiro
 Species: Rabbit
 Sex: --
 Weight: --
 Source: Davidson's Mill

Reviewer: M. Perry
 Report Date: 7-23-87
 Report No.: T-6778

Dosage: 0.1 ml
 Test Material: Triamine 3-Way Lawn Weed Killer
 Quality Assurance (40 CFR §160.12): Present

Summary:

1. Toxicity Category: 3
2. Classification: Guideline

Procedure (Deviations From §81-4): A dose of 0.1 ml was placed into the conjunctival sacs of the test animals. Eyes were observed at 1, 24, 48, and 72 hours after treatment.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	0/6	0/6				
Iris	0/6	0/6	0/6	0/6				
Conjunctivae								
Redness	1/6	2/6	0/6	0/6				
Chemosis	0/6	0/6	0/6	0/6				
Discharge	0/6	0/6	0/6	0/6				

Comments: Since irritation was present in two of six test animals at twenty-four hours, this product has been placed into eye category three.

Tox Chem. No.: 559, 3159, 320B File Last Updated

Current date: 1-31-92

Study/Species/Lab/Study# Date	Material	MRID No.	Results	Tox. Cat.	Core Grade
Eye Irritation: Rabbit, Hazelton, 50705856, 9-30-85	2,4-D... 4.5% 2,4-DP... 4.5% mCPP... 4.5%	259762	Opacity and irritation cleared by day 14	2	M.
Eye Irritation: Rabbit, Cosmopolitan, 1451D, 2-6-86	2,4-D... 0.32% 2,4-DP... 0.32% mCPP... 0.32%	261901	No positive reactions	4	Min
Eye Irritation: Rabbit, Cosmopolitan, 1550D, 7-12-86	2,4-D... 3.2% 2,4-DP... 3.2% mCPP... 3.2%	264843	No positive reactions after 1hr	4	Min
Eye Irritation: Rabbit, Product Safety, T-6778, 7-23-87	2,4-D... 2.2% 2,4-DP... 2.2% mCPP... 2.2%	403673-01	2/6 positive for redness at 24 hrs	3	Gui