FEB 13 1996

MEMORANDUM

Subject: EPA File Symbol/EPA Reg. No.: 4787-EG/Glyfos™ Herbicide

From: Carol E. Glasgow, Ph.D., Toxicologist carol
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division (7505C)

To: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (7505C)

Applicant: Cheminova, Inc.
Oak Hill Park
1700 Route 23, Suite 210
Wayne, New Jersey 07470

FORMULATION FROM LABEL:

Active Ingredient (s):	% by weight
Glyphosate, N-(phosphonomethyl) glycine, in the form of its isopropylamine salt	41.0
Inert ingredient(s)	59.0

BACKGROUND: Cheminova Inc. submitted six studies (acute oral, dermal, inhalation, primary eye and dermal irritation, dermal sensitization) to support registration of its new product referenced above. Studies performed by Inveresk Research International. MRID numbers were 435300-02C through -07C. These studies reviewed by CDPR.

RECOMMENDATION: RSB/PRS findings are as follows:

All studies are **Acceptable**. Inveresk Research International does not conduct individual quality assurance inspections on short-term studies, but rather inspects at intervals according to a pre-determined schedule. They did, however, audit the final study report. Quality Assurance is not on California's checklist.

2.

TOXICITY PROFILES

Acute oral toxicity	IV	Acceptable
Acute dermal toxicity	III	Acceptable
Acute inhalation toxicity	~~IV~~ III per review	Acceptable
Primary eye irritation	III	Acceptable
Primary dermal irritation	IV UCW	Acceptable
Dermal sensitization	No 3/22/96	Acceptable

LABELING: The signal word for this product is "Caution" as the acute dermal toxicity and primary eye irritation studies are category III. Language required for the label should include the following:

> Harmful if absorbed through skin. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

Statements of practical treatment language should include the following:

> ***If in eyes:*** Flush eyes with plenty of water. Call a physician if irritation persists.
> ***If on skin:*** Wash with plenty of soap and water. Get medical attention.

Study for eye irritation submitted 10/28/98 changed category for this product to II Warning. See review dated 11/8/99. All other categories remain same. UCW 2/12/99

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ID #: 004787-00023 GLYPOS

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if absorbed through skin. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Wash thoroughly with soap and water after handling.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

4.

TO: Ann Prichard, Program Specialist
Pesticide Registration Branch

FROM: Medical Toxicology Branch Date: December 13, 1995

PRODUCT REGISTRATION RECOMMENDATION SHEET

Formulated Product Name: Glyfos
Chemical Code #: 1855
SB 950 #: 241
Document #: 51834-005 ID #: 157131-EPAE
EPA #: 4787-8 EG
Company Sponsor: Cheminova Agro A/S

RECOMMENDATION:

Submitted as Addition Data in conjunction with the EPA/CDPR Sharing Project.

The data reviewed are adequate to make a complete acute toxicological evaluation of the subject product.

All potential hazards associated with the use of the subject product, as indicated by the data reviewed, are adequately identified on the product label.

Registration is recommended.

Charles Kahn
Associate Pesticide Review Scientist

12/13/95
Date

Staff Toxicologist

12-14-95
Date

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TO--File: Registration **Program Specialist:** Ann Prichard
Branch: Registration
FROM--Medical Toxicology

DATA PACKAGE SUMMARY AND RECOMMENDATION SHEET

Active Ingredient: Glyphosate
Formulated Product Name: Glyfos
Formulation: 41.0% Glyphosate and 59.0% Inert ingredients
Chemical Code #: 1855
SB 950 #: 241
Document #: 51834-005 **ID #:** 157131-EPAE
EPA #: 4787-0 EG
Company Sponsor: Cheminova Agro A/S

SUMMARY: ("One-liners" from each study worksheet, significant information not mentioned in worksheets, other pertinent information for ongoing review or registration. Attach additional sheets if needed)

Glyfos (Compound No. 3607) and the subject product are the same formulation

Glyfos (Compound No. 3607) Acute Toxicity Categories

Acute Oral LD50	IV
Acute Dermal LD50	III
Acute Inhalation LC50	III
Eye Irritation	III
Dermal Irritation	IV

Glyfos (Compound No. 3607) Acute Toxicity Studies

Acute Oral LD50
51834-005; 142544; Acute Oral LD50; 811; rat; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); oral dose of 5000 mg/kg (dosed at a concentration of 500 mg/ml distilled water); mortalities 0/10; clinical observations- hypokinesia, piloerection, soiled coat, chromodacryorrhoea (eyes and nose) and salivation; no meaningful effect on body weight; necropsy- no gross post mortem observations; LD50 > 5000 mg/ kg; Toxicity Category IV; study acceptable. (Kahn, 12/11/95)

Acute Dermal LD50
51834-005; 142548; Acute Dermal LD50; 814; rat; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); dermal dose of 2000 mg/kg; 5/sex/dose; 24 hour exposure period (occluded); mortalities 0/10; clinical observations- no abnormalities; no effect on body weight; necropsy- no gross findings; LD50 > 2000 mg/kg; Toxicity Category III; study acceptable. (Kahn, 12/11/5)

Acute Inhalation LC50
51834-005; 142549; Acute Inhalation LC50; 813; rat; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 7/20/89; IRI Project No. 640023; Glyfos (Compound No. 3607 - yellow liquid); inhalation dose of 4.86 mg/l (gravimetric value) and 6.99 mg/l (nominal value); 5/sex/dose; 4 hour

exposure period - nose only; 43% respirable particles (< 3 µm); MMAD (± GSD): 3.5 (± 2.2) µm; mortalities 0/10; clinical observations- red staining around the snout, subduedness, piloerection and general unkempt appearance; weight gain appeared normal; necropsy- slight pale mottling on lungs; LC50 > 4.86 mg/l (gravimetric value); Toxicity Category III; study acceptable. (Kahn, 12/11/95)

Eye Irritation

51834-005; 142550; Eye Irritation; 814; rabbit; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); dosed with 0.1 ml/eye; 6 rabbit eyes tested; mortalities 0/6; at Day 1 post-dose -Grade 1 (2/6) iris , -Grade 2 (6/6) conjunctival irritation; at Day 7 post-dose -No eye irritation; Toxicity Category III; study accepted. (Kahn 12/11/95)

Dermal Irritation

51834-005; 142551; Dermal Irritation; 815; rabbit; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); dermal dose of 0.5 ml/site; 4 hours exposure period (semi-occluded); 6 rabbits tested; mortalities 0/6; at 24 hours post patch removal -Grade 1 (1/6) erythema; at 48 and 72 hours post patch removal -No skin irritation; Toxicity Category IV; study acceptable. (Kahn, 12/11/95)

CONCLUSIONS: Do data support registration, if applicable? For formulated product, do data support registration of product as labelled?

The submitted Glyfos (Compound No. 3607) acute studies have been reviewed and all the required studies are acceptable.

RECOMMENDATIONS: What type of registration action is being requested? In case of ongoing registration, register or do not register? What other specific studies or data are requested?

Submitted as Addition Data in conjunction with the EPA/CDPR Sharing Project.

The data reviewed are adequate to make a complete acute toxicological evaluation of the subject product.

All potential hazards associated with the use of the subject product, as indicated by the data reviewed, are adequately identified on the product label.

Registration is recommended.

Charles Kahn
Associate Pesticide Review Scientist

12/13/95
Date

Staff Toxicologist

Date

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CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

DEPARTMENT OF PESTICIDE REGULATION

MEDICAL TOXICOLOGY BRANCH

TOXICOLOGY STUDY EVALUATION WORKSHEET
(acute and special studies)

I. STUDY IDENTIFICATION

Active Ingredient: Glyphosate
Formulated Product Name: Glyfos (Compound No. 3607)
Chemical Code #: 1855
SB 950 #: 241 **ID #:** 157131-EPAE
Document #: 51834-005 **Record #:** 142544
EPA #: NA 4787-64 MRID 435300-02C
Study Type: 811 - Acute Oral LD50
Full Study Title: Glyfos - Acute Oral Toxicity Study In Rats
Company Sponsor: Cheminova Agro A/S
Conducting Laboratory: Inveresk Research International, Musselburgh, EH21 7UB, Scotland
Report Date: June 14, 1989
Study Interval: November 15, 1988 to November 30, 1988

II. SUMMARY OF WORKSHEET

A. **STUDY STATUS: Is report complete?** No
Is study acceptable? Yes

- \- **Meets EPA guidelines**
- Yes **Minor variances from guidelines**
- \- **Major variances from guidelines**
- \- **Could be upgraded with additional information (see VI-A)**

Yes **Has useful data**
- \- **Insufficient data**
- \- **Non EPA validated study**

Other_____

B. **CONCLUSIONS: Does this study as reported demonstrate a possible significant adverse health effect?:** No **If so, in what area?** NA

C. **ONE LINER-One or two sentence summary of the study:**
51834-005; 142544; Acute Oral LD50; 811; rat; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); oral dose of 5000 mg/kg (dosed at a concentration of 500 mg/ml distilled water); mortalities 0/10; clinical observations- hypokinesia, piloerection, soiled coat, chromodacryorrhoea (eyes and nose) and salivation; no meaningful effect on body weight; necropsy- no gross post mortem observations; LD50 > 5000 mg/kg; Toxicity Category IV; study acceptable. (Kahn, 12/11/95)

D. **ARE DATA ADEQUATE TO SUPPORT REGISTRATION (if applicable)?:** Yes

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Charles Kahn
Associate Pesticide Review Scientist **Date** 12/14/95

Staff Toxicologist **Date** 12-14-95

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III. PROTOCOL SUMMARY

A. ANIMALS, ROUTE OF ADMINISTRATION, AND DURATION OF TREATMENT:

Species: Rat
Strain: Sprague-Dawley
Source of animals: Charles River (U.K.) Limited, Manston, Kent, England
Age at start: 6-8 weeks (weighing 148-204 g at dosing)
Route of administration: Gavage
Vehicle: Distilled water
Period of treatment: Single dose

B. BACKGROUND (including relationship of this study to other studies): NA

C. TREATMENT LEVELS AND GROUP SIZE:

	Units (mg/kg)
	5000
# Male Rats:	5
# Female Rats:	5
	Mortality
# Dead Male Rats:	0
# Dead Female Rats:	0

IV. STUDY DESIGN AND EVALUATION

A. TEST PROCEDURES AND REMARKS (e.g., OK, specific parameters; asterisks denote deficiencies, NA indicates not applicable or no comment).

1. **Test article:** Glyfos (Compound No. 3607 - yellow liquid)
* 2. **Analysis of dosing material:** Not reported
3. **Animal selection:** OK
4. **Animal husbandry:** Housed by sex in polypropylene cages with mesh floors with a maximum of five animals per cage - Temperature 19-20°C and the mean Relative Humidity was 48%
5. **Mortality:** See III-C
6. **Number of animals:** See III-C
* 7. **Randomization of animals:** Not reported
8. **Dose level selection:** OK
9. **Route of administration:** OK
10. **Exposure conditions:** OK
11. **Controls:** OK
12. **Observations:** Observed for mortality or other signs of gross toxicity frequently on day of dosing and at least once daily thereafter for 14 days
13. **Necropsies:** OK
14. **Appropriateness of methods:** OK
15. **Treatment of results:** OK
16. **Test report:** OK
17. **Consistency:** OK
18. **Good Laboratory Practice:** OK
19. **Other:** OK

B. ELABORATION OF METHODS OR PROTOCOL DESCRIPTION (if needed): NA

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RESULTS

A. **EFFECTS REPORTED:**
Clinical observations- hypokinesia, piloerection, soiled coat, chromodacryorrhoea (eyes and nose) and salivation. No meaningful effect on body weight. Mortalities 0/10. Necropsy- no gross post mortem observations.

B. **ACUTE TOXICITY VALUE(LD50,LC50,etc):**
LD50 > 5000 mg/kg

C. **TOXICITY CATEGORY:**
IV

VI. DISCUSSION

A. **MAJOR DEFICIENCIES (if present).** None **What are they and can they be corrected with additional information?** NA **Be specific:** NA

B. **DISCUSSION OF RESULTS (if necessary). Were there significant adverse health effects?** No **Are there any recommendations specific to this study?** NA

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CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

DEPARTMENT OF PESTICIDE REGULATION

MEDICAL TOXICOLOGY BRANCH

TOXICOLOGY STUDY EVALUATION WORKSHEET
(acute and special studies)

I. STUDY IDENTIFICATION

Active Ingredient: Glyphosate
Formulated Product Name: Glyfos (Compound No. 3607)
Chemical Code #: 1855
SB 950 #: 241 **ID #:** 157131-EPAE
Document #: 51834-005 **Record #:** 142548
EPA #: NA 4787-EG MRID 435300-03 C
Study Type: 812 - Dermal LD50
Full Study Title: Glyfos - Acute Dermal Toxicity Study In Rats
Company Sponsor: Cheminova Agro A/S
Conducting Laboratory: Inveresk Research International, Musselburgh, EH21 7UB, Scotland
Report Date: June 14, 1989
Study Interval: November 15, 1988 to November 30, 1988

II. SUMMARY OF WORKSHEET

A. **STUDY STATUS: Is report complete?** No
Is study acceptable? Yes

- \- **Meets EPA guidelines**
- Yes **Minor variances from guidelines**
- \- **Major variances from guidelines**
- \- **Could be upgraded with additional information (see VI-A)**

Yes **Has useful data**
\- **Insufficient data**
\- **Non EPA validated study**
Other_____

B. **CONCLUSIONS: Does this study as reported demonstrate a possible significant adverse health effect?** No **If so, in what area?** NA

C. **ONE LINER-One or two sentence summary of the study:**
51834-005; 142548; Acute Dermal LD50; 814; rat; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); dermal dose of 2000 mg/kg; 5/sex/dose; 24 hour exposure period (occluded); mortalities 0/10; clinical observations- no abnormalities; no effect on body weight; necropsy- no gross findings; LD50 > 2000 mg/kg; Toxicity Category III; study acceptable. (Kahn, 12/11/5)

D. **ARE DATA ADEQUATE TO SUPPORT REGISTRATION (if applicable)?:** Yes

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Charles Kahn
Associate Pesticide Review Scientist

12/13/95
Date

Staff Toxicologist

12-14-95
Date

10

III. PROTOCOL SUMMARY

A. ANIMALS, ROUTE OF ADMINISTRATION, AND DURATION OF TREATMENT:

Species: Rat
Strain: Sprague-Dawley
Source of animals: Charles River (UK) Limited, Manston, Kent, England
Age at start: 6-8 weeks (weighing 191-304 g at dosing)
Route of administration: Dermal - occluded
Vehicle: None reported
Period of treatment: Single (24 hour exposure)

B. BACKGROUND (including relationship of this study to other studies): NA

C. TREATMENT LEVELS AND GROUP SIZE:

	Units (mg/kg)
	2000
# Male Rats:	5
# Female Rats:	5
	Mortality
# Dead Male Rats:	0
# Dead Female Rats:	0

IV. STUDY DESIGN AND EVALUATION

A. TEST PROCEDURES AND REMARKS (e.g., OK, specific parameters; asterisks denote deficiencies, NA indicates not applicable or no comment).

1. **Test article:** Glyfos (Compound No. 3607 - yellow liquid)
2. **Analysis of dosing material:** Dosed as received
3. **Animal selection:** OK
4. **Animal husbandry:** Housed by sex in polypropylene cages with mesh floors with a maximum of five animals per cage - Temperature 19-20°C and the mean Relative Humidity 48%
5. **Mortality:** See III-C
6. **Number of animals:** See III-C
7. * **Randomization of animals:** Not reported
8. **Dose level selection:** OK
9. **Route of administration:** OK
10. **Exposure conditions:** OK
11. **Controls:** OK
12. **Observations:** Observed for mortality or other signs of gross toxicity frequently on day of dosing and at least once daily thereafter for 14 days
13. **Necropsies:** Gross necropsies all animals
14. **Appropriateness of methods:** OK
15. **Treatment of results:** OK
16. **Test report:** OK
17. **Consistency:** OK
18. **Good Laboratory Practice:** OK
19. **Other:** OK

B. ELABORATION OF METHODS OR PROTOCOL DESCRIPTION (if needed): NA

V. RESULTS

A. EFFECTS REPORTED:
Clinical observations- no abnormalities. No effect on body weight. Mortalities 0/10. Necropsy- no gross findings.

B. ACUTE TOXICITY VALUE(LD50, LC50, etc):
LD50 > 2000 mg/kg

C. TOXICITY CATEGORY:
III

VI. DISCUSSION

A. MAJOR DEFICIENCIES (if present). None **What are they and can they be corrected with additional information?** NA **Be specific:** NA

B. DISCUSSION OF RESULTS (if necessary). Were there significant adverse health effects? No **Are there any recommendations specific to this study?** NA

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CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH
TOXICOLOGY STUDY EVALUATION WORKSHEET
(acute and special studies)

I.STUDY IDENTIFICATION

Active Ingredient: Glyphosate
Formulated Product Name: Glyfos (Compound No. 3607)
Chemical Code #: 1855
SB 950 #: 241 **ID #:** 157131-EPAE
Document #: 51834-005 **Record #:** 142549
EPA #: MRID 4787-EG MRID 435300-04C
Study Type: 813 - Acute Inhalation LC50
Full Study Title: Glyfos - Acute Inhalation Toxicity Study In Rats
Company Sponsor: Cheminova Agro A/S
Conducting Laboratory: Inveresk Research International, Musselburgh, EH21 7UB, Scotland
Report Date: July 20, 1989
Study Interval: February 10, 1989 to February 25, 1989

II. SUMMARY OF WORKSHEET

A. **STUDY STATUS: Is report complete?** No
Is study acceptable? Yes

- Meets EPA guidelines
Yes Minor variances from guidelines
- Major variances from guidelines
- Could be upgraded with additional information (see VI-A)

Yes Has useful data
- Insufficient data
- Non EPA validated study
Other_____

B. **CONCLUSIONS: Does this study as reported demonstrate a possible significant adverse health effect?** No **If so, in what area?** NA

C. **ONE LINER-One or two sentence summary of the study:**
51834-005; 142549; Acute Inhalation LC50; 813; rat; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 7/20/89; IRI Project No. 640023; Glyfos (Compound No. 3607 - yellow liquid); inhalation dose of 4.86 mg/l (gravimetric value) and 6.99 mg/l (nominal value); 5/sex/dose; 4 hour exposure period - nose only; 43% respirable particles (< 3 µm); MMAD (± GSD): 3.5 (± 2.2) µm; mortalities 0/10; clinical observations- red staining around the snout, subduedness, piloerection and general unkempt appearance; weight gain appeared normal; necropsy- slight pale mottling on lungs; LC50 > 4.86 mg/l (gravimetric value); Toxicity Category III; study acceptable. (Kahn, 12/11/95)

D. **ARE DATA ADEQUATE TO SUPPORT REGISTRATION (if applicable)?:** Yes

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Charles Kahn
Associate Pesticide Review Scientist

12/13/95
Date

Staff Toxicologist

12-14-95
Date

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III. PROTOCOL SUMMARY

A. ANIMALS, ROUTE OF ADMINISTRATION, AND DURATION OF TREATMENT:

Species: Rat
Strain: Sprague-Dawley
Source of animals: Charles River (U.K.) Limited, Manston, Kent, England
Age at start: Not reported (weighing 122-142 g)
Route of administration: Inhalation (nose only)
Vehicle: None reported
Period of treatment: Single (4 hour exposure period)

B. BACKGROUND (including relationship of this study to other studies): NA

C. TREATMENT LEVELS AND GROUP SIZE:

	Units (mg/l)*
	4.86
# Male Rats:	5
# Females Rats:	5
	Mortality
# Dead Males Rats:	0
# Dead Females Rats:	0

* Gravimetric Value
6.99 mg/l Nominal Value
3.5 µm Mass Median Aerodynamic Diameter

IV. STUDY DESIGN AND EVALUATION

A. TEST PROCEDURES AND REMARKS (e.g., OK, specific parameters; asterisks denote deficiencies, NA indicates not applicable or no comment).

1. **Test article:** Glyfos (Compound No. 3607 - yellow liquid)
2. **Analysis of dosing material:** Dosed as received
3. **Animal selection:** OK
4. **Animal husbandry:** Housed 1 or 2 rats/cage by sex in suspended polypropylene cages - Temperature 20-23°C and Relative Humidity 36-43%
5. **Mortality:** See III C
6. **Number of animals:** See III C
7. * **Randomization of animals:** Not reported
8. **Dose level selection:** OK
9. **Route of administration:** OK
10. **Exposure conditions:** OK
11. **Controls:** OK
12. **Observations:** Observed for mortality or other signs of gross toxicity 1/2 hour post-dose and at least once daily thereafter for 14 days
13. **Necropsies:** Surviving animals
14. **Appropriateness of methods:** OK
15. **Treatment of results:** OK
16. **Test report:** OK
17. **Consistency:** OK
18. **Good Laboratory Practice:** OK
19. **Other:** NA

B. ELABORATION OF METHODS OR PROTOCOL DESCRIPTION (if needed): NA

V. RESULTS

A. EFFECTS REPORTED:
Clinical observations- red staining around the snout, subduedness, piloerection and general unkempt appearance. Weight gain appeared normal. Mortalities 0/10. Necropsy- slight pale mottling on lungs.

B. ACUTE TOXICITY VALUE(LD50,LC50,etc):
LC50 > 4.86 mg/l (gravimetric value).

C. TOXICITY CATEGORY:
III

VI. DISCUSSION

A. MAJOR DEFICIENCIES (if present). None **What are they and can they be corrected with additional information?** NA **Be specific:** NA

B. DISCUSSION OF RESULTS (if necessary). Were there significant adverse health effects? No **Are there any recommendations specific to this study?:**
NA

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CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

DEPARTMENT OF PESTICIDE REGULATION

MEDICAL TOXICOLOGY BRANCH

TOXICOLOGY STUDY EVALUATION WORKSHEET
(acute and special studies)

I.STUDY IDENTIFICATION

Active Ingredient: Glyphosate
Formulated Product Name: Glyfos (Compound No. 3607)
Chemical Code #: 1855
SB 950 #: 241 **ID #:** 157131-EPAE
Document #: 51834-005 **Record #:** 142550
EPA #: 4787-EG MRID 435300-05C
Study Type: 814 - Eye Irritation
Full Study Title: Glyfos - Primary Eye Irritation Test In Rabbits
Company Sponsor: Cheminova Agro A/S
Conducting Laboratory: Inveresk Research International, Musselburgh, EH21 7UB, Scotland
Report Date: June 14, 1989
Study Interval: January 17, 1989 to January 26,1989

II. SUMMARY OF WORKSHEET

A. **STUDY STATUS: Is report complete?** No
Is study acceptable? Yes

- \- Meets EPA guidelines
- Yes Minor variances from guidelines
- \- Major variances from guidelines
- \- Could be upgraded with additional information (see VI-A)

- Yes Has useful data
- \- Insufficient data
- \- Non EPA validated study
- Other _____

B. **CONCLUSIONS: Does this study as reported demonstrate a possible significant adverse health effect?** None **If so, in what area?** NA

C. **ONE LINER-One or two sentence summary of the study:**
51834-005; 142550; Eye Irritation; 814; rabbit; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); dosed with 0.1 ml/eye; 6 rabbit eyes tested; mortalities- 0/6; at Day 1 post-dose -Grade 1 (2/6) iris , -Grade 2 (6/6) conjunctival irritation; at Day 7 post-dose -No eye irritation; Toxicity Category III; study accepted. (Kahn 12/11/95)

D. **ARE DATA ADEQUATE TO SUPPORT REGISTRATION (if applicable)?** Yes

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Charles Kahn
Associate Pesticide Review Scientist

12/13/95
Date

Staff Toxicologist

12-14-95
Date

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III. PROTOCOL SUMMARY

A. ANIMALS, ROUTE OF ADMINISTRATION AND DURATION OF TREATMENT:

Species: Rabbit
Strain: New Zealand White
Source of animals: Cheshire Rabbit Farms Limited, Duddon Lodge, Tarporley, Cheshire, England
Age at start: Young adults
Route of administration: Test material placed in the conjunctival sac of the right eye of each test animal while the other eye served as the control.
Vehicle: Undiluted
Period of treatment: Single

B. BACKGROUND (including relationship of this study to other studies): NA

C. TREATMENT LEVELS AND GROUP SIZE:

	Units (ml/eye)
# Rabbits:	0.1 / 6

	Mortality
# Dead Rabbits:	0

IV. STUDY DESIGN AND EVALUATION

A. TEST PROCEDURES AND REMARKS (e.g., OK, specific parameters; asterisks denote deficiencies, NA indicates not applicable or no comment).

1. **Test article:** Glyfos (Compound No. 3607 - yellow liquid)
2. **Analysis of dosing material:** Dosed as received
3. **Animal selection:** OK
4. **Animal husbandry:** Housed individually in aluminum cages with grid floors - Temperature 18-19°C and Mean Relative Humidity 51%
5. **Mortality:** See III-C
6. **Number of animals:** See III-C
7. * **Randomization of animals:** Not reported
8. **Dose level selection:** OK
9. **Route of administration:** OK
10. **Exposure conditions:** OK
11. **Controls:** Untreated eyes served as controls
12. **Observation:** Eyes were examined at 1, 24, 48 and 72 hours and 7 post-dose
13. **Necropsies:** Not required
14. **Appropriateness of methods:** OK
15. **Treatment of results:** OK
16. **Test report:** OK
17. **Consistency:** OK
18. **Good Laboratory Practice:** OK
19. **Other:** OK

B. ELABORATION OF METHODS OR PROTOCOL DESCRIPTION (if needed): NA

V. RESULTS

A. EFFECTS REPORTED:
Mortalities 0/6. At Day 1 post-dose -Grade 1 (2/6) iris , -Grade 2 (6/6) conjunctival irritation. At Day 7 post-dose -No eye irritation.

B. ACUTE TOXICITY VALUE(LD50, LC50, etc):
NA

C. TOXICITY CATEGORY:
III

VI. DISCUSSION

A. MAJOR DEFICIENCIES (if present). None **What are they and can they be corrected with additional information?** NA **Be specific:** NA

B. DISCUSSION OF RESULTS (if necessary). Were there significant adverse health effects? None **Are there any recommendations specific to this study?**
NA

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CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

DEPARTMENT OF PESTICIDE REGULATION

MEDICAL TOXICOLOGY BRANCH

TOXICOLOGY STUDY EVALUATION WORKSHEET
(acute and special studies)

I. STUDY IDENTIFICATION

Active Ingredient: Glyphosate
Formulated Product Name: Glyfos (Compound No. 3607)
Chemical Code #: 1855
SB 950 #: 241 **ID #:** 157131-EPAE
Document #: 51834-005 **Record #:** 142551
EPA #: 100 4787-EG MRID 435300-06
Study Type: 814 - Dermal Irritation
Full Study Title: Glyfos Primary Skin Irritation Study In Rabbits
Company Sponsor: Cheminova Agro A/S
Conducting Laboratory: Inveresk Research International, Musselburgh, EH21 7UB, Scotland
Report Date: June 14, 1989
Study Interval: November 14, 1988 November 18, 1988

II. SUMMARY OF WORKSHEET

A. **STUDY STATUS: Is report complete?** No
Is study acceptable? Yes

- Meets EPA guidelines
Yes Minor variances from guidelines
- Major variances from guidelines
- Could be upgraded with additional information (see VI-A)

Yes Has useful data
- Insufficient data
- Non EPA validated study
Other_____

B. **CONCLUSIONS: Does this study as reported demonstrate a possible significant adverse health effect?:** No **If so, in what area?** NA

C. **ONE LINER-One or two sentence summary of the study:**
51834-005; 142551; Dermal Irritation; 815; rabbit; Inveresk Research International, Musselburgh, EH21 7UB, Scotland; 6/14/89; IRI Project No. 241496; Glyfos (Compound No. 3607 - yellow liquid); dermal dose of 0.5 ml/site; 4 hours exposure period (semi-occluded); 6 rabbits tested; mortalities- 0/6; at 24 hours post patch removal -Grade 1 (1/6) erythema; at 48 and 72 hours post patch removal -No skin irritation; Toxicity Category IV; study acceptable. (Kahn, 12/11/95)

D. **ARE DATA ADEQUATE TO SUPPORT REGISTRATION (if applicable)?** Yes

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Charles Kahn
Associate Pesticide Review Scientist

12/13/95
Date

Staff Toxicologist

12-14-95
Date

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III. PROTOCOL SUMMARY

A. ANIMALS, ROUTE OF ADMINISTRATION, AND DURATION OF TREATMENT:

Species: Rabbit
Strain: New Zealand White
Source of animals: Cheshire Rabbit Farms Limited, Duddon Lodge, Tarporley, Cheshire, England
Age at start: Young Adults
Route of administration: Dermal (semi- occluded)
Vehicle: None reported
Period of treatment: Single (4 hour exposure)

B. BACKGROUND (including relationship of this study to other studies): NA

C. TREATMENT LEVELS AND GROUP SIZE:

	Units (ml/site)
# Rabbits:	0.5 / 6

	Mortality
# Dead Rabbits:	0

IV. STUDY DESIGN AND EVALUATION

A. TEST PROCEDURES AND REMARKS (e.g., OK, specific parameters; asterisks denote deficiencies, NA indicates not applicable or no comment).

1. **Test article:** Glyfos (Compound No. 3607 - yellow liquid)
2. **Analysis of dosing material:** Dosed as received
3. **Animal selection:** OK
4. **Animal husbandry:** Housed individually in aluminum cages with grid floors - Temperature 18-20°C and Mean Relative Humidity 51%
5. **Mortality:** See III-C
6. **Number of animals:** See III-C
* 7. **Randomization of animals:** Not reported
8. **Dose level selection:** OK
9. **Route of administration:** OK
10. **Exposure conditions:** OK
11. **Controls:** OK
12. **Observations:** Observed for skin irritation at 1/2, 24, 48 and 72 hours post patch removal
13. **Necropsies:** Not required
14. **Appropriateness of methods:** OK
15. **Treatment of results:** OK
16. **Test report:** OK
17. **Consistency:** OK
18. **Good Laboratory Practice:** OK
19. **Other:** OK

B. ELABORATION OF METHODS OR PROTOCOL DESCRIPTION (if needed): NA

V. RESULTS

A. EFFECTS REPORTED:
Mortalities- 0/6. At 24 hours post patch removal -Grade 1 (1/6) erythema. At 48 and 72 hours post patch removal -No skin irritation.

B. ACUTE TOXICITY VALUE (LD50, LC50, etc):
NA

C. TOXICITY CATEGORY:
IV

VI. DISCUSSION

A. MAJOR DEFICIENCIES (if present). None What are they and can they be corrected with additional information? NA Be specific: NA

B. DISCUSSION OF RESULTS (if necessary). Were there significant adverse health effects? No Are there any recommendations specific to this study? NA

State of California

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PESTICIDE EVALUATION
Worker Health & Safety

Date: December 28, 1995

Phone: 324-3930

Subject: Product Name : Glyphos
I.D. No. : EPA-157131E
EPA Reg. No. : 4787-[redacted] EG MRID 435300-07L
Doc. No. : 51834-005
Company : Cheminova LTD.
A.I. : Glyphosate (41.0%)
Use : Herbicide

Recommendation : Register

Summary of Registration Request:

The proposed Section 3 Registration product is intended to be used to control or destroy unwanted herbaceous plants in labeled areas, including industrial, recreational, and other public areas, for habitat management, ornamentals and christmas trees, stump treatment, for renovation of turfgrasses, and other labeled areas. The product is applied by aerial or ground-based equipment at a rate of 8 - 48 fluid ounces per acre (0.25 - 1.5 pounds active ingredient). To prepare solutions ranging from 1/2% - 10%, mix 2 quarts - 10 gallons in 100 gallons of water.

Applicators and other handlers must wear: long-sleeved shirt, long pants, shoes plus socks, and protective eyewear.

Dermal Sensitization:

Title: Glyfos - Dermal Sensitization Study in Guinea Pigs (DPR Rec. No. 142569)

Test Substance: Glyfos - Compound No. 3607 (contains 4 pounds/gallon of the IPA salt of glyphosate.

Test Animals: Female Dunkin-Hartley albino guinea pigs.

Method: Magnusson-Kligman - Following a preliminary range finding test to assess the suitable concentrations for injection and topical application, the injection concentration of 0.55 and topical application concentration of 50% were chosen based upon findings. For the test, 20 guinea pigs were assigned to the test group, 20 to the control group. For induction, 20 guinea pigs received six intradermal injections, two each containing 0.10 ml Freund's Complete Adjuvant, 0.10 ml test material, and 0.05 ml test material emulsified with 0.05 ml Freund's Complete Adjuvant. Six days after the injection phase, the test material was applied at a concentration of 50% v/v in distilled water to the pretreated area of each of the animals in the test group. Following a two week rest, both the test and control groups were challenged with the test material at a concentration of 50% v/v in distilled water. Irritation was determined at 24 and 48 hours after removal of the challenge patch. Scoring was as follows: 0, 1, 2, 3; where 3 was equal to intense erythema. Historical positive control data generated using DNCB as the test material was completed on May 13, 1988 when 95% of the test group animals reacted positively.

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Conclusion: The test material did not elicit a dermal sensitization reaction under conditions of the test.

Additional Data Required: None.

Labeling: The signal word, precautionary statements, and protective equipment requirements have been reviewed. The labeling is acceptable.

Richard Bireley
(Assoc. Pest. Review Scientist)

James R. Sanborn
(Staff Toxicologist)

cc: Ann Prichard

SURNAME

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