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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

November 29, 2004

MEMORANDUM

Subject: Name of Pesticide Product: Gramoxone Inteon
EPA File Symbol: 100-RERT
DP Barcode: D309349
Decision No.: 348898
PC Code: 061601 Paraquat dichloride

From: Breann Hanson, Toxicologist *B. Hanson*
Technical Review Branch *JCH*
Registration Division (7505C)

To: Hope Johnson, RM Team 25
Herbicide Branch
Registration Division (7505C)

Applicant: Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419

FORMULATION FROM LABEL:

<u>Active Ingredient:</u>			<u>% by wt.</u>
061601	Paraquat dichloride	CAS No. 1910-42-5	30.1%
<u>Inert Ingredients:</u>			69.9%
Total:			100.0%

AUG 17 2005
K

ACTION REQUESTED:

The Product Manager requests:

"The registrant, Syngenta, has submitted an application for a new formulation of paraquat dichloride. The formulation is designed to gel if ingested, thus minimizing entry to intestine. They have submitted the five pack of acute tox (inhalation study is cited, and i have blown back a copy for your review), along with toxicokinetic study in the dog to show how the gelling effect helps lessen the toxicity. Please review these studies for acceptance. This product is a me-too with 100-1009, so please review to see if this product is toxicologically substantially similar to 100-1009 cyclone. I have included MRID's 46364503-46364518, along with the CSF, the application letter, the data matrix, the label, and the me-too label and csf for comparison. NOTE: MRID's 46364511-46364518 are for the 200 g/l formulation that will be used in Mexico. The 240 g/l formulation will be used here in the U.S. However, Jim Jones agreed to review the Mexican formulation studies for Mexico under the NAFTA Agreement. For further information, contact Luis Suguiyama 305-6027..."

BACKGROUND: Syngenta Crop Protection, Inc. has submitted 2 sets of 5 pack acute toxicity studies in support of registration for Gramoxone Inteon, EPA File Symbol: 100-RERT. The submission included a CSF, label, application, data matrix and letter from the sponsor. The studies were conducted at SafePharm Laboratories Ltd., Derbyshire, UK (MRID numbers 463645-03 through -06), Product Safety Laboratories, Dayton, NJ (MRID number 463645-07), or Central Toxicology Laboratory, Cheshire, UK (MRID numbers 463645-12 through -16). Two of the submitted studies (MRIDs 463645-08 and -09) will not be reviewed by TRB due to being extraneous to this registration. The 4 toxicokinetic studies have been forwarded to HED. No acute inhalation toxicity study was submitted due to the fact that the company has agreed to take a category I classification for the inhalation route.

RECOMMENDATIONS: The studies have been reviewed and are classified as acceptable. Because actual studies have been submitted no determination of similarity with 100-1009 has been made. The acute toxicity profile for the 240 g/L Gramoxone Inteon formulation, EPA File Symbol: 100-RERT, is:

Acute oral toxicity	II	Acceptable	MRID 46364503
Acute dermal toxicity	II	Acceptable	MRID 46364514*
Acute inhalation toxicity	I	Cited	MRID 00046105
Primary eye irritation	II	Acceptable	MRID 46364506
Primary skin irritation	III	Acceptable	MRID 46364504
Dermal sensitization	Negative	Acceptable	MRID 46364507

* although a study (MRID 46364505) was submitted for the 240 g/L formulation in which the category for acute dermal toxicity is III, the study sent in for the 200 g/L formulation has a more restrictive category II for dermal toxicity. It is TRB's recommendation that this more restrictive

study be used to register the 240 g/L formulation. The signal word remains DANGER.

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 000100-01217

PRODUCT NAME: Gramoxone Inteon

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: DANGER

POISON ☠

SPANISH SIGNAL WORD: PELIGRO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

Restricted Use Pesticide due to toxicity categories. For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

Fatal if inhaled. Do not breathe spray mist. May be fatal if swallowed or absorbed through skin. Causes substantial but temporary eye injury. Do not get in eyes, on skin, or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wear coveralls worn over short-sleeved shirt and short pants, socks, chemical resistant footwear, and chemical-resistant gloves (such as Natural Rubber, Selection Category A).

For handling activities, use a non-powered, NIOSH-approved air purifying cartridge respirator equipped with an organic-vapor (OV) removing cartridge plus an N-, R- or P-series filter, OR a non-powered air purifying canister-type respirator equipped with an organic vapor canister that uses an N-, R-, or P-series air-purifying filter.

USER SAFETY RECOMMENDATIONS:

Remove and wash contaminated clothing before reuse. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

First Aid:

If inhaled:

- Move the person to fresh air.
- If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
- Call a poison control center or doctor for further treatment advice.

If swallowed:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to by a poison control center or doctor.

-Do not give anything to an unconscious person.

If in eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

If on skin:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a Note to Physician which addresses the category I Acute Inhalation Toxicity. The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

The acute toxicity profile for the 200 g/L Gramoxone Inteon formulation, EPA File Symbol: 100-RERT, is:

Acute oral toxicity	III	Acceptable	MRID 46364515
Acute dermal toxicity	II	Acceptable	MRID 46364514
Acute inhalation toxicity	I	Cited	MRID 00046105
Primary eye irritation	II	Acceptable	MRID 46364512
Primary skin irritation	IV	Acceptable	MRID 46364513
Dermal sensitization	Negative	Acceptable	MRID 46364516

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 000100-01217

PRODUCT NAME: Gramoxone Inteon

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: DANGER

POISON ☠

SPANISH SIGNAL WORD: PELIGRO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

Restricted Use Pesticide due to toxicity categories. For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

Fatal if inhaled. Do not breathe spray mist. May be fatal if absorbed through skin. Causes substantial but temporary eye injury. Harmful if swallowed. Do not get in eyes, on skin, or on clothing. Wear coveralls worn over long-sleeved shirt and long pants, socks, chemical-resistant footwear, and chemical-resistant gloves (such as Natural Rubber, Selection Category A). Wear protective eyewear (goggles, face shield, or safety glasses).

For handling activities, use a non-powered, NIOSH-approved air purifying cartridge respirator equipped with an organic-vapor (OV) removing cartridge plus an N-, R- or P-series filter, OR a non-powered air purifying canister-type respirator equipped with an organic vapor canister that uses an N-, R-, or P-series air-purifying filter.

Follow the manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry. When mixing and loading wear a chemical resistant apron. For overhead exposure wear chemical-resistant headgear. When cleaning equipment wear a chemical-resistant apron.

USER SAFETY RECOMMENDATIONS:

Remove and wash contaminated clothing before reuse. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

First Aid:

If inhaled:

- Move the person to fresh air.
- If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
- Call a poison control center or doctor for further treatment advice.

If on skin:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

If in eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

If swallowed:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to by a poison control center or doctor.
- Do not give anything to an unconscious person.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a Note to Physician which addresses the category I Acute Inhalation Toxicity. The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Acute Oral Toxicity - SD rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid)

CITATION: Pooles, A. (2004) Paraquat 240 g/l SL Formulation (A7813K): Acute Oral Toxicity in the Rat. Laboratory Study Identification: 006/438. Unpublished study prepared by SafePharm Laboratories Ltd. August 3, 2004. MRID 46364503.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46364503), 6 female Sprague-Dawley rats (Age: 8-12 weeks, Weight: 203-234 g; Source: Charles River (UK) Ltd., Kent, UK) were given a single oral dose of Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid) by oral gavage. The study was initiated at a dose of 175 mg/kg in one female, and due to survival of that animal an additional 5 females were dosed at either 175 or 550 mg/kg following the up-and-down procedure. Individual animal body weights were recorded prior to test substance administration and again on days 7 and 14, or at death. Clinical checks for mortality and signs of toxicity were made four times post-dosing on initial study day and at least once daily for 14 days. All animals were necropsied on study day 14.

The 3 animals dosed at 175 mg/kg survived, gained weight and appeared healthy throughout the study. No gross internal findings were observed at necropsy.

The 3 animals dosed at 550 mg/kg died by study day 4. One animal was killed *in extremis* on study day 3. Signs of toxicity noted in 2/3 animals included hunched posture, piloerection and laboured respiration and/or decreased respiratory rate. Lethargy and ataxia were also noted in one animal, as well as emaciation. At necropsy, animals that died during the study were noted as having abnormally red lungs, dark liver and dark kidneys. No gross internal findings were observed for the animal killed *in extremis*.

Oral LD₅₀ Females = 310 mg/kg (95% C.I. = 175-550 mg/kg)

Based on the LD₅₀ in female rats, Paraquat 240 g/l SL Formulation (A7813K) is classified as EPA Toxicity Category II.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Main Test

Dosing Sequence	Animal No.	Sex	Dose level (mg/kg)	Sort-Term Outcome	Long-Term Outcome
1	1-0	F	175	S	S
2	2-0		550	D	D
3	3-0		175	S	S
4	4-0		550	D	D
5	5-0		175	S	S
6	6-0		550	D	D

S = survival D = death

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program
Date/Time: Tuesday, November 23, 2004, 12:55:41 PM
Data file name: work.dat
Last modified: 11/23/2004 12:55:41 PM

Test/Substance: paraquat
Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	1-0	175	O	O
2	2-0	550	X	X
3	3-0	175	O	O
4	4-0	550	X	X
5	5-0	175	O	O
6	6-0	550	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.
Stopping criteria met: 5 reversals in 6 tests. LR criterion.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
175	3	0	3
550	0	3	3
All Doses	3	3	6

Statistical Estimate based on long term outcomes:
Estimated LD50 = 310.2 (Based on an assumed sigma of 0.5).
Approximate 95% confidence interval is 175 to 550.

A. Mortality - As noted in table.

B. Clinical observations - The 3 animals dosed at 175 mg/kg survived, gained weight and appeared healthy throughout the study.

The 3 animals dosed at 550 mg/kg died by study day 4. One animal was killed *in extremis* on study day 3. Signs of toxicity noted in 2/3 animals included hunched posture, piloerection and laboured respiration and/or decreased respiratory rate. Lethargy and ataxia were also noted in one animal, as well as emaciation.

C. Gross Necropsy - No gross internal findings were observed at necropsy for the animals surviving the study or the one animal killed *in extremis*.

Findings at necropsy for the remaining animals included abnormally red lungs, dark liver and dark kidneys.

D. Reviewer's Conclusions: Agree with study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Acute Dermal Toxicity - SD Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid)

CITATION: Pooles, A. (2004) Paraquat 240 g/l SL Formulation (A7813K): Acute Dermal Toxicity (Limit Test) in the Rat. Laboratory Study Identification: 006/439. Unpublished study prepared by SafePharm Laboratories Ltd. August 3, 2004. MRID 46364505.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46364505), 5/sex of Sprague-Dawley rats (Age: 8-12 weeks; Weight: 238-268 g males, 208-224 g females; Source: Charles River (UK) Ltd., Kent, UK) were dermally exposed to a single application of Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid) at 2,000 mg/kg. At first only 2 animals were treated (1 male, 1 female). Afterwards an additional 8 animals were treated. The test material was applied evenly to each exposure area, approximately 10% of the total BSA, covered with gauze and then semi-occluded with self-adhesive bandages for 24 hours. Individual animal body weights were recorded prior to test substance administration and again on days 7 and 14, or after death. Clinical checks for mortality and signs of toxicity were made four times post-application on initial study day and at least once daily for 14 days. Animals were also graded for dermal irritation (Draize) after removal of the dressings and once daily for 14 days. All animals were necropsied on study day 14.

2/5 females were killed *in extremis* during the study. All remaining animals survived the study. Survivors gained weight throughout the study, except for 2 females which lost weight during the first week of the study. Signs of toxicity noted in females included hunched posture, lethargy, ataxia, decreased respiratory rate, laboured or increased respiration, dehydration, emaciation, pallor of the extremities and red/brown staining around the snout and eyes. Females recovered from these symptoms by study day 12. Males appeared normal throughout the study. Dermal irritation noted during the study included well-defined erythema, crust formation and hardened light brown-coloured scabs, small superficial scattered scabs and glossy skin. At necropsy, abnormally red lungs were noted in one of the females killed *in extremis*. No gross internal findings were observed at necropsy for the remaining animals.

Dermal LD₅₀ Males => 2,000 mg/kg
Females => 2,000 mg/kg
Combined => 2,000 mg/kg

Based on the dermal LD₅₀ of 2,000 mg/kg, Paraquat 240 g/l SL Formulation (A7813K) is

classified as EPA Toxicity Category III.

This acute dermal study is classified acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg)	Mortality/Number Tested		
	Males	Females	Combined
2000	0/5	2/5	2/10

A. Mortality - As noted in table.

B. Clinical observations - 2/5 females were killed *in extremis* during the study. All remaining animals survived the study. Survivors gained weight throughout the study, except for 2 females which lost weight during the first week of the study. Signs of toxicity noted in females included hunched posture, lethargy, ataxia, decreased respiratory rate, laboured or increased respiration, dehydration, emaciation, pallor of the extremities and red/brown staining around the snout and eyes. Females recovered from these symptoms by study day 12. Males appeared normal throughout the study. Dermal irritation noted during the study included well-defined erythema, crust formation and hardened light brown-coloured scabs, small superficial scattered scabs and glossy skin.

C. Gross Necropsy - At necropsy, abnormally red lungs were noted in one of the females killed *in extremis*. No gross internal findings were observed at necropsy for the remaining animals.

D. Reviewer's Conclusions: Agree with study author.

Date: Nov. 29, 2004

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

STUDY TYPE: Primary Eye Irritation - NZW Rabbit, OPPTS 870.2400; OECD 405

TEST MATERIAL: Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid)

CITATION: Pooles, A. (2004) Paraquat 240 g/l SL Formulation (A7813K): Acute Eye Irritation in The Rabbits. Laboratory Study Identification: 006/407. Unpublished study prepared by SafePharm Laboratories Ltd. July 14, 2004. MRID 46364506.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46364506), 0.1 mL of undiluted Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid) was instilled into the conjunctival sac of the right eye of 3 male young adult New Zealand albino rabbits (Source: David Percival Ltd., Cheshire, UK). The untreated left eye served as a control. At first only one animal was treated and an assessment of the initial pain reaction was made. The two remaining animals were given one drop of local anaesthetic into both eyes prior to instillation. Animals were then observed at 1, 24, 48, 72 hours and on days 7, 10, 14, 17, 21 and for two treated eyes on days 24 and 28, post-instillation. Irritation was scored according to Draize.

No corneal opacity or iritis was noted at any point during the study. One hour after instillation 3/3 eyes exhibited conjunctivitis redness, chemosis and discharge (scores 1-2). Positive effects were noted in 2/3 eyes through study day 10. 1 eye experienced positive discharge (score 2) through study day 24. 1 treated eye exhibited an area of haemorrhage over the nictitating membrane at 24-hours. Haemorrhaging was noted in all treated eyes at 48 and 72-hours. Fur loss around the treated eye was noted in 3/3 treated eyes on study days 10, 14 and 17, with this loss persisting in one eye to the 21-day observation.

The test substance is mildly irritating. In this study, Paraquat 240 g/l SL Formulation (A7813K) is classified as EPA Toxicity Category II.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested										
	Hours				Days						
	1	24	48	72	7	10	14	17	21	24	28
Corneal Opacity	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Conjunctivae											
Redness*	3/3	3/3	3/3	3/3	3/3	1/3	0/3	0/3	0/3	0/3	0/3
Chemosis*	1/3	1/3	2/3	1/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Discharge*	0/3	3/3	3/3	3/3	3/3	2/3	1/3	1/3	1/3	1/3	0/3

*Score of 2 or more required to be considered "positive"

A. Observations - No corneal opacity or iritis was noted at any point during the study. One hour after instillation 3/3 eyes exhibited conjunctivitis redness, chemosis and discharge (scores 1-2). Positive effects were noted in 2/3 eyes through study day 10. 1 eye experienced positive discharge (score 2) through study day 24. 1 treated eye exhibited an area of haemorrhage over the nictitating membrane at 24-hours. Haemorrhaging was noted in all treated eyes at 48 and 72-hours. Fur loss around the treated eye was noted in 3/3 treated eyes on study days 10, 14 and 17, with this loss persisting in one eye to the 21-day observation.

B. Reviewer's Conclusions: Agree with the study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Primary Dermal Irritation - NZW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid)

CITATION: Pooles, A. (2004) Paraquat 240 g/l SL Formulation (A7813K): Acute Dermal Irritation In The Rabbit. Laboratory Study Identification: 006/406. Unpublished study prepared by SafePharm Laboratories Ltd. July 13, 2004. MRID 46364504.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46364504), 3 young adult New Zealand albino rabbits (1 male, 2 females; Source: David Percival Ltd., Cheshire, UK) were dermally exposed to 0.5 mL of undiluted Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid). Initially only one animal was treated and after consideration of the skin reactions in this animal two additional animals were treated. The test substance was introduced under a gauze patch, placed on the dose site on each animal and then secured with a strip of surgical adhesive tape for 4 hours. Animals were then observed for up to 28 days, to assess the reversibility of skin reactions. Dermal irritation was scored according to the Draize system at 1, 24, 48, 72 hours post-patch removal for all animals and up through study days 7, 10, 14, 17, 21, 24 and 28.

One hour post-patch removal well-defined erythema (score 2) and very slight oedema (score 1) was noted at 2/3 treated sites. This irritation persisted at 72 hours for both treated sites, persisting to the 7-day observation in one animal. Very slight erythema (score 1) was noted at the other treated site from 24-hours to study day 14. One animal had extreme weight loss at the 72-hour observation and was killed for humane reasons. One skin site appeared normal at the 21-day observation while the other site appeared normal on study day 28.

Increased salivation, loss of skin elasticity, crust formation, reduced regrowth of fur, loss of skin flexibility and slight desquamation were also noted during the study.

In this study, the formulation is moderately irritating to the skin. Paraquat 240 g/l SL Formulation (A7813K) is classified as EPA Toxicity Category III.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

INDIVIDUAL SKIN IRRITATION SCORES

ERYTHEMA/EDEMA

Animal Number	Sex	Hours				Days						
		1	24	48	72	7	10	14	17	21	24	28
91	M	0/0	1/0	1/0	1/0	1/0	1/0	1/0	0/0	0/0	0/0	0/0
30 ^a	F	2/1	2/1	2/1	2/1	-	-	-	-	-	-	-
31	-	2/1	2/1	2/2	2/2	2/2	- ^b	0/0	0/0	0/0	0/0	0/0
Severity of Irritation - Mean Score		1.3/0.6	1.6/0.6	1.6/1.0	1.6/1.0	1.5/1.0	1/0	0.5/0	0/0	0/0	0/0	0/0

^a Animal 30 was killed for humane reasons after the 72-hour observation period.

^b A reading for erythema and oedema could not be made to crust formation.

A. Observations - One hour post-patch removal well-defined erythema (score 2) and very slight oedema (score 1) was noted at 2/3 treated sites. This irritation persisted at 72 hours for both treated sites, persisting to the 7-day observation in one animal. Very slight erythema (score 1) was noted at the other treated site from 24-hours to study day 14. One animal had extreme weight loss at the 72-hour observation and was killed for humane reasons. One skin site appeared normal at the 21-day observation while the other site appeared normal on study day 28.

B. Results - Test substance is moderately irritating to the skin.

C. Reviewer's Conclusions - Agree with study author.

Date: Nov. 29, 2004

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: Paraquat (240 g/L) and PP796 (1.5 g/L) SL (A7813K) (Paraquat: 22.3% w/w, Batch Reference: J4267/75-2; clear green liquid)

CITATION: Merkel, D. (2004) Dermal Sensitization Study in Guinea Pigs (Buehler Method) with Paraquat (240 g/L) and PP796 (1.5 g/L) SL (A7813K). Laboratory Study Identification: 15409. Unpublished study prepared by Product Safety Laboratories. July 23, 2004. MRID 46364507.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46364507) with Paraquat (240 g/L) and PP796 (1.5 g/L) SL (A7813K) (Paraquat: 22.3% w/w, Batch Reference: J4267/75-2; clear green liquid), 30 male young adult Hartley guinea pigs (Weight: 382-480 g males; Source: Elm Hill Breeding Labs, Chelmsford, MA) were tested using the Buehler method. Once a week for 3 weeks, 0.4 mL of a 10% w/w mixture of the test substance in distilled water was applied to the dose site of each animal using a lint patch and secured with surgical tape to 20 test animals. After 6 hours of exposure, the patches were removed. 24 and 48 hours after each induction the animals were scored for dermal irritation. Thirteen days after the last induction dose challenge doses of 0.2 mL of a 1% w/w mixture of the test substance in distilled water and a 0.3% w/w mixture were applied to the right side of the test animals and to a set of 10 naive control guinea pigs for 6 hours. Approximately 24 and 48 hours after challenge, the animals were graded for dermal irritation. The procedures were validated using alpha-Hexylcinnamaldehyde (HCA) as the positive control substance.

All animals survived and appeared healthy throughout the study. During the induction phase of the study, very faint to faint erythema (score 0.5-1) was noted for most of the treated sites. During the challenge phase, very faint erythema (score 0.5) was noted for 12/20 test sites treated with the 1% w/w mixture at the 24 hour reading. Irritation persisted at 5/20 to 48 hours. Naive controls treated with the 1% w/w mixture exhibited very faint erythema at 2/10 treated sites at the 24 hour reading. Irritation cleared from these sites by 48 hours. Very faint erythema was noted for 2/20 test sites treated with the 0.3% w/w mixture, with irritation clearing by 48 hours. In control animals, very faint erythema was noted for 2/10 treated sites, with irritation clearing by 48 hours.

Based on the results of this study, Paraquat (240 g/L) and PP796 (1.5 g/L) SL (A7813K) does not have to be labeled as a dermal sensitizer.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary

dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig .

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE

A. Induction - Once a week for 3 weeks, 0.4 mL of a 10% w/w mixture of the test substance in distilled water was applied to the dose site of each animal using a lint patch and secured with surgical tape to 20 test animals. After 6 hours of exposure, the patches were removed. 24 and 48 hours after each induction the animals were scored for dermal irritation.

B. Challenge - Thirteen days after the last induction dose challenge doses of 0.2 mL of a 1% w/w mixture of the test substance in distilled water and a 0.3% w/w mixture were applied to the right side of the test animals for 6 hours. Approximately 24 and 48 hours after challenge, the animals were graded for dermal irritation.

C. Naive Controls - A naive control group of 10 animals were tested with 0.2 mL of the 1% w/w and 0.3% w/w mixture at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - All animals survived and appeared healthy throughout the study. During the induction phase of the study, very faint to faint erythema (score 0.5-1) was noted for most of the treated sites. During the challenge phase, very faint erythema (score 0.5) was noted for 12/20 test sites treated with the 1% w/w mixture at the 24 hour reading. Irritation persisted at 5/20 to 48 hours. Naive controls treated with the 1% w/w mixture exhibited very faint erythema at 2/10 treated sites at the 24 hour reading. Irritation cleared from these sites by 48 hours. Very faint erythema was noted for 2/20 test sites treated with the 0.3% w/w mixture, with irritation clearing by 48 hours. In control animals, very faint erythema was noted for 2/10 treated sites, with irritation clearing by 48 hours.

B. Positive control - Results were appropriate with a HCA study to validate test procedures. The positive control study was completed July 2, 2004. This test was completed July 23, 2004.

C. Reviewer's Conclusions: Agree with study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Acute Oral Toxicity - Wistar rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid)

CITATION: Johnson, I. (2003) Paraquat 200 g/l SL Formulation (A3879BU): Acute Oral Toxicity Study in the Rat - Up and Down Procedure. Laboratory Study Identification: AR7304. Unpublished study prepared by Central Toxicology Laboratory. July 15, 2003. MRID 46364515.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46364515), 7 female Wistar Alpk rats (Age: 8-12 weeks, Weight: 166-254 g; Source: Rodent Breeding Unit, Cheshire, UK) were given a single oral dose of Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid) by oral gavage. The study was initiated at a dose of 175 mg/kg in one female, and due to survival of that animal an additional 6 females were dosed at either 175, 550 or 2,000 mg/kg following the up-and-down procedure. Individual animal body weights were recorded prior to test substance administration and again on days 8 and 15, or at death. Clinical checks for mortality and signs of toxicity were made immediately post-dosing and a further twice on initial study day and at least once daily for 15 days. All animals were necropsied on study day 15, or as soon as possible after death.

The 1 animal dosed at 175 mg/kg survived, gained weight and appeared healthy throughout the study. No gross internal findings were observed at necropsy.

1/3 animals dosed at 550 mg/kg were killed *in extremis* on study day 6. The surviving animals either gained weight or equalled their initial body weight by the end of the study. Slight toxicity was seen until study day 4 in one animal, while the other animal showed no signs of toxicity. No gross internal findings were observed at necropsy.

3/3 animals dosed at 2,000 mg/kg died during the study. One was found dead on study day 1, one was found dead on study day 2 and the remaining was killed *in extremis* on study day 2. At necropsy, findings included contents of the stomach and/or intestines stained blue, staining of the mouth and fluid stomach contents were noted.

Oral LD₅₀ Females = 550 mg/kg (95% C.I. = 186.5 to 1640)

Based on the LD₅₀ in female rats, Paraquat 200 g/l SL Formulation (A3879BU) is classified as EPA Toxicity Category III.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Main Test					
Dosing Sequence	Animal No.	Sex	Dose level (mg/kg)	Sort-Term Outcome	Long-Term Outcome
1	21	F	175	S	S
2	32		550	S	S
3	47		2000	D	D
4	563		550	S	S
5	34		2000	D	D
6	48		550	S	D
7	130		2000	D	D

S = survival D = death

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Wednesday, November 24, 2004, 12:33:46 PM

Data file name: work.dat

Last modified: 11/24/2004 12:33:46 PM

Test/Substance: paraquat (200 g/l)

Test type: Main Test

Limit dose (mg/kg): 2000

Assumed LD50 (mg/kg): Default

Assumed sigma (mg/kg): 0.5

Recommended dose progression: 2000, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	21	175	O	O
2	32	550	O	O
3	47	2000	X	X
4	563	550	O	O
5	34	2000	X	X
6	48	550	O	X
7	130	2000	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

Stopping criteria met: 5 reversals in 6 tests.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
175	1	0	1
550	2	1	3
2000	0	3	3

All Doses 3 4 7

Statistical Estimate based on long term outcomes:

Estimated LD50 = 550 (The one dose with partial response).

95% PL Confidence interval is 186.5 to 1640.

A. Mortality - As noted in table.

B. Clinical observations - The 1 animal dosed at 175 mg/kg survived, gained weight and appeared healthy throughout the study.

1/3 animals dosed at 550 mg/kg were killed *in extremis* on study day 6. The surviving animals either gained weight or equalled their initial body weight by the end of the study. Slight toxicity was seen until study day 4 in one animal, while the other animal showed no signs of toxicity.

3/3 animals dosed at 2,000 mg/kg died during the study. One was found dead on study day 1, one was found dead on study day 2 and the remaining was killed *in extremis* on study day 2.

C. Gross Necropsy - No gross internal findings were observed at necropsy for the animals dosed at 175 or 550 mg/kg.

At necropsy, findings for animals dosed at 2,000 mg/kg included contents of the stomach and/or intestines stained blue, staining of the mouth and fluid stomach contents were noted.

D. Reviewer's Conclusions: Agree with study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Acute Dermal Toxicity - Wistar Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid)

CITATION: Johnson, I. (2003) Paraquat 200 g/l SL Formulation (A3879BU): Acute Dermal Toxicity Study in the Rat. Laboratory Study Identification: CR3618. Unpublished study prepared by Central Toxicology Laboratory. July 16, 2003. MRID 46364514.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46364514), 15/sex of Wistar Aplk rats (Age: 8-12 weeks; Weight: 245-322 g males, 176-277 g females; Source: Rodent Breeding Unit, Cheshire, UK) were dermally exposed to a single application of Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid) at either 500, 1,000 or 2,000 mg/kg. The test material was applied to the shorn back of each animal for 24 hours using an occlusive dressing. Individual animal body weights were recorded prior to test substance administration and again on days 8 and 15, or after death. Clinical checks for mortality and signs of toxicity were made twice post-application on initial study day and at least once daily for 15 days. Animals were also graded for dermal irritation (Draize) after removal of the dressings and once daily for 14 days. All animals were necropsied on study day 15, or as soon as possible after death.

1/5 male dosed at 500 mg/kg was killed *in extremis* on study day 4. The remaining 4/5 males and 5/5 females survived the study. One female failed to gained body weight. There were no signs of toxicity in the surviving animals. Scabs and wet sores were apparent on some animals while moderate skin irritation, persisting to study termination, was noted in all animals. At necropsy, the male killed *in extremis* was noted as having stained fur and nares. Animals that survived to study termination were noted as having scabs and, in addition, females had thickened scaly skin.

3/5 males dosed at 1,000 mg/kg were found dead on study days 3 or 4 while 1/5 females were killed *in extremis*. All remaining animals survived the study and gained weight. There were no signs of toxicity in the surviving animals. Slight to moderate skin irritation, scabs and wet sores were apparent on animals. At necropsy, the males killed *in extremis* had no gross internal findings while the female had discoloured liver, lungs and nares, scabs and froth in the lumen. Animals that survived to study termination were noted as having scabs and, in addition, males had thickened skin.

All animals dosed at 2,000 mg/kg were found dead or killed *in extremis* on study day 2 or 3. Slight or moderate skin irritation was noted in most animals. At necropsy staining of the fur was

noted on all animals and several animals had distended stomachs while two had staining of the mouth or nares.

Dermal LD₅₀ Males => 805 mg/kg (95% C.I = 423-1264 mg/kg)

Females => 1,231 mg/kg (95% C.I. = 928-1632 mg/kg)

Based on the dermal LD₅₀ of 805 mg/kg and 1,231 mg/kg, Paraquat 200 g/l SL Formulation (A3879BU) is classified as EPA Toxicity Category II.

This acute dermal study is classified acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg)	Mortality/Number Tested		
	Males	Females	Combined
500	1/5	0/5	1/10
1000	3/5	1/5	4/10
2000	5/5	5/5	10/10

A. **Mortality** - As noted in table.

B. **Clinical observations** - 1/5 male dosed at 500 mg/kg was killed *in extremis* on study day 4. The remaining 4/5 males and 5/5 females survived the study. One female failed to gained body weight. There were no signs of toxicity in the surviving animals. Scabs and wet sores were apparent on some animals while moderate skin irritation, persisting to study termination, was noted in all animals.

3/5 males dosed at 1,000 mg/kg were found dead on study days 3 or 4 while 1/5 females were killed *in extremis*. All remaining animals survived the study and gained weight. There were no signs of toxicity in the surviving animals. Slight to moderate skin irritation, scabs and wet sores were apparent on animals.

All animals dosed at 2,000 mg/kg were found dead or killed *in extremis* on study day 2 or 3. Slight or moderate skin irritation was noted in most animals.

C. Gross Necropsy - In animals dosed at 500 mg/kg, at necropsy the male killed *in extremis* was noted as having stained fur and nares. Animals that survived to study termination were noted as having scabs and, in addition, females had thickened scaly skin.

In animals dosed at 1000 mg/kg, at necropsy the males killed *in extremis* had no gross internal findings while the female had discoloured liver, lungs and nares, scabs and froth in the lumen. Animals that survived to study termination were noted as having scabs and, in addition, males had thickened skin.

In animals dosed at 2000 mg/kg, at necropsy staining of the fur was noted on all animals and several animals had distended stomachs while two had staining of the mouth or nares.

D. Reviewer's Conclusions: Agree with study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Primary Eye Irritation - NZW Rabbit, OPPTS 870.2400; OECD 405

TEST MATERIAL: Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid)

CITATION: Johnson, I. (2003) Paraquat 200 g/l SL Formulation (A3879BU): Eye Irritation Study in the Rabbit. Laboratory Study Identification: FB6020. Unpublished study prepared by Central Toxicology Laboratory. August 1, 2003. MRID 46364512.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46364512), 0.1 mL of undiluted Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid) was instilled into the conjunctival sac of the left eye of 3 female young adult New Zealand albino rabbits (Source: Charles River UK Ltd., Kent, UK and Harlan Interfauna UK Ltd., Oxfordshire, UK). The untreated right eye served as a control. At first only one animal was treated and an assessment of the initial pain reaction was made. Animals were then observed at 1, 24, 48, 72 hours and on days 4, 7, 10, 14 and 17 days post-instillation. Irritation was scored according to Draize.

1 hour after instillation 3/3 eyes exhibited slight corneal opacity (score 1), iritis (score 1), conjunctivitis redness, chemosis and discharge (scores 1-2). All signs of irritation were resolved by study day 17, apart from slight discharge in 2 animals. Positive effects cleared within 10 days. Additional signs noted included comprised lachrymatory, Harderian or mucoid discharge, erythema, oedema, thickening and convolution of the eyelids, haemorrhage of the conjunctiva and nictitating membrane, dried secretion around the periorbital skin, irregular corneal surface and hair loss around the periorbital area. Two animals also exhibited salivation and few faeces.

The test substance is moderately irritating. In this study, Paraquat 200 g/l SL Formulation (A3879BU) is classified as EPA Toxicity Category II.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested								
	Hours				Days				
	1	24	48	72	4	7	10	14	17
Corneal Opacity	3/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Iritis	3/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Conjunctivae									
Redness*	2/3	3/3	3/3	3/3	3/3	2/3	0/3	0/3	0/3
Chemosis*	2/3	3/3	1/3	0/3	0/3	0/3	0/3	0/3	0/3
Discharge*	3/3	0/3	1/3	1/3	1/3	0/3	2/3	2/3	0/3

*Score of 2 or more required to be considered "positive"

A. Observations - 1 hour after instillation 3/3 eyes exhibited slight corneal opacity (score 1), iritis (score 1), conjunctivitis redness, chemosis and discharge (scores 1-2). All signs of irritation were resolved by study day 17, apart from slight discharge in 2 animals. Positive effects cleared within 10 days. Additional signs noted included comprised lachrymatory, Harderian or mucoid discharge, erythema, oedema, thickening and convolution of the eyelids, haemorrhage of the conjunctiva and nictitating membrane, dried secretion around the periorbital skin, irregular corneal surface and hair loss around the periorbital area. Two animals also exhibited salivation and few faeces.

B. Reviewer's Conclusions: Agree with the study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Primary Dermal Irritation - NZW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid)

CITATION: Johnson, I. (2003) Paraquat 200 g/l SL Formulation (A3879BU): Skin Irritation Study in the Rabbit. Laboratory Study Identification: EB5012. Unpublished study prepared by Central Toxicology Laboratory. May 22, 2003. MRID 46364513.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46364513), 3 female young adult New Zealand albino rabbits (Source: Charles River UK Ltd., Kent, UK) were dermally exposed to 0.5 mL of undiluted Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid). Initially only one animal was treated and after consideration of the skin reactions in this animal two additional animals were treated. The test substance was applied to the left flank of each animal, covered with a gauze patch and secured with a strip of surgical tape for 4 hours. Animals were then observed for up to 34 days to assess the reversibility of skin reactions. Dermal irritation was scored according to the Draize system at 1, 24, 48, 72 hours post-patch removal for all animals and in intervals for up to 34 days.

One hour post-patch removal very slight erythema (score 1) was noted at 2/3 treated sites. Irritation increased thereafter. At 72 hours very slight to moderate erythema (score 1-2) was noted in all animals, as well as very slight to slight oedema (score 1-2) for 2/3 animals. Erythema and oedema was seen in all animals up through 11 days, but not after. Additional signs of irritation noted included desquamation, scabbing, wrinkling, thickening and areas of new skin. Animals recovered from all signs of dermal irritation by study day 34.

In this study, the formulation is slightly irritating to the skin. Paraquat 200 g/l SL Formulation (A3879BU) is classified as EPA Toxicity Category IV.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

INDIVIDUAL SKIN IRRITATION SCORES

ERYTHEMA/EDEMA

Animal Number	Sex	Hours				Days			
		1	24	48	72	4	7	8	11
62	F	0/0	1/0	1/0	1/0	1/1	NA*	2/1	2/1
72		1/0	1/1	2/1	2/1	2/1	2/0	NA*	0/0
73		1/0	1/1	2/2	2/2	2/2	2/0	NA*	0/0
Severity of Irritation - Mean Score		0.66/ 0.0	1.0/ 0.66	1.66/ 1.0	1.66/ 1.0	1.66/ 1.33	2/ 0	2/ 1	0.66/ 0.33

*NA - animal was not scored.

A. Observations - One hour post-patch removal very slight erythema (score 1) was noted at 2/3 treated sites. Irritation increased thereafter. At 72 hours very slight to moderate erythema (score 1-2) was noted in all animals, as well as very slight to slight oedema (score 1-2) for 2/3 animals. Erythema and oedema was seen in all animals up through 11 days; but not after. Additional signs of irritation noted included desquamation, scabbing, wrinkling, thickening and areas of new skin. Animals recovered from all signs of dermal irritation by study day 34.

B. Results - Test substance is slightly irritating to the skin.

C. Reviewer's Conclusions - Agree with study author.

Reviewer: Breann Hanson
Risk Manager (EPA): Hope Johnson, RM 25

Date: Nov. 29, 2004

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid)

CITATION: Johnson, I. (2003) Paraquat 200 g/l SL Formulation (A3879BU): Skin Sensitization Study in the Guinea Pig. Laboratory Study Identification: GG7729. Unpublished study prepared by Central Toxicology Laboratory. August 26, 2003. MRID 46364516.

SPONSOR: Syngenta Crop Protection, Inc., P.O. Box 18300, Greensboro, NC 27419

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46364516) with Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid), 30 female young adult Hartley guinea pigs (Weight: 300-344 g males; Source: Harlan Interfauna UK Ltd., Oxon, UK) were tested using the Buehler method. Three times a week for 3 weeks, 0.4 mL of a 25% w/v mixture of the test substance in distilled water (for the first 3 inductions) or a 10%w/v mixture (for the final 6 inductions) was applied to the dose site of each animal using a lint patch and covered with an occlusive dressing to 20 test animals. During this phase 10 naive control guinea pigs were treated in the same manner but with deionized water only. After 6 hours of exposure, the patches were removed. 24 hours after each induction the animals were scored for dermal irritation. Two weeks after the last induction dose challenge doses of 0.1-0.2 mL of a 10% w/v mixture of the test substance in distilled water and a 5% w/v mixture were applied to either flank of the test animals and to the naive control guinea pigs for 6 hours. Approximately 24 and 48 hours after challenge, the animals were graded for dermal irritation. The procedures were validated using alpha-Hexylcinnamaldehyde (HCA) as the positive control substance.

Irritation was noted for all test animals during the induction phase while there were no signs of irritation in any of the control animals. There were no signs of irritation in any animal at challenge. One test animal was humanely killed prior to the 7th induction due to severe signs of toxicity.

Based on the results of this study, Paraquat 200 g/l SL Formulation (A3879BU) does not have to be labeled as a dermal sensitizer.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality

statements were provided.

I. PROCEDURE

A. Induction - Three times a week for 3 weeks, 0.4 mL of a 25% w/v mixture of the test substance in distilled water (for the first 3 inductions) or a 10%w/v mixture (for the final 6 inductions) was applied to the dose site of each animal using a lint patch and covered with an occlusive dressing to 20 test animals. During this phase 10 naive control guinea pigs were treated in the same manner but with deionized water only. After 6 hours of exposure, the patches were removed. 24 hours after each induction the animals were scored for dermal irritation.

B. Challenge - Two weeks after the last induction dose challenge doses of 0.1-0.2 mL of a 10% w/v mixture of the test substance in distilled water and a 5% w/v mixture were applied to either flank of the test animals and to the naive control guinea pigs for 6 hours. Approximately 24 and 48 hours after challenge, the animals were graded for dermal irritation.

C. Naive Controls - A naive control group of 10 animals were tested with the test substance at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - Irritation was noted for all test animals during the induction phase while there were no signs of irritation in any of the control animals. There were no signs of irritation in any animal at challenge. One test animal was humanely killed prior to the 7th induction due to severe signs of toxicity.

B. Positive control - Results were appropriate with a HCA study to validate test procedures. The positive control study was completed May 31, 2003 This test was completed May 2, 2003.

C. Reviewer's Conclusions: Agree with study author.

1. DP BARCODE: D309349

2. PC CODE: 061601

3. CURRENT DATE: 29/NOV/2004

4. TEST MATERIAL:

^a Paraquat 240 g/l SL Formulation (A7813K) (Paraquat: 22.3%, Batch Reference: J4267/75-2; green liquid)

^b Paraquat (240 g/L) and PP796 (1.5 g/L) SL (A7813K) (Paraquat: 22.3% w/w, Batch Reference: J4267/75-2; clear green liquid)

^c Paraquat 200 g/l SL Formulation (A3879BU) (Paraquat: 18.416%, Batch Reference: J6470/11/1; clear green liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat ^a SafePharm Laboratories Ltd. 006-438/08-03-2004	46364503	LD ₅₀ = 310 mg/kg (95% C.I.= 175-550 mg/kg) (females)	II	A
Acute dermal toxicity/rat ^a SafePharm Laboratories Ltd. 006-439/08-03-2004	46364505	LD ₅₀ > 2,000 mg/kg (males, females combined)	III	A
Primary eye irritation/rabbit ^a SafePharm Laboratories Ltd. 006-407/07-14-2004	46364506	no corneal opacity or iritis noted. 3/3 conjunctivitis at 1 hour, no positive effects on day 28	II	A
Primary dermal irritation/rabbit ^a SafePharm Laboratories Ltd. 006-406/07-13-2004	46364504	moderate irritant	III	A
Dermal sensitization/guinea pig ^b Product Safety Laboratories 15409/07-23-2004	46364507	is not a sensitizer	—	A

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat ^c Central Toxicology Laboratory AR7304/07-15-2003	46364515	LD ₅₀ = 550 mg/kg (95% C.I.= 186.5 - 1640 mg/kg) (females)	III	A
Acute dermal toxicity/rat ^c Central Toxicology Laboratory CR3618/07-16-2003	46364514	LD ₅₀ = 805 mg/kg (males) LD ₅₀ = 1231 mg/kg (females)	II	A
Primary eye irritation/rabbit ^c Central Toxicology Laboratory FB6020/08-01-2003	46364512	3/3, opacity, iritis, conjunctivitis at 1 hour, no positive effects on day 10.	II	A
Primary dermal irritation/rabbit ^c Central Toxicology Laboratory EB5012/05-22-2003	46364513	slight irritant	IV	A
Dermal sensitization/guinea pig ^c Central Toxicology Laboratory GG7729/08-26-2003	46364516	is not a sensitizer	—	A

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived



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FEDERAL EXPRESS

June 19, 2006

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**SUBJECT: SUBMISSION OF ADDITIONAL INFORMATION RELATED TO SAFETY
IMPROVEMENT OF GRAMOXONE INTEON, EPA REG. NO. 100-1217**

Dear Mr. Tompkins:

Syngenta Crop Protection is herein submitting additional information related to the safety improvement of Gramoxone Inteon. This information was presented at a meeting with USEPA on April 24, 2006. Included are:

- 1) Attachment A: *Gramoxone Inteon and Improved Safety*, a document reviewing the information presented at the meeting by Dr. Mike Clapp,
- 2) Attachment B: A review of global paraquat incidence data,
- 3) Attachment C: *Declaration of Sir Colin Berry*
- 4) A study, not previously submitted; "*Gramoxone Effects of Increased Emetic Levels on Toxicokinetics in the Dog*" which is listed on the attached Transmittal Document.

This information is submitted for informational purposes. The submission is outside the scope of PRIA. If you have any questions regarding this submission please contact me at 336-632-6324.

Kind Regards,

Jerry Wells
Senior Regulatory Product Manager

**VOLUME 1 OF 2 OF SUBMISSION
(TRANSMITTAL DOCUMENT)**

1. Name and Address of Submitter

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2. Regulatory Action in Support of which this Package is Submitted

SUBMISSION OF ADDITIONAL INFORMATION RELATED TO SAFETY
IMPROVEMENT OF GRAMOXONE INTEON, EPA REG. NO. 100-1217

3. Transmittal Date

6/19/2006

4. List of Submitted Studies

MRID NUMBER	VOLUME NUMBER	STUDY TITLE	EPA GUIDELINE NUMBER
	1 OF 2	Transmittal document	NA
	2 OF 2	Effects of Increased Emetic Levels on Toxicokinetics in the Dog;(XD1328, 026698-RES,T003396-06), (09003aeb801feed9),(445557)	NA

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ATTACHMENT A:

***GRAMOXONE INTEON AND IMPROVED
SAFETY, A DOCUMENT REVIEWING THE
INFORMATION PRESENTED AT THE
MEETING BY DR. MIKE CLAPP***

GRAMOXONE INTEON AND IMPROVED SAFETY

May 31, 2006

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A listing of the formulations discussed in this document is given below.

<i>Product Reference</i>	<i>Paraquat a.i. concentration</i>	<i>Inteon Technology (Y or N)</i>	<i>Comments</i>
<i>Gramoxone</i>	<i>200 g/l</i>	<i>No</i>	<i>Global formulation, not registered in US</i>
<i>Gramoxone US</i>	<i>360 g/l</i>	<i>No</i>	<i>Registered in US as Cyclone Concentrate (alternative brand name Gramoxone Max) US Voluntary cancellation requested</i>
<i>Inteon</i>	<i>200 g/l</i>	<i>Yes</i>	<i>Global formulation, not registered in US, separation problems (also called A3879BU)</i>
<i>Inteon US</i>	<i>240 g/l</i>	<i>Yes</i>	<i>Registered in US as Gramoxone Inteon (also called A7813K)</i>

GRAMOXONE INTEON AND IMPROVED SAFETY

1. Introduction

Gramoxone Inteon (referred to as Inteon or Inteon US hereafter in this document) is a novel formulation of paraquat developed by Syngenta. The formulation was specifically developed to improve the acute oral toxicity in the event of ingestion by humans. To test the new formulation, the dog was selected as the most appropriate surrogate for humans. Tests in the dog indicate a significant improvement in acute oral toxicity indicated by reduced paraquat absorption and survival. All dogs survived a dose containing greater than ten times the amount of paraquat shown to be lethal to dogs with non-Inteon formulations (referred to as Gramoxone or Gramoxone US hereafter in this document) in previous studies. The principle components of the formulation responsible for this improvement are a natural alginate (that causes the liquid formulation to gel under the acidic conditions of the stomach), emetic and purgative. This technology is expected to result in fewer deaths following accidental or intentional paraquat ingestions in humans.

2. Rationale for reduced oral toxicity in the Inteon formulation

Inteon formulations have been designed to offer improved oral safening compared to previously registered Gramoxone formulations through a reduction in the amount of paraquat absorbed following ingestion. A natural alginate that immediately gels when entering the low pH environment of the stomach has been included in Inteon formulations. The amount of emetic has also been increased three-fold in Inteon formulations compared to the currently sold Gramoxone formulation. The increase in emetic was made to ensure efficacy of the emetic after gelling of the formulation in the stomach. The purpose of these changes is to cause the formulation to gel in the stomach and for the gel mass in turn to cause the pyloric valve at the base of the stomach to constrict, holding paraquat in the stomach and allowing the critical time needed for the emetic to reach the brain and cause vomiting. Paraquat expelled in this manner does not reach the intestine where most absorption would occur, thereby minimizing exposure (Heylings et al 1991). A purgative, magnesium sulphate is also added to the Inteon formulation to help purge any product that does pass into the intestines, further minimizing exposure time.

3. Method of assessing improvement in oral toxicity of Inteon

In order to investigate the benefit of the combination of alginate gelling and emetic effect, as well as evaluate consequent oral safening, a vomiting species is required and the dog was selected (see No. 8 for additional considerations for selecting the dog as a surrogate for humans). Oral safening (degree of toxicity) has been evaluated for the Inteon formulations by measuring plasma paraquat levels in the dog after administration. Due to animal welfare concerns, lethality studies with paraquat in the dog are not

permitted under the animal experimentation Project Licence administered through the UK Home Office. The main parameters evaluated to reflect the paraquat absorbed following oral dosing have been the peak plasma level and the 24 hour area under the curve (AUC) value. For the same animal welfare reasons, no concurrent Gramoxone dose response was included in the study design as all doses except the lowest have been shown to be lethal to the dog or are above such a lethal dose. Two formulations are reported, Inteon (a 200g/l paraquat formulation with built in wetters for use outside the US and Inteon US (a 240g/l paraquat formulation without built in wetters for use in the US). The basic study design was to dose three dogs with a dose (8 mg paraquat/kg bw) just below the lethal threshold for Gramoxone (approximately 10 mg paraquat/kg bw) and monitor paraquat plasma levels. The same dogs would be dosed 30 days later at a higher dose if they met certain health criteria. The doses used in the assessment of Inteon were 8, 16, 32, 64, and 128mg/kg bw. The Inteon US assessment was done after that of Inteon and based on the Inteon results, the Inteon US doses selected were 32, 64, and 128mg/kg bw.

10mg/kg
*

4. The lethal dose of non- Inteon paraquat formulations in the dog

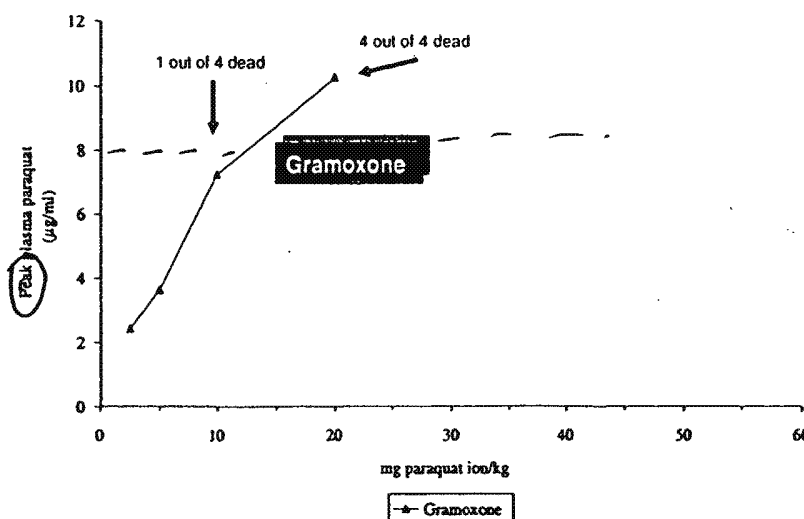
The established toxicity of Gramoxone in the dog from studies in 1987 is shown in Figure 1, where the peak plasma level is correlated with deaths observed. This provides a rationale for not testing Gramoxone at doses higher than 8mg/kg since these would be expected to result in mortality (Swain 2005; Cockrill and Goburdhum 1988). The calculated LD50 was 12 mg/kg, which is consistent with Widdop et al (1977) who reported deaths at 10mg/kg bw.

*

Figure 1

Swain & Cockrill
10 & 12 mg/kg LD50

GRAMOXONE: Peak Plasma Paraquat Levels in Dogs (1987 Study)



Peak

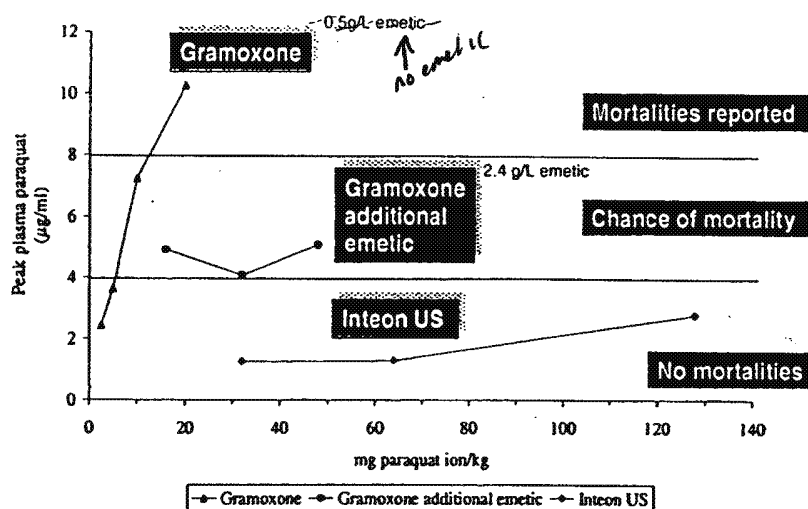
One dog died at 10 mg paraquat ion/kg. All dogs were administered a further dose of 10 mg paraquat ion/kg 30 days later.

5. The effect of increasing emetic levels in non- Inteon formulations on reducing oral toxicity in dog

The effect of increasing the emetic level in a Gramoxone (non- Inteon) formulation was established in a research study in 1990. The peak plasma levels are shown in Figure 2 and the 24h area under the curve (AUC) are shown in Figure 3. Increasing the amount of emetic in Gramoxone reduced absorption of paraquat (peak plasma) at dose levels up to 48mg/kg bw, but at this dose the overall systemic exposure resulted in mortality (2 out of 3 dogs were humanely killed following a dose of 48 mg paraquat/kg bw with the high emetic formulation). The peak plasma level of paraquat is fairly constant (between 4 to 5ug/ml) across administered doses of 16 to 48 mg paraquat ion/kg for the formulation with high emetic, but the 24 hour paraquat plasma AUC increases significantly between 32 and 48 mg paraquat ion /kg with mortality observed at the higher dose level. Increasing the emetic level alone therefore, confers some, but limited oral safening (Swain and Heylings 2006). Increasing the emetic level in the Gramoxone formulation produced earlier emesis than that observed with Inteon US (at approx 3 vs. 15 minutes). Therefore, increasing emetic level alone reduced time to emesis and reduced peak plasma and AUC levels but only offered minimal improvement in preventing lethality compared with Inteon US which showed a greater than 10X improvement.

Figure 2

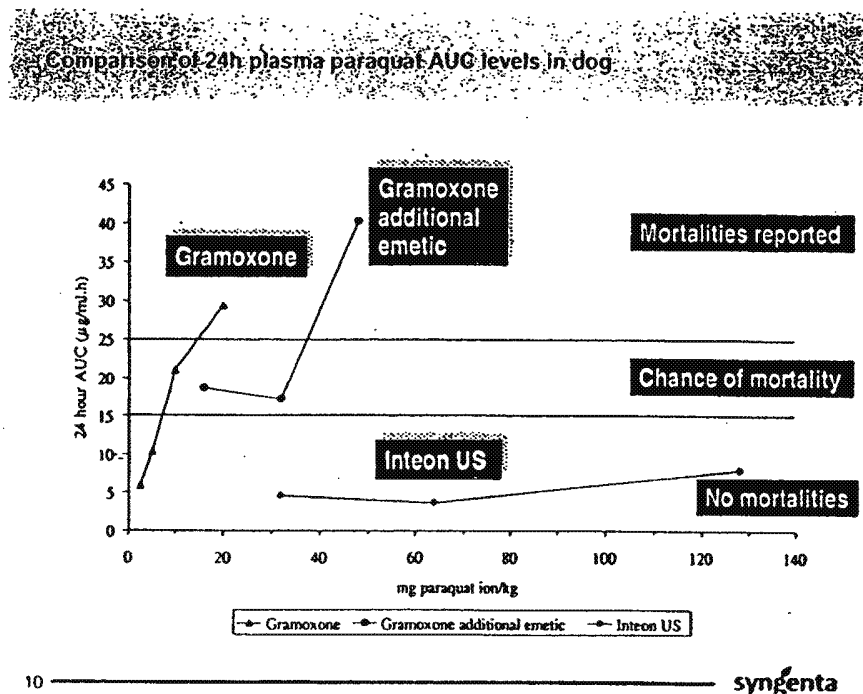
Gramoxone influence of increased emetic on peak plasma paraquat levels in dog



4

syngenta

Figure 3



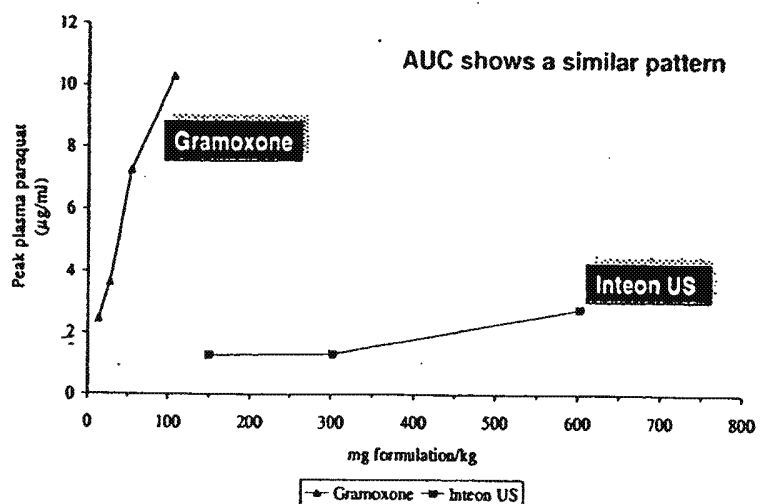
6. Comparison of oral toxicity in the dog between Inteon and Gramoxone

Inteon US has a much greater impact on reducing paraquat exposure (based on plasma peak or AUC) in dog than increasing emetic. Figure 3 shows the 24h AUC values for Gramoxone, Gramoxone with increased emetic, and Inteon US. The Inteon US formulation resulted in lower levels of systemic absorption of paraquat in the dog, as measured by both peak plasma level and 24h AUC over a dose range of more than 10 fold greater than that for Gramoxone. The acid-triggered gelling with Inteon holds the formulation in the stomach resulting in productive emesis and a consequent reduced systemic exposure. Examining this in terms of the amount of formulation ingested (rather than a normalised mg/kg of paraquat ion) results in a similar picture as shown in Figure 4.

The pharmacokinetic and oral toxicity data indicate that Inteon US affords a greater than 10-fold improvement in oral safety over non-Inteon formulations in dogs and as dogs are an excellent surrogate for humans a significant improvement in human survival following paraquat ingestion is expected.

Figure 4

GRAMOXONE INTEON: Lower Peak Plasma Paraquat Levels in Dog



11

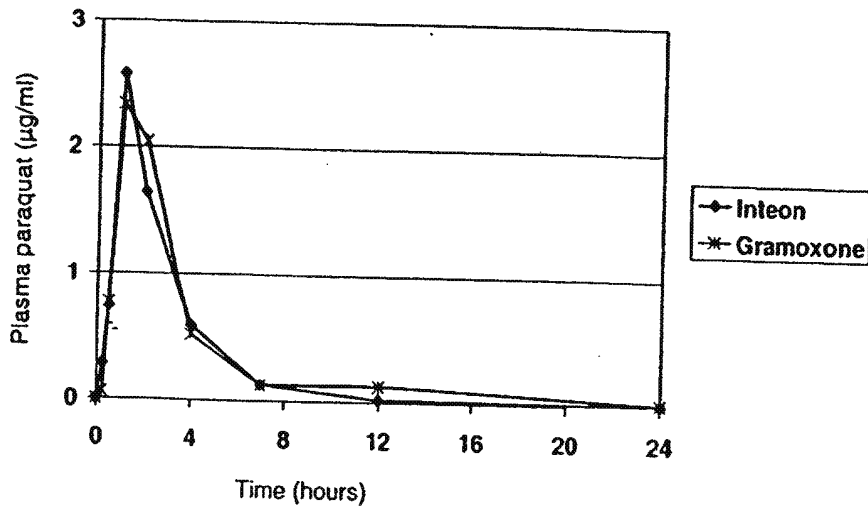
Humar-Jacobs formulation

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7. Comparison of oral toxicity in dog between Inteon and Gramoxone at a sublethal dose

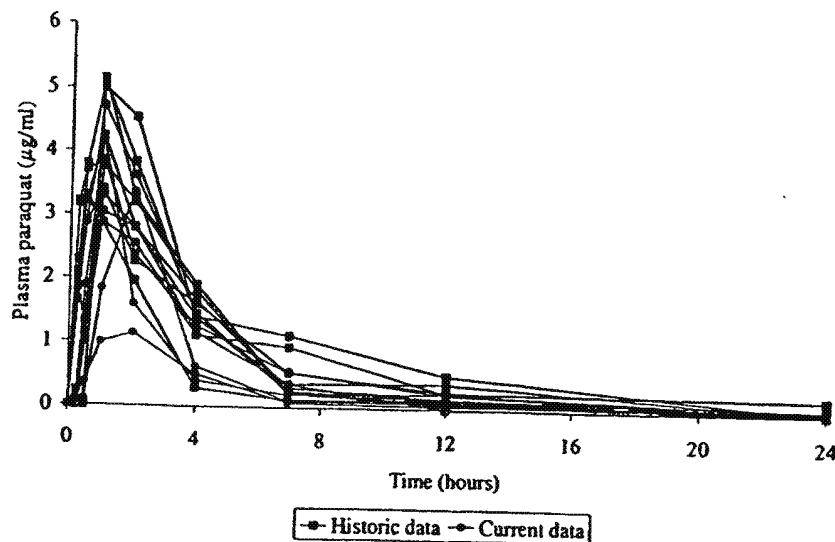
Dogs given a sublethal dose (8 mg paraquat/kg) of Inteon had lower paraquat peak plasma levels when the levels are compared with those seen in historical studies (1988-1991) with Gramoxone where dogs were dosed with the same level of paraquat (Heylings *et al* 2004). However, due to the results of one outlier dog, there does not appear to be an improvement when the paraquat peak plasma levels from the average of 3 dogs dosed with Inteon are compared to levels seen in a contemporaneous study with Gramoxone (Brammer *et al* 2004) (Figure 5).

Figure 5



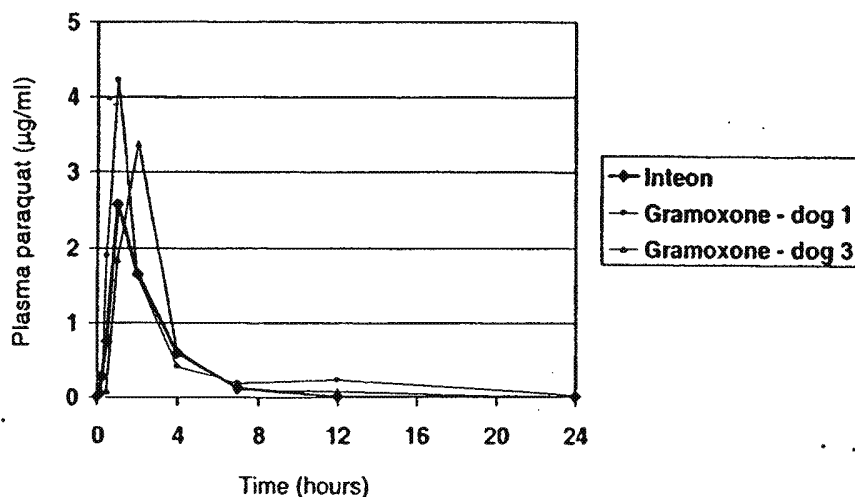
In the Brammer *et al* (2004) study, plasma levels of dogs dosed with Gramoxone were higher when compared to dogs dosed at the same level with Inteon for two of the three dogs tested. One dog dosed with Gramoxone, however, showed an atypical and unusually low value. This is clearly shown in Figure 6, where one of the three dogs in red (the contemporaneous control dogs referred to above) is an outlier with regard to the other two dogs and also all the other historical dogs.

Figure 6



If the results from the one dog are removed as an outlier, the peak plasma levels (approximately 3.5 ug/ml) of the remaining two dogs dosed with Gramoxone at 8 mg/kg are consistent with the historical control (Figure 7). The mean peak plasma level (approximately 2.5 ug/ml) in dogs dosed with the same level of Inteon indicate the Inteon formulation does reduce exposure at the sublethal dose.

Figure 7



In view of the results of the dog studies with Inteon (no lethal effects up to 128mg/kg), the 8 mg/kg dose level was not repeated in the Inteon US study (the doses used in the Inteon US study were 32, 64 and 128 mg/kg). Therefore, there is a "weight of evidence" to support a significant improvement in oral toxicity at the low dose of Inteon US.

8. The selection of the dog as an acceptable surrogate for human safety

The main requirements for an animal model for assessing the toxicity of Inteon/Inteon US are for similarity in the gastro-intestinal (GI) tract, stomach pH, an ability to vomit, and ability to respond to the centrally acting emetic PP796. The relevant characteristics of the dog and human have been compared (Figures 8 & 9; Berry, 2005). They fully support the dog being an appropriate surrogate for use in toxicokinetic studies to reach a determination of human responses to ingestion of Inteon formulations.

Figure 8

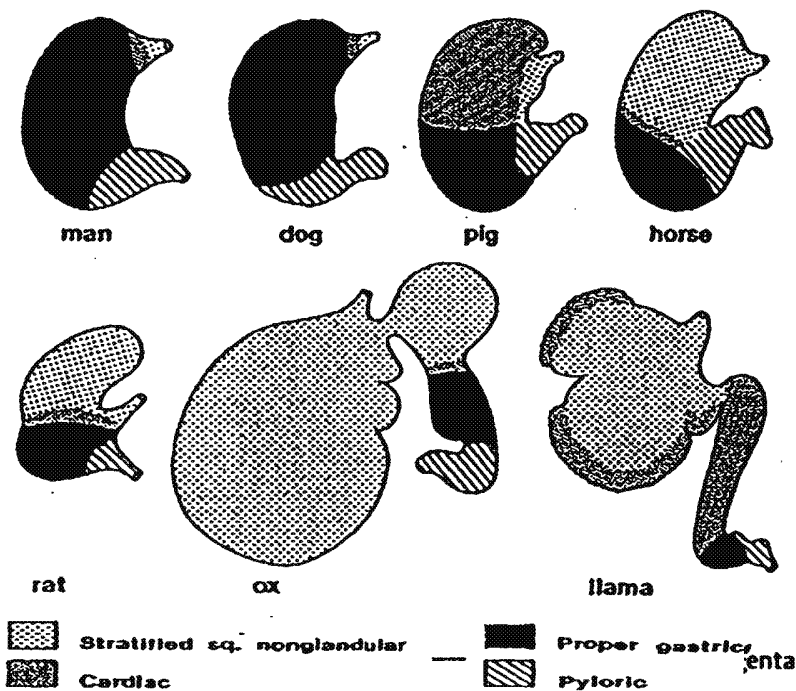


Figure 9

Human: Dog - Comparison of GI Anatomy and Physiology			
	Characteristic	Human	Dog
Relevant Similarities	Chamber	Single/glandular	Single/glandular
	Capacity	1-1.6 L	~2 L
	pH fasted	1.4 - 2.1	1.5
	Gastric Mucosa	Predominantly "Proper Gastric" (see diagrams)	
	Emptying rates	1-2 hrs	1-2 hrs
	Proportional GI lengths (%):		
	Small	80	85
	Cecum	3	2
	Colon	17	13
Potentially Relevant Differences	Vomiting	Initiated by local irritation and/or similar neural reflex pathways to/from CNS	
	Total GI Transit Time	8 - 72 hrs	6 - 8 hrs
	Small Intestine Transit time	3-4 hrs	>4 to <8 hrs

20 From: Karak, TT (1995). Comparison of the gastrointestinal anatomy, physiology, and biochemistry of humans and commonly used laboratory animals. *Biopharm & Drug Disp.* 16: 351-380. **syngenta**

9. The relevant endpoint for evaluating oral safety improvement in humans

Accidental or intentional ingestions in humans may result in fatalities due to an initial organ failure (including renal and hepatic failure) or a subsequent progressive pulmonary fibrosis. The different scenarios are determined by the amount ingested. In the event of a lower intake of paraquat such that these two phases are not encountered, a recovery is normally made and the individual survives. The intention of the Inteon technology is to provide a reduction in the amount of paraquat being absorbed relative to existing Gramoxone formulations for any given amount ingested, and consequently reduce the number of fatalities from what would otherwise have been a fatal dose. Therefore, the relevant parameter for assessing improved oral safety in humans is lethality arising from rapid organ failure or subsequent progressive lung fibrosis.

In the toxicity studies conducted with the dog, physical condition and lethality were directly assessed through observation. Clinical chemistry was also undertaken, and at the end of the study, animals were subject to post mortem examination and histopathological examination. All the dogs tolerated well the highest dose of Inteon US (128mg paraquat/kg, equivalent to 602 mg formulation/kg bodyweight) and there was no clinical evidence of toxicity from pulmonary auscultation or clinical chemistry. There was minimal bodyweight loss, which was quickly recovered. Small discoloured areas of less than 1 cm² were present in the lungs of a single animal at post mortem, and these were areas of minimal interstitial fibrosis and associated change. These changes are considered to be treatment related but not progressive, and not life-threatening. This fully supports a dose of 602 mg formulation/kg bodyweight of Inteon US formulated product as the appropriate dose for risk assessment and the one of relevance to assessing oral safening in humans. This dose level provides an improvement over existing Gramoxone formulations of approximately 10 fold.

10. Progression of lung lesions in humans surviving paraquat ingestion

One of three dogs receiving the highest dose of Inteon US (greater than 10X the known lethal dose of Gramoxone) showed a small non-progressive lung lesion when lungs were examined after being sacrificed at the conclusion of the study (10 days after the last dose). The lesion was not considered life threatening or progressive. In human cases where an individual survives an accidental or intentional ingestion of paraquat, the reports from the literature indicate that the lung lesion does not subsequently progress with time, and that some recovery is seen. The recovery of respiratory function in survivors of acute paraquat poisoning has been studied (Lin et al 1995; Bismuth et al 1996). The results demonstrate that paraquat induced respiratory function impairments progressively recover, at least partially with time. In addition, pulmonary structure damage improved as shown in the follow-up chest radiographs. A third paper (Yamashita et al 2000) which is based on a group of only 12 patients is more difficult to interpret and concluded that patients surviving paraquat poisoning should be followed up with detailed lung function studies.

11. Species differences in paraquat lethality between human and dog

The median lethal dose (MLD) for Gramoxone in the dog is approximately 12 mg paraquat ion/kg. An estimate of the MLD in humans is 50-80 mg/kg paraquat ion, derived from Pond (1990) assuming a bodyweight of 60kg (Figure 10). Therefore, the dog is more sensitive to paraquat lethality compared to humans.

Figure 10

Species differences in acute oral toxicity

Species	Median Lethal Dose (MLD) paraquat ion mg/kg	Inteon US mg formulation/kg
Dog	~12	Non-lethal at 602 (128mg paraquat ion/kg)
Human	50 – 80 (15-25 ml Gramox.) (Pond, 1990)	

12. The ratio of intentional and accidental paraquat ingestions in the US

An analysis of Syngenta Poison Control Center Database (Prosar) for the 6 year period 2000 – 2005 revealed 29 cases of paraquat poisoning in the US. Eleven (38%) of these were classified as deliberate (intentional) and 18 (62%) as accidental. The accidental cases included people ingesting material decanted into drinks bottles, a man denying a suicide attempt, someone ingesting what he thought was tobacco spit, a doctor suspecting paraquat poisoning without confirming paraquat exposure and a 15 month old child drinking from a container in the back of a car. In 2 accidental cases there was predominantly topical exposure. Very often the information was from a third party and not the patient themselves and therefore, factual information is limited and in many cases detailed hospital records were not available. Ten of eleven people who intentionally ingested paraquat (91%) died and 8 of the 16 people who accidentally ingested paraquat (50%) died as a result.

13. Ingested volumes in the rest of the world and survival

Data collected from 563 cases of deliberate ingestion from several countries mainly in the Asia Pacific region shows that approximately 50% of those deliberately ingesting paraquat formulations consumed less than 50mls in volume of paraquat formulation (10g paraquat ion) (Submitted to EPA August 2005). Although the median amount of paraquat ion ingested varies from country to country and may differ from region to region within these countries. The overall survival rate of this population was approximately 25%.

14. Typical ingested volumes for accidental and deliberate ingestions in the US and survival

In 7 out of 11 of the intentional ingestions reported by PROSAR for the years 2000-2005 the amount ingested is unknown, in 3 cases it was approximately 3-8 ounces (90-240mls) and in one case a sip. The latter individual, a 16 year old girl was the only one out of the 11 to survive.

Of the accidental ingestions, the amount ingested was unknown in 55% (10/18) of the cases. Two were topical exposures, and the amount ingested for the other six ranged from a sip to 2 swallows, although there was an estimation of 100ml ingested by a 13 year old child who survived. Considering the Syngenta product contains an olfactory alert it is possible, but difficult, to envisage someone consuming more than one mouthful (~15ml) accidentally. The overall survival from accidental ingestions, excluding the topical exposures who survived, was just under 50%.

From the records available in the cases considered it is very difficult to establish the amount ingested with any accuracy, although the greater survival in the case of accidental ingestions suggests less volume is ingested.

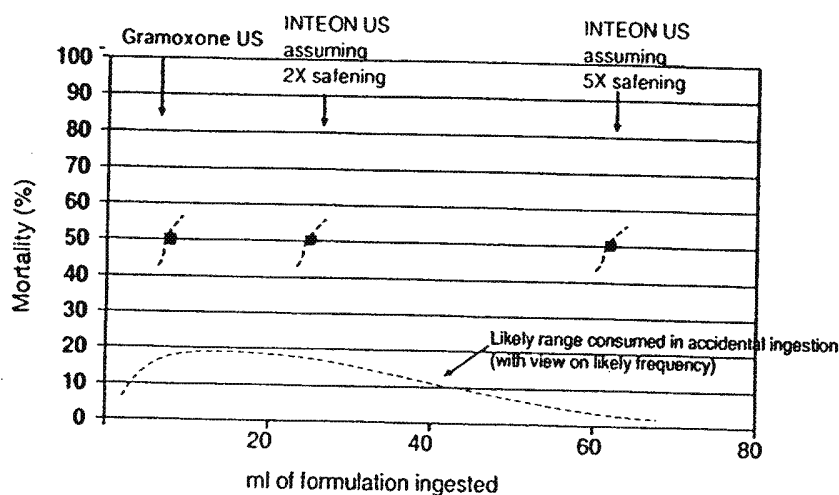
15. Significance of the improvement in oral toxicity on reducing human fatalities

Inteon US has been shown to be non-lethal in the dog at doses up to 128 mg/kg paraquat ion, a dose greater than ten times the MLD for Gramoxone in the dog (approximately 12 mg/kg paraquat ion). This level of safening in the dog, a more sensitive species than humans, indicates a real and significant safening and reduction in lethality. From these results, and the similarities between dog and man in the mechanism of toxicity and relevant anatomy and physiology, a significant improvement in oral toxicity is to be expected in humans. The oral toxicity improvement from Inteon is expected to be particularly relevant to ingestions that are accidental or to intentional ingestions of lower volumes of formulation. Effectively, a shift to the right is expected in the toxicity curve for survival against paraquat ingestion, as illustrated schematically in Figure 11. In this figure, the shift in the 50% mortality point is illustrated starting from a value of 50mg/kg for Gramoxone (source taken from Pond in Section 11 above), and scaling from this to

Gramoxone US and then to Inteon US with 2x or 5x assumed safening factors (well below the 10X suggested by the dog data). The likely (anticipated) range of volumes consumed in accidental ingestions is also shown, although the available data for this category are limited and of varying quality as discussed in Section 13 above. This Figure is shown for illustrative purposes only.

Figure 11

Possible improvement in human survival following accidental ingestion of INTEON US compared with Gramoxone US (illustrative schematic only)



16. Relationship between paraquat plasma levels and human survival

The measurement of paraquat plasma concentration has proved to be a reliable indicator of the prognosis of the intoxication. Based on results from 79 patients with a reasonably well established time of ingestion, Proudfoot *et al* (1979) found that those patients whose plasma paraquat concentration did not exceed 2.0, 0.6, 0.3, 0.16, and 0.1 mg/l at 4, 6, 10, 16, and 24 hours after ingestion, survived. This semi-logarithmic plot has become known as the predictive line, or 'Proudfoot's curve'. Subsequently, using a sample size of 219 patients, Hart *et al* (1984) were able to calculate the probability of survival of the patient from the initial paraquat plasma concentration. It was noted that the line denoting a 50% probability of survival correlated well with Proudfoot's curve.

17. Status of Sri Lanka observational monitoring survey

Syngenta has undertaken a survey of paraquat poisonings in Sri Lanka to monitor the effect of introducing an Inteon formulation on the survival of humans following

ingestion. Nine hospitals are involved in this survey and data have included the estimated dose of paraquat ingested and outcome. The data collected before the introduction of Inteon comprised some 350 cases, and there were 224 cases confirmed with Inteon when the survey was closed at Jan. 26, 2006. The data are now under evaluation and a summary of findings is expected in June 2006 following review by the independent scientific advisory panel that is overseeing the survey. The formulation in Sri Lanka is a 200g/l Inteon formulation containing built-in wetters and is different to that developed for the US. During the period of the survey it became apparent that the formulation was not optimal and suffered a degree of separation as illustrated in Figure 12. This formulation separation resulted in a reduction in the degree of safening in studies in dogs. Despite this, there was still an improved safening over Gramoxone (Figure 13). The Inteon formulation in Sri Lanka is therefore considered to be sub-optimal for demonstrating the full potential of a homogeneous Inteon formulation, like that developed for, and registered in the US. A fully homogeneous Inteon formulation would be expected to show greater improvement in safety than the data that will be generated from the Sri Lanka survey.

Inteon US is a formulation without built-in wetters and does not (cannot) suffer the same separation issue as the Sri Lanka formulation. Inteon US has a greater improvement in oral safety in the dog than the Inteon formulation undergoing evaluation in Sri Lanka.

Figure 12

Inteon Sri Lankan formulation: Illustration of formulation separation

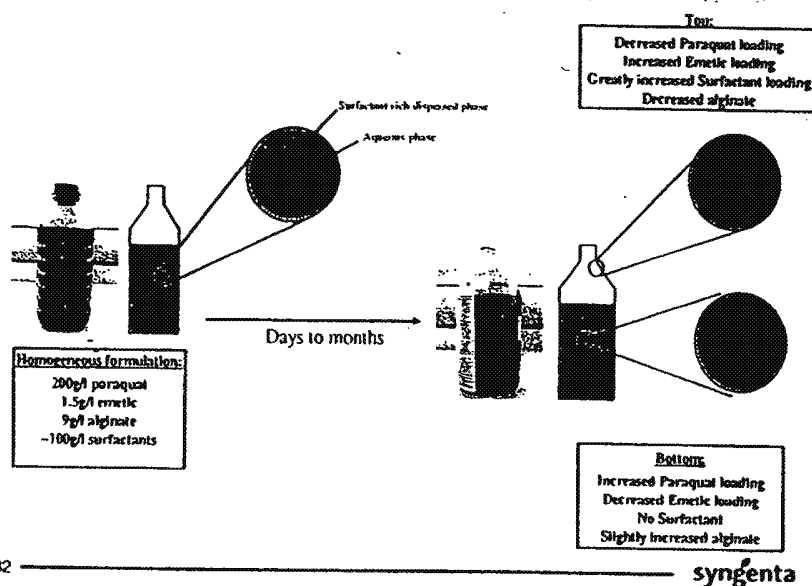
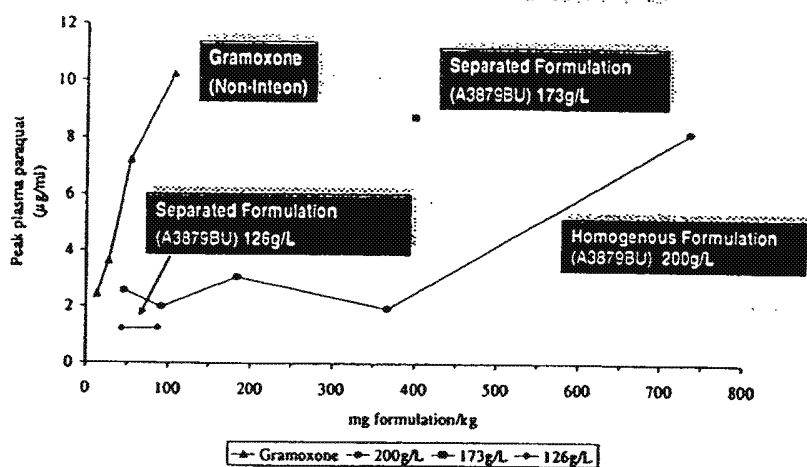


Figure 13

Inteon formulation in Sri Lanka: Plasma Paraquat Levels in Dogs



Separated Inteon formulation significantly reduced paraquat levels in dogs from Syngenta

18. Impact of Inteon formulations on lesions on the lips and mouth as reported in the literature with Gramoxone

Swallowing Gramoxone has been reported to produce a caustic lesion including the lips and mouth, but recovery is also reported (Bismuth *et al* 1995). In animal tests, Inteon formulations have been found to show reduced irritancy to skin and eye compared with Gramoxone, but the extent to which this may offer a benefit in poisoning cases is not established. A comparison of Inteon US with Gramoxone in rabbit irritation tests is shown in Figures 14 -16, showing a reduced irritancy for the Inteon formulation.

Figure 14

Skin Irritation Comparisons

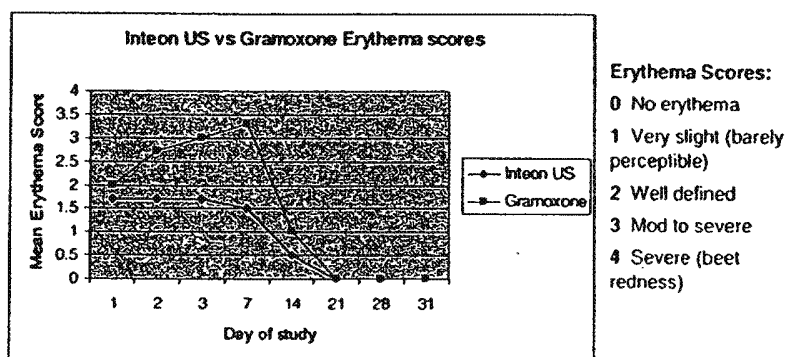
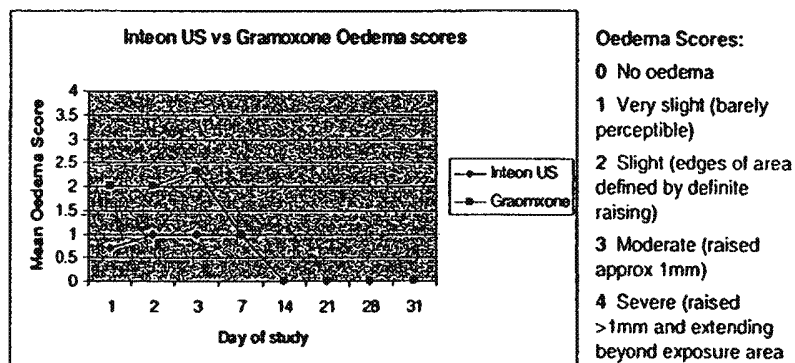


Figure 15

Skin Irritation Comparisons

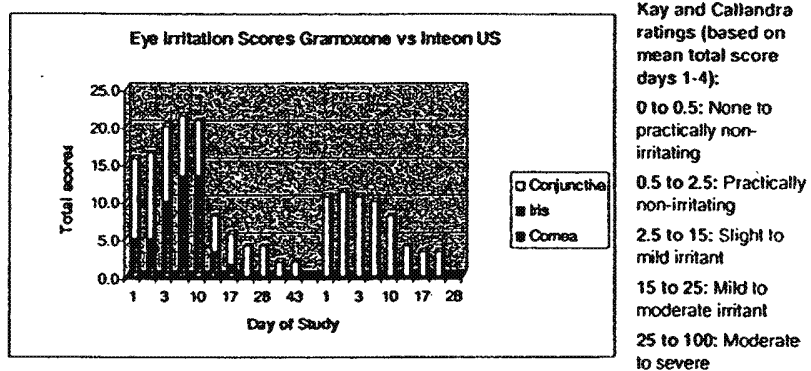


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Figure 16

Eye Irritation Comparisons



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syngenta

19. Summary

Intentional or accidental ingestions occur with paraquat as with many other materials. Over the years, Syngenta has introduced formulation improvements to deter ingestion, including colour and stench, and has introduced an emetic to reduce paraquat absorption. Syngenta has now introduced alginate technology into a new formulation (Inteon) that clearly shows reduced paraquat absorption and 10-fold safening (reduction in volume to cause lethality) in the dog. The data indicate that changing to Inteon formulations will save lives in the USA and internationally.

20. References

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Paraquat Human poisonings:

Estimates of the amount of paraquat ingested are not routinely recorded by hospitals and poison centres since the main objective for the medic is treatment with the aim of saving life. However, we have been able to compile data collected from some cases of deliberate ingestion from several countries mainly in the Asia Pacific region (Table 1). This data shows that the median amount of paraquat ion ingested varies from country to country and may differ from region to region within these countries. The estimates provided are for total paraquat ingested and, since bodyweights of the patients were not recorded, these are estimated values derived using amounts of the Gramoxone 200g/l formulation (with built in wetting agents). Hence, a dose of 10g paraquat ion would equate to approximately 50mls of end-use product formulation.

The same data as presented in Table 1 has also been plotted in Figure 1 as amount of paraquat ingested for the cumulative population. The data presented in Figure 1 demonstrates that approximately 50% of those deliberately ingesting paraquat formulations consumed less than 50mls in volume of paraquat formulation (10g paraquat ion). For some subpopulations this figure is as low as 25mls of paraquat formulation (5g paraquat ion). Based upon this data, the greater than 10 fold reduction in toxicity in the dog and the perceived benefits that the INTEON formulation can bring to the marketplace, Syngenta believes that the INTEON formulations will have a significant improvement on survival in humans (deliberately or accidentally) ingesting paraquat formulations at the volumes of ingestion documented and presented.

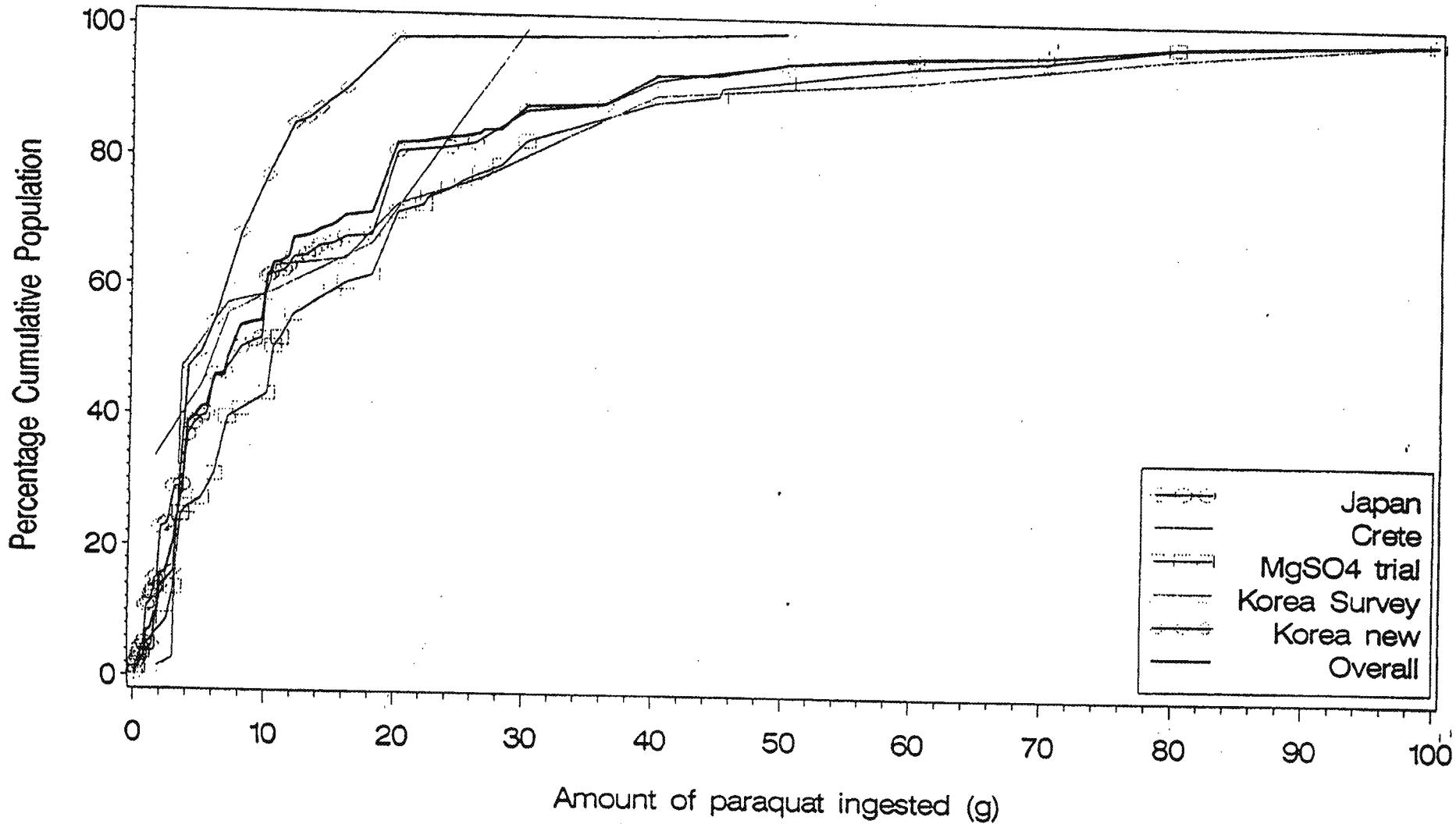
Table 1

Estimates of median amount of paraquat ion ingested and resulting survival rates for different sub-populations

Source	Years	No of cases	Survival rate	Median amount (g) paraquat ion ingested (mls of Gramoxone formulation)
ICI Japan	1979-1985	209	25%	9.6 (~48.0)
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a data only reported fatalities, not used in subsequent analysis

Figure 1. Cumulative population data for human poisonings from paraquat ingestion.



Ingestion Incidents in the United States

Over the last five years, Syngenta has received approximately one to five reports of intentional or accidental ingestions of paraquat-containing formulations per year in the United States. On average, approximately two to four people per year are involved in lethal or life-threatening incidents in the United States as a result of accidental or intentional ingestion of paraquat-containing herbicides. The majority of the intentional ingestion incidents were self-harm attempts, and the majority of accidental ingestion incidents involved illegal removal and storage in soda or sport's drink containers that were subsequently and accidentally consumed.

Similar to the rest of the world, poison control centers or hospitals in the United States rarely obtain a detailed or accurate description of the quantity of paraquat or end-use formulation consumed. However, based on Syngenta's experience in the United States over the last five years, there appears to be a general trend:

- **Accidental Ingestions:** Individuals who accidentally drink paraquat-containing formulations tend to consume only one swallow of the liquid formulation (e.g., Gramoxone), which is often rapidly vomited out. The amount of one swallow can be debated, however it is likely to be in the range of < 0.5 to 2 ounces (< 15 - 60 ml) of liquid. Due to the liquid nature of the formulation, complete emesis is unlikely to be achieved (due to incompleteness of regurgitation from the small intestines), and the ingestion of this volume of Gramoxone Max formulation can be lethal, even though rapid emesis occurred.
- **Intentional Ingestions:** There is large variability and uncertainty regarding the volumes consumed during intentional ingestions incidents. Furthermore, the reliability of the reported volumes is questionable due to the poor quality of investigation or minimal fact-gathering activities. Nevertheless, based on our experience, most intentional ingestion cases involve the ingestion of relatively small volumes of Gramoxone (e.g., < 2 to 4 ounces). In some rarer instances, however, large amounts (e.g., < 8 to 24 ounces) appear to have been consumed.

The Value of the Emetic in Paraquat formulations

As part of a series of continuing stewardship measures to address accidental ingestion of paraquat, mainly as a result of grossly negligent practices such as decanting into drinks bottles, Syngenta (formerly ICI) introduced a potent emetic, the phosphodiesterase inhibitor PP796, into all its paraquat formulations, along with a dye (blue green colour) and olfactory alert. This is now recommended in the FAO specification (2003) for all paraquat formulations.

Paraquat is rapidly absorbed from the gastrointestinal tract resulting in peak plasma paraquat levels 1-2 hours after ingestion. The main site of absorption is the jejunum (Heylings 1990) and if emesis occurs within 30 minutes, it was originally proposed that this may limit the amount of paraquat absorbed, and thus improve survival. Since the incorporation of the emetic, dye and alerting agent, survival data collected confirms this theory.

Between 1980 and 1988 the London Centre of the National Poisons Information Service collected data on all reported cases of paraquat ingestion and compared the outcome of cases

involving the 'old', formulation without emetic, with the 'new', formulation with emetic. (Bramley and Hart, 1983; Denduyts-Whitehead et al 1985; Onyon and Volans, 1987). It could be conclusively demonstrated that the formulation with emetic induced earlier vomiting, and the difference between the number of patients in each group (emetic vs. non-emetic) who vomited either before or after 30 minutes (or not at all) was highly statistically significant (Meredith and Vale 1995). Furthermore, it was possible to show that following ingestion of the formulation with emetic, vomiting was more likely to occur as the quantity of paraquat ingested increased demonstrating the positive effect of the emetic.

A detailed scientific review by Garnier et al (2003) concluded that poisoning as a result of accidental ingestion of paraquat was now rare in Europe because of improved farmer training and the addition of alerting agents and emetic to commercial products. A 20 year survey from the National Poisons Information Centre (London) noted in 2001 that most of the cases of poisonings from mistaken ingestion of paraquat occurred in the early 1980s, at the start of the study, with the last one recorded in 1992, confirming the virtual disappearance of fatalities due to accidental ingestion since their peak in the early 1970's (Northall and Wilks, 2001). There are no comparative statistics available for developing countries, but it is believed that the introduction of safety and alerting agents (colour and stench) and emetic have made significant contributions to the reduction in instances of mistaken ingestion (Sabapathy, 1995).

With new formulations based upon INTEON technology and acid triggered gelling there is an opportunity for more productive emesis prior to passage of paraquat into the small intestines. Limiting the passage of paraquat into the small intestines, the primary site of absorption, is expected to significantly reduce paraquat absorption and consequentially improve the survival rate of humans who ingest paraquat (accidental or intentional). Previous research studies in the dog showed that early emesis was achieved with liquid formulation and dosing the emetic in combination with paraquat dichloride or paraquat formulations shortened the time to emesis (Figure 2). However despite shortening the time to emesis it resulted in higher paraquat exposure with increasing paraquat doses due to passage of the formulation into the small intestines. The threshold for emesis within 30mins with liquid formulations was between 0.02 and 0.19mg PP796/kg. With the INTEON triggered gel formulations emesis does not occur as quickly but is more productive as demonstrated by the reduced paraquat absorption across a large dose range (16 fold). The threshold dose for emesis within 30 mins with INTEON formulations is approximately 0.2mg PPR796/kg (Figure 2).

From data reported by Meredith and Vale 1987, showed that an increased incidence of emesis within 30mins occurred following the inclusion of the emetic in the formulation and this was dependent on dose. All those ingesting 25mls (5g paraquat ion) or greater vomited within 30mins, this equates to a dose of 0.205mg PP796/kg (Figure 3).

In conclusion, Syngenta believes that the inclusion of increased emetic (PP796) and acid triggered gels will have a beneficial effect by causing a more productive expulsion of paraquat following oral ingestion, thus reducing the amount of paraquat absorbed systemically. The results of the detailed scientific review of Garnier et al (2003) are consistent with the current formulations, which include emetic, resulting in very low incidences of fatalities following accidental ingestions.

MJLC 15th August 2005

Figure 2 Time to emesis vs. dose of emetic in the dog for liquid and acid triggered gel .. INTEON formulations

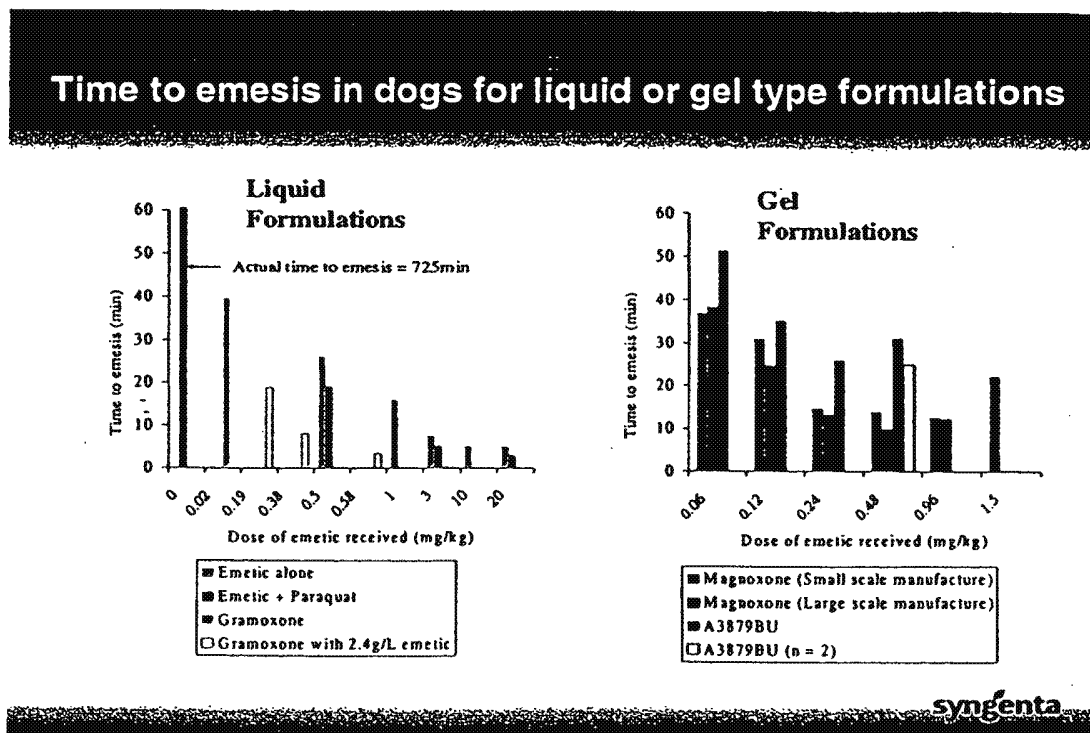
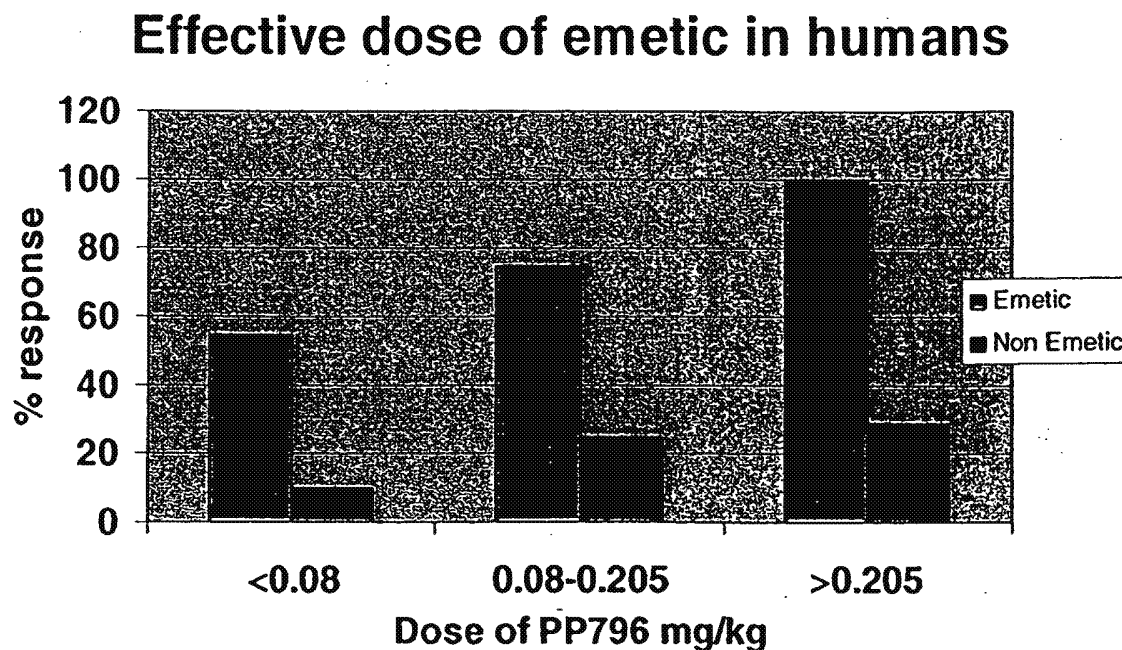


Figure 3 Incidence of spontaneous vomiting within 30minutes of ingestion of an emeticised or non emeticised formulation of the paraquat formulation, Gramoxone



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ATTACHMENT B:

**A REVIEW OF GLOBAL PARAQUAT
INCIDENCE DATA**

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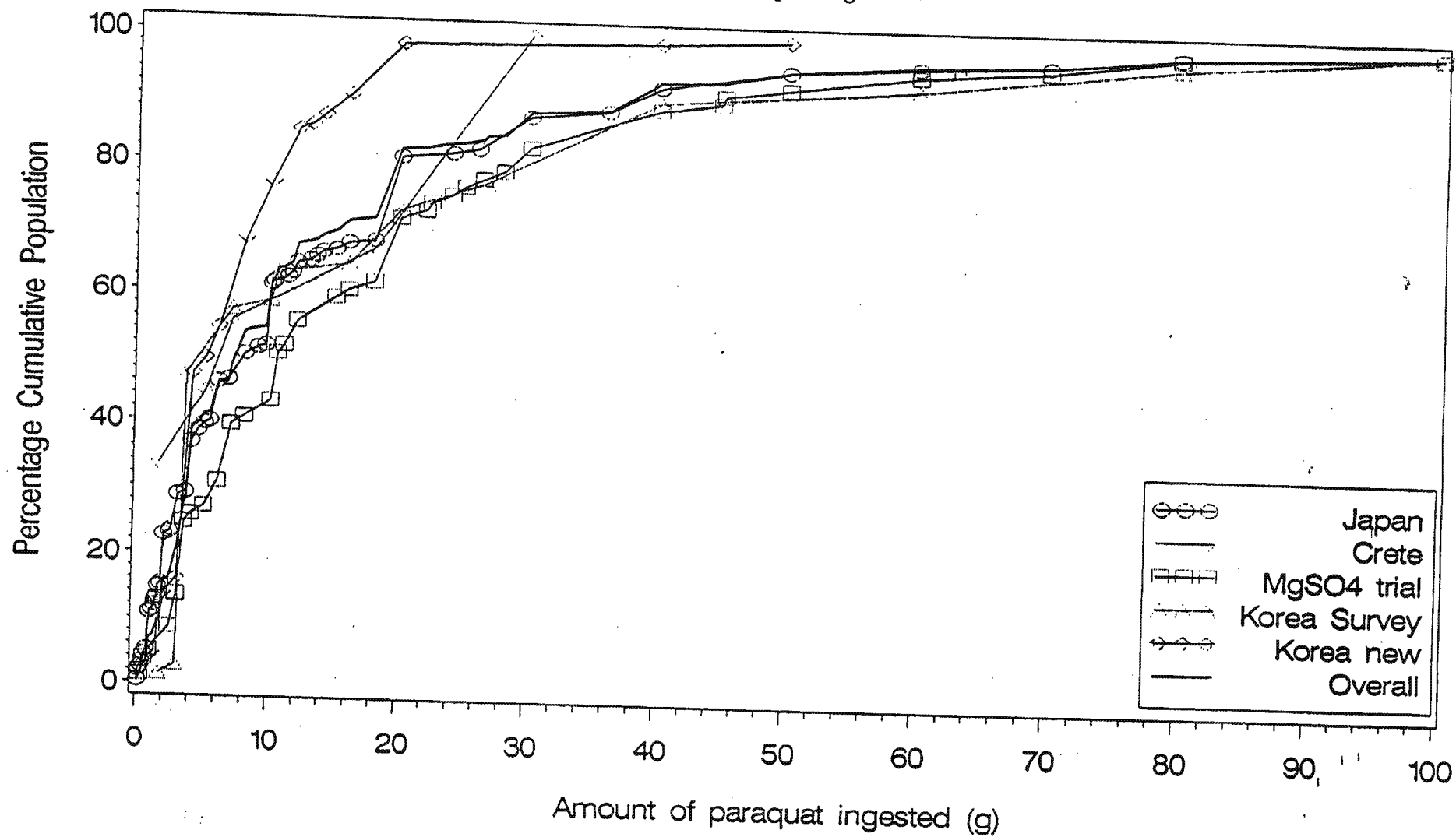
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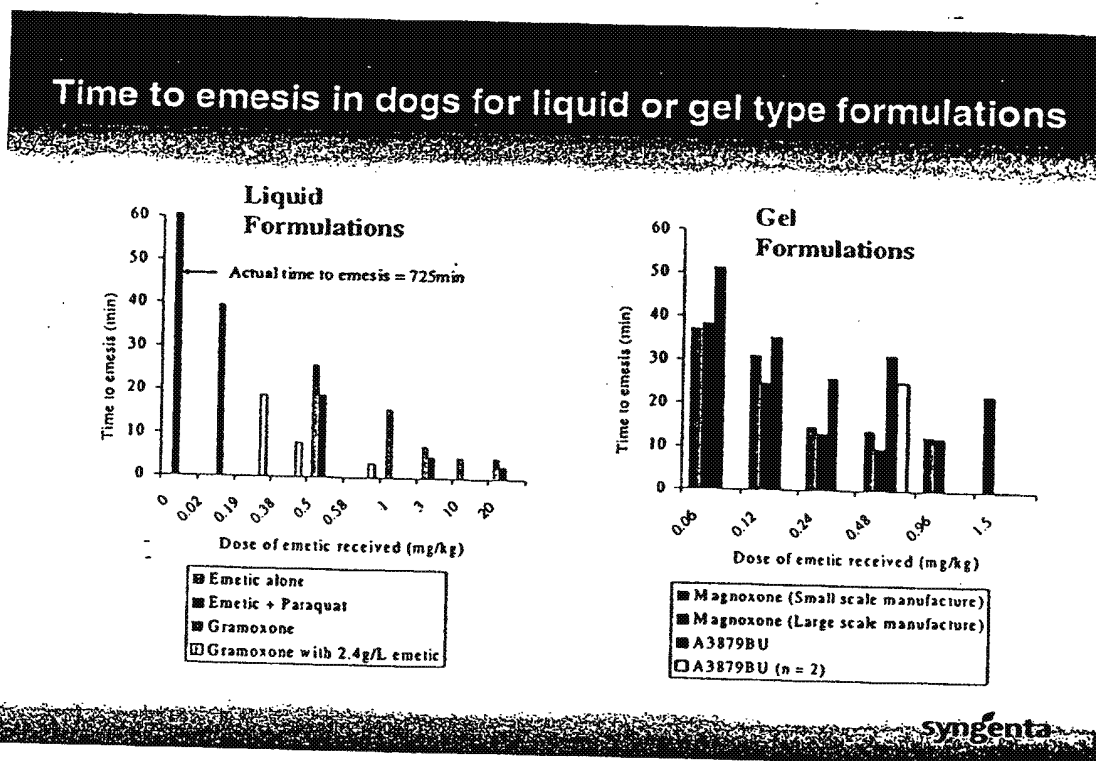
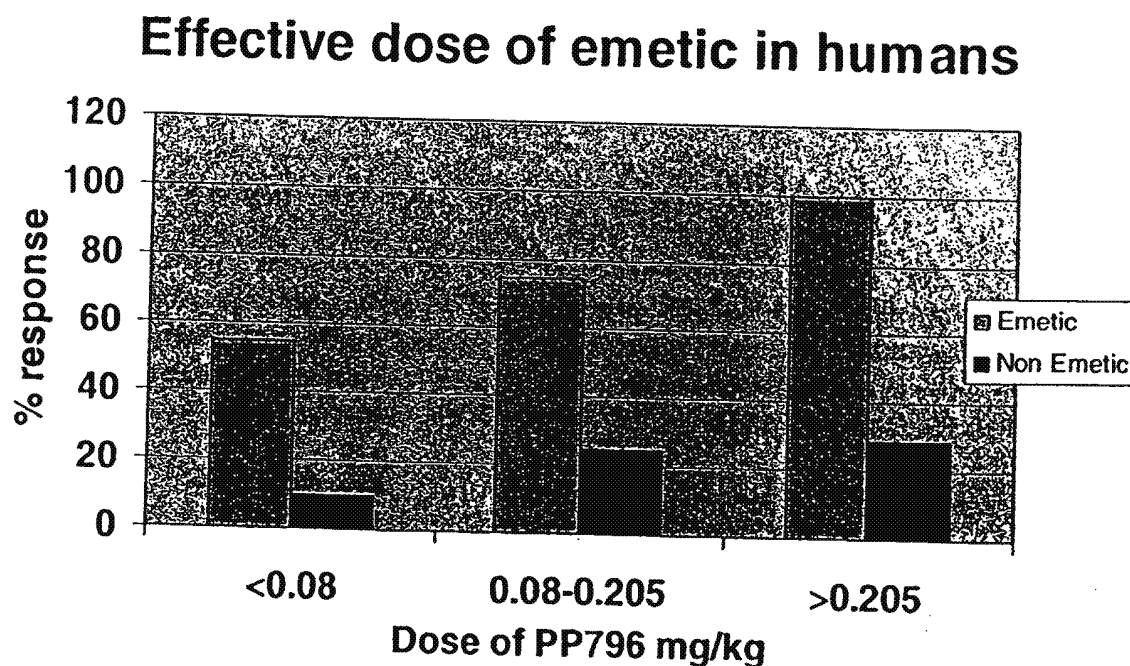


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ATTACHMENT C:

DECLARATION OF SIR COLIN BERRY

1/16/06

Declaration of Sir Colin Berry

- I, Sir Colin Berry, declare under penalty of perjury that the following is true and correct
1. I am Professor Emeritus of Pathology at Queen Mary, London. I am presently in active pathology practice and act as consultant in toxicology for regulatory agencies, pharmaceutical and agrochemical companies and for groups with environmental concerns. I serve on the advisory boards of "Sense about Science", the Scientific Alliance and am a consultant at the Science Media Center of the Royal Institution.
 2. I was a member of the UK regulatory body for Pesticides for more than 20 years in various capacities; serving as Chairman of the Advisory Committee on Pesticides for 10 years – reporting to six government departments. I have also been Chairman of the Committee of Dental and Surgical Materials and served on the Committee of Safety of Medicines. In these capacities I have taken part in a number of reviews of many compounds, including UK, EU and WHO related reviews of Paraquat. My present publications relate mainly to risk evaluation and assessment and I have recently addressed the Parliamentary and Scientific Committee on related issues.
 3. CV attached
 4. I have been asked to provide my opinion as an expert in toxicology and pesticide testing on the reliability of Syngenta data for predicting human responses to ingestion of Syngenta's Inteon formulation.
 5. This Declaration explains the biochemical mechanism of the Inteon formulation in the digestive tracks of mammals, the results of tests of Inteon when ingested by dogs, and the science supporting the application of these data to assessing the consequences of Inteon ingestion by humans.

Biochemical Mechanism of Inteon

6. The main site of absorption of paraquat is the small intestine, particularly the jejunum (the central section of the small intestine), with limited absorption from either the oesophagus or stomach (Heylings, 1991). The oral toxicity of paraquat may therefore be reduced by limiting the exposure of the small intestine to ingested paraquat material.
7. The key to Inteon's safety mechanism is the formation of an alginate gel in the stomach that helps prevent the release of any paraquat into the small intestine. Alginates are non-toxic carbohydrates of polymannuronic and polyguluronic acid and are commonly used in the food industry as gelling agents. They are also used therapeutically, for example in treating dyspepsia (Mandel *et al*, 2000) and wound healing (Agren, 1996). An alginate that gels under low pH conditions (pH 1-3) was selected for Inteon, as the material remains liquid and flowable as a formulation, but if it is swallowed and reaches the acidic conditions of the stomach, it forms a semi-solid gel. This change holds the material in the stomach, and allows emesis (vomiting) to be more effective in removing the semi-solid material than it would be in removing a liquid. Inteon also contains an emetic agent that induces vomiting following ingestion.

8. The gelling process reduces the amount of paraquat that might be released to the small intestine.

Results of Toxicity Study on Inteon Formulation in Dogs

9. Inteon formulations have been shown to reduce the systemic absorption of paraquat in the dog, resulting in a greater than ten-fold reduction in oral toxicity when compared with non-Inteon paraquat formulations (Brammer et al. 2004).

Extrapolation from dogs to humans

10. The choice of the dog in Syngenta's experiments depends on this species having the necessary digestive attributes, including a vomit reflex. The vomit reflex is controlled centrally by the vomit centre in the brain, responding to changes in cAMP (a molecule that regulates several biological processes) – which is the same in dog and man. This is significant because phosphodiesterase inhibitors, like Syngenta's emetic agent (PP796), work through a cAMP-regulated process. It is worth noting that other species such as the rat were deemed inappropriate since rats do not vomit.
11. The toxicokinetics processes for paraquat (and many drugs and other chemicals) are similar in dog and humans. Dogs, like humans are omnivores and intermittent feeders. The physiology of digestion in both species is also very similar.

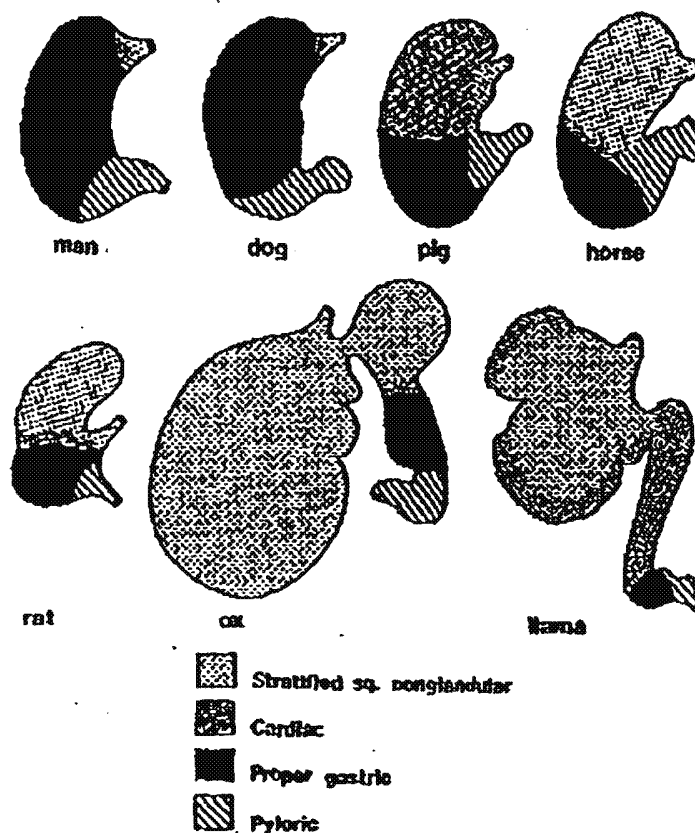
Reactions to paraquat in dog and human

12. Data in man indicates that the plasma paraquat kinetic profile and area under the curve (AUC) at a minimally toxic dose is similar between dog and man. Across species there are differences in the acute oral lethal dose which is thought to be due to differences in the amount of paraquat absorbed from the gastrointestinal tract. Analysis of the 0-24h AUC across these species shows similar paraquat systemic exposure at a peri-lethal oral dose (Heylings, 1994).

Comparable gastrointestinal tract characteristics

13. It was concluded by Kararli (1995) that current data indicated that no single animal can mimic the gastrointestinal tract characteristics in humans. However, in considering stomach morphology and emptying characteristics, the dog and human were found to be very similar. The Inteon technology is predominantly focused on the interactions within the stomach in order to prevent the ingested dose from reaching the intestine. The stomach size, volume and pH are similar between dog and man.

Figure 1. Variations in the type and distribution of gastric lining tissue in different mammals. The dog and human are closest in structure of stomach tissue. (Stomachs are not drawn to scale).



Humans have a highly regulated gastrointestinal physiology. The human digestive system is sensitive to a variety of potentially ingested toxins and is particularly sensitive to topical irritants of the gastric mucosa (lining tissue), some bacterial and viral toxins, and foods and drinks that have a high salinity. Vomiting can be initiated centrally or locally.

14. Local irritation by compounds (such as alcohol or paraquat) is a slow and inefficient emetic stimulus, while centrally acting emesis (mediated via the hypothalamus) is very efficient in all higher mammals. The vomit centre, once triggered, causes a complete closure of the pyloric sphincter, followed by gastric muscle contraction from the pylorus upwards through the fundus. Following relaxation of the oesophageal sphincter, the pressure effect expels the gastric contents very effectively. There is no anatomical or physiological reason why human vomiting should be less effective than that seen in dogs.

Emesis in dogs and humans

15. The efficiency of emesis (vomiting) generally depends on the dose of the emetic and the physical constitution of the stomach contents. When ingested, the Inteon product gels and stays in the stomach while the human receives a dose of the emetic (PP796) that causes prompt emesis, coupled with closure of the pylorus. Human vomiting will be as productive as vomiting by the dog. From analysis of poisoning data reported by Meredith and Vale (1987), the threshold dose of the PP796 emetic required to produce emesis in 100 percent of human patients within 30 minutes was greater than or equal to 0.2mg/kg. It is important to note that this is also the threshold dose in the administration of Inteon formulations in the dog (Brammer et al 2004).

Conclusion

16. The similarities between the human and dog gastrointestinal systems, including similar stomach emptying and emesis processes, allow for valid extrapolation from dog toxicokinetics studies to reach a determination of human responses to ingestion of Inteon formulation.

References

1. Heylings JR (1991). Gastrointestinal absorption of paraquat across the isolated mucosa of the rat. *Toxicol. Appl. Pharmacol.* 107, 482-493.
2. Mandel KG, Daggy BP, Brodic DA, Jacoby HI (2000). Alginate-raft formulations in the treatment of heartburn and acid reflux. *Aliment Pharmacol Ther.* 14(6):669-90
3. Agren MS (1996). Four alginate dressings in the treatment of partial thickness wounds: A comparative experimental study. *J. Plast. Surg.* 49:129-1:34.
4. Schiller LR (1999). Clinical pharmacology and use of laxatives and lavage solutions. *J. Clin. Gastroenterol.* 28(1):1-8
5. Brammer A, Heylings JR and Swain C (2004). Paraquat 240 g/L SL formulation (A7813K): Toxicokinetic study in the dog. Syngenta Report No: CTL/XD7355/REGULATORY/REPORT. (MRID 46364510, Submission Date: Sept. 16, 2004.)
6. Meredith and Vale, JA (1995). Treatment of paraquat poisoning: gastrointestinal decontamination. In *Paraquat Poisoning: Mechanisms, Prevention, Treatment*, Ed Bismuth, C. and Hall, A.H., Marcel Dekker, New York, pp. 297-314.
7. Karali (1995). Comparison of the gastrointestinal anatomy, physiology, and biochemistry of humans and commonly used laboratory animals. *Biopharmaceutics & Drug Disposition* 16 351-380.

January 16th, 2006


Sir Colin Berry

NOTE Missing reference to be added

References

1. Heylings JR (1991). Gastrointestinal absorption of paraquat across the isolated mucosa of the rat. *Toxicol. Appl. Pharmacol.* 107, 482-493.
2. Mandel KG, Daggy BP, Brodie DA, Jacoby HI (2000). Alginate-raft formulations in the treatment of heartburn and acid reflux. *Aliment Pharmacol Ther.* 14(6):669-90
3. Agren MS (1996). Four alginate dressings in the treatment of partial thickness wounds: A comparative experimental study. *J. Plast. Surg.* 49:129-134.
4. Schiller LR (1999). Clinical pharmacology and use of laxatives and lavage solutions. *J. Clin. Gastroenterol.* 28(1):1-8
5. Brammer A, Heylings JR and Swain C (2004). Paraquat 240 g/l SL formulation (A7813K): Toxicokinetic study in the dog. Syngenta Report No: CTL/XD7355/REGULATORY/REPORT. (MRID 46364510, Submission Date: Sept 16, 2004.)
6. Meredith and Vale, JA (1995). Treatment of paraquat poisoning: gastrointestinal decontamination. In *Paraquat Poisoning: Mechanisms, Prevention, Treatment*, Ed Bismuth, C. and Hall, A.H., Marcel Dekker, New York, pp. 297-314.
7. Kararli (1995). Comparison of the gastrointestinal anatomy, physiology, and biochemistry of humans and commonly used laboratory animals. *Biopharmaceutics & Drug Disposition* 16 351-380.
8. Heylings (1994) Paraquat: Acute Oral Toxicity - A species comparison. Syngenta Report No CTL/R/1175.

January 16th, 2006

Sir Colin Berry



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

June 26, 2006

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SYNGENTA CROP PROTECTION, INC.
ATTN: REGULATORY AFFAIRS
PO Box 18300
GREENSBORO, NC 27419-8300

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 20-JUN-06. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

JUL 06 2006

Rt

Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419-8300
www.syngenta.com



FEDERAL EXPRESS

June 19, 2006

Mr. Jim Tompkins, PM 25
Document Processing Desk
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

**SUBJECT: SUBMISSION OF ADDITIONAL INFORMATION RELATED TO SAFETY
IMPROVEMENT OF GRAMOXONE INTEON, EPA REG. NO. 100-1217**

Dear Mr. Tompkins:

Syngenta Crop Protection is herein submitting additional information related to the safety improvement of Gramoxone Inteon. This information was presented at a meeting with USEPA on April 24, 2006. Included are:

- 1) Attachment A: *Gramoxone Inteon and Improved Safety*, a document reviewing the information presented at the meeting by Dr. Mike Clapp,
- 2) Attachment B: A review of global paraquat incidence data,
- 3) Attachment C: *Declaration of Sir Colin Berry*
- 4) A study, not previously submitted; "*Gramoxone Effects of Increased Emetic Levels on Toxicokinetics in the Dog*" which is listed on the attached Transmittal Document.

This information is submitted for informational purposes. The submission is outside the scope of PRIA. If you have any questions regarding this submission please contact me at 336-632-6324.

Kind Regards,

A handwritten signature in cursive script that reads "Jerry Wells".

Jerry Wells
Senior Regulatory Product Manager

VOLUME 1 OF 2 OF SUBMISSION
(TRANSMITTAL DOCUMENT)

1. Name and Address of Submitter

Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419

2. Regulatory Action in Support of which this Package is Submitted

SUBMISSION OF ADDITIONAL INFORMATION RELATED TO SAFETY
IMPROVEMENT OF GRAMOXONE INTEON, EPA REG. NO. 100-1217

3. Transmittal Date

6/19/2006

4. List of Submitted Studies

MRID NUMBER	VOLUME NUMBER	STUDY TITLE	EPA GUIDELINE NUMBER
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1 OF 2

Transmittal document

NA

46865501

2 OF 2

Effects of Increased Emetic Levels on
Toxicokinetics in the Dog;(XD1328,
026698-RES,T003396-06),
(09003aeb801feed9),(445557)

NA

*Entered 7/12/06
t*

COMPANY OFFICIAL: JERRY WELLS
(NAME)

Jerry Wells
(SIGNATURE)

COMPANY NAME: SYNGENTA CROP PROTECTION, INC.

COMPANY CONTACT: JERRY WELLS 336-632-6324
(NAME) (PHONE)



Syngenta Crop Protection, Inc.
P.O. Box 18300
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July 14, 2006

Document Processing Desk
Office of Pesticide Programs (H7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Jim Tompkins, Team 25

SUBJECT: Syngenta Crop Protection, Inc., Additional Data and Information Relevant to Memorandum from Nicole Zinn, Biological Analysis Branch, EPA and Jin Kim, Biological and Economic Analysis Branch, EPA to Hope Johnson, Registration Division, EPA, Paraquat Assessment, D323223, dated 12-7-05.

Dear Mr. Tompkins:

Syngenta is submitting new data and information validating the improvement in human safety of the Inteon formulation of paraquat. These data provide an important addition to the factual record necessary regarding BEAD's analysis of the benefits and risks of the new paraquat safety standard set by the Inteon formulation. Syngenta requests that this new data and information be evaluated and acknowledged in a follow up to the Dec. 7, 2005 BEAD assessment. Attached to this letter for the Agency's review are three documents:

- (A) An abstract summarizing findings following intensive observational monitoring in Sri Lanka before and after the introduction of an Inteon formulation. The abstract was prepared for a presentation in August 2006 and the results indicate a statistically significant improvement in oral toxicity in humans following ingestion of paraquat formulated with the Inteon[®] technology compared to a non-Inteon formulation available in Sri Lanka before the introduction of the Inteon formulation;
- (B) A treating physician's case report of a person in the United States who survived the intentional ingestion of a large amount of Gramoxone Inteon; and
- (C) Descriptions of fatal incidents involving unintentional human ingestion of the non-Inteon formulation from 2000 to 2005 that were reported to the poison control center, PROSAR.

Syngenta will submit within the next few weeks comprehensive comments on the December BEAD analysis, including additional factual information that is critical to BEAD's assessment of the risks and benefits of Inteon.

The following new data and information provided with this letter provide BEAD with important new and more complete information to undertake this analysis with a much higher level of reliability.

(A) Large scale monitoring data on the reduced oral toxicity of Inteon in humans following ingestion are now available. An observational monitoring program underway before and after the introduction of an Inteon formulation in Sri Lanka shows a significant improvement in survivability following ingestion of Inteon compared to the non-Inteon formulation. The results of this intensive monitoring program will be presented in a scientific paper at the Asia Pacific Association of Medical Toxicologists' Congress (to be held in Sri Lanka from 6 - 8 August, 2006). The submitted abstract is now available and is attached (Attachment A). The monitoring program demonstrates a statistically significant improvement in survivability following ingestion (primarily intentional ingestion at higher volumes) of Gramoxone Inteon vs. non-Inteon paraquat. Of note, the Inteon formulation available in Sri Lanka was found to have a separation problem after introduction compromising the full potential for improvement in safety. The separation was caused by addition of wetters (adjuvants) to the Sri Lankan formulation. The U.S. formulation does not contain wetters, and, therefore, offers even greater promise for improving survivability following ingestion.

(B) A recent paraquat ingestion incident in the United States followed up with physician monitoring and reporting also validates the improved toxicity of Inteon. As explained in the enclosed case report from Fermin Barrueto, Jr., M.D. (Attachment B), an individual intentionally drank a large volume (approximately 4 ounces) of Gramoxone Inteon, the new formulation registered in the U.S. The individual was treated and survived. The patient would have most likely died if a non-Inteon formulation were ingested, since 4 ounces of formulation is greater than 10 times the typical lethal dose of a non-Inteon paraquat containing formulation. There was also an incident reported last month [submitted to U.S. EPA under FIFRA § 6(a)(2)] where an individual intentionally drank a large volume (exact amount unknown) of non-Inteon Gramoxone in Canada. The individual died on the same day of ingestion.

(C) Paraquat incident data collected from the poison control center PROSAR is more up-to-date than the data analyzed by BEAD and indicates a significantly higher number of fatal outcomes resulting from unintentional ingestion of the non-Inteon formulation. It should be noted that all of these incidents involved the non-Inteon formulation of paraquat, which is no longer being produced or sold by Syngenta in the U.S. In the benefits section of the assessment, BEAD presented a quantitative valuation of the cases of unintentional deaths and illness that may be potentially avoided as a result of paraquat reformulation. BEAD obtained the incident data from a variety of sources (e.g., TESS database), adjusting these numbers for potential under-reporting and area coverage, and provided the estimated number of cases. Based on their analysis, BEAD estimated the total number of fatal unintentional cases to be 2.4 per year; they indicated that 6 deaths were reported over an 11-year period.

An analysis of PROSAR data for the 6 year period 2000 - 2005 revealed 29 actual cases of paraquat poisoning in the US. Eleven (38%) of these were classified as deliberate (intentional) and 18 (62%) as accidental. The accidental cases included people ingesting material decanted into drink bottles, a man denying a suicide attempt, someone ingesting what he thought was tobacco spit, a doctor suspecting paraquat poisoning without confirming paraquat exposure and a 15 month old child drinking from a container in the back of a car. In 2 accidental cases there was

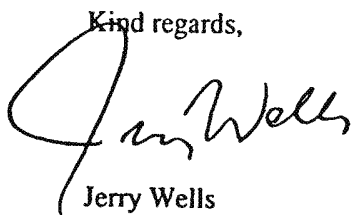
predominantly topical exposure. Very often the information obtained was from a third party and not the patient themselves and therefore, factual information is limited and in many cases detailed hospital records were not available. Ten of eleven people who intentionally ingested non-Inteon paraquat (91%) died and 8 of the 16 people who accidentally ingested non-Inteon paraquat (50%) died as a result (see Attachment C).

Based on Syngenta's analysis of the PROSAR data, there were 8 cases of unintentional ingestions resulting in death since the formation of Syngenta (2000-2005) calculating to an average of 1.3 deaths per year over this 6 year period. This figure is more indicative of the recent trend and significantly higher than the 0.6 deaths per year (1993-2003) used by BEAD in their assessment. Using this higher number of deaths and the BEAD analysis methodology taking into account potential under-reporting and coverage, the estimated number of unintentional deaths per year would be calculated to be 5.9 $[(8 \text{ deaths}/0.911)*4]/6 \text{ years}$. The Total Value in Table 7 of BEAD's assessment would then be \$37,878,000 (value of a statistical life of \$6,420,000 X 5.9 deaths per year).

Syngenta requests that the Agency evaluate this important new data and information and acknowledge in a follow up document to the BEAD analysis that 1) there is now scientific evidence available that the Inteon technology has been shown to reduce oral toxicity to humans and 2) to revise the upper benefit from \$15,443,322 to \$37,878,000. As noted above, the benefits of Gramoxone Inteon should also include the prevention of deaths in some portion of the intentional ingestions. Therefore, the benefits even after the adjustment suggested above are still likely significantly understated as BEAD's analysis only included unintentional incidents.

Thank you for your consideration of this new and important data and information. If you have any questions concerning the data and information please contact me at 336-632-6324.

Kind regards,



Jerry Wells
Senior Regulatory Product Manager

Attachments

ATTACHMENT A

Improvement in survival following paraquat ingestion after introduction of a new formulation with INTEON® technology in Sri Lanka.

Wilks MF (1), Fernando R (2,10), Ariyananda PL (3), Eddleston M (4,10), Berry DJ (5), Tomenson JA (6), Buckley NA (7,10), Jayamanne S (8,10), Gunnell D (9), Dawson A (10). 1. Syngenta Crop Protection AG, Basel, Switzerland; 2. Department of Forensic Medicine and Toxicology, University of Colombo and National Poisons Information Centre, Sri Lanka; 3. Faculty of Medicine, University of Ruhuna, Sri Lanka; 4. Centre for Tropical Medicine, University of Oxford, UK; 5. Syngenta, Alderley Park, Macclesfield, UK; 6. Causation Limited, Macclesfield, UK; 7. Australian National University Medical School, Canberra, Australia; 8. Polonnaruwa Base Hospital, Sri Lanka; 9. Department of Social Medicine, University of Bristol, UK; 10. South Asian Clinical Toxicology Research Collaboration (SACTRC)

Objective: To compare the outcome of poisoning cases following the introduction of a new paraquat formulation, developed to have reduced oral toxicity, with the standard formulation of paraquat. **Methods:** Cases of paraquat poisoning presenting to nine base and general/teaching hospitals across Sri Lanka over a 26 month period were included. The survey protocol was approved by three Ethical Committees covering all hospitals and an independent Scientific Advisory Panel was established to oversee data collection and analysis. Informed consent was obtained from patients presenting following paraquat ingestion (or from their relatives), and a questionnaire was used to collect details of the circumstances of ingestion, treatment and outcome. Plasma and/or urine samples were obtained to identify which formulation had been ingested. Patients discharged from hospital were followed up after 3 months to ascertain survival. Starting in December 2003, data were collected over a 26 month period. During the first 10 months the only product containing paraquat available for sale in Sri Lanka was a standard 200g/l formulation. In October 2004, a novel 200g/l formulation with INTEON® technology (containing an alginate that converts to a gel under stomach acid conditions, increased levels of emetic, and a purgative) designed to reduce the amount of paraquat available for absorption was introduced. Problems were experienced with an apparent phase separation of the INTEON® formulation during the survey period, but it was decided to continue with the survey since it was felt that this was unlikely to influence the study's assessment of the safening potential of INTEON® technology. Survival analyses were performed using both non-parametric analyses (Kaplan-Meier and log rank trend tests) and semi-parametric methods (Cox's proportional hazards (PH) with adjustment for potential confounding factors). **Results:** Data from 586 patients were included in the analysis; 297 cases were recorded prior to October 2004 (standard formulation), and 289 cases had confirmed or probable INTEON® ingestion (195 confirmed by plasma or urine test). The average age of patients was 30 years and the majority were male (79%). Most (94%) were cases of deliberate ingestion. A higher proportion of patients having ingested INTEON® vomited within 15 min (55% vs. 38%), and fewer received gastric lavage (40% vs. 55%). The new formulation improved overall survival ($p=0.005$, log rank test) from 25.6% to 35.3% (difference 9.7%; 95% CI 2.3% - 17.1%). Survival was strongly associated with estimated ingestion volume, and the beneficial effect of INTEON® was apparent across the dose range. Cox PH regression analyses consistently showed a significant, approximately 2-fold reduction in toxicity (i.e. a shift in the dose response by a factor of 2) for INTEON® compared to standard product, suggesting a reduction of paraquat absorption. There was a small overall increase in median time to death from 0.9 days for standard product to 1.5 days for INTEON®, however, this effect was more apparent in those patients who had ingested lower doses (0-30ml) where median time to death increased from 2.8 days (IQR 0.7 - 8.7) to 5.0 days (IQR 2.0 - 9.5) thus raising the possibility of more time being available for treatments to be effective. **Conclusion:** The survey has shown that INTEON® technology significantly improves the survival of patients following paraquat ingestion. Formulation developments have now overcome the phase separation problems and it is expected that this may lead to a further reduction in toxicity.

ATTACHMENT B

(Email from Fermin Barrueto Jr., MD, Assistant Professor – Department of Emergency Medicine, University of Maryland School of Medicine, Medical Toxicologist)

A Severe Paraquat Ingestion that Survived

A 27 year old man, in a suicide attempt, ingested ½ a cup (4 ounces) of Gramoxone® (Syngenta), a 43% solution of paraquat, that was in his landscaping truck. Forty-five minutes after the ingestion, the patient vomited several times and went to the Emergency Department (ED). He complained of burning in his chest and mouth. He was admitted and had an esophagogastroduodenoscopy (EGD) performed which showed gastritis and superficial ulcerations of the esophagus, stomach and proximal duodenum. The patient was discharged after 24 hours of observation and returned to the ED 4 days later with hemoptysis and shortness of breath. He was immediately transferred to a tertiary care facility. He has no past medical or surgical history. He takes no prescription or herbal medications. Social history revealed he drinks alcohol 2-3 days a week and has used marijuana and cocaine in the past. Vital signs at the tertiary care facility were: temperature, 102.3°F; pulse, 108/minute; blood pressure, 132/71 mmHg; respiratory rate 31/minute; pulse oximetry, 90% on room air. This is a well nourished male in moderate respiratory distress. Head and neck exam revealed no oropharyngeal burns or ulcerations. Lung examination revealed diffuse rhonchi and tachypnea but no accessory muscle use. Cardiovascular examination revealed tachycardia but no murmur, rub or gallop. Abdominal examination was benign and neurologic examination revealed an alert and oriented man with no focal deficits.

Laboratory investigation included a comprehensive metabolic panel that revealed: Na⁺, 132 meq/L; K⁺, 3.0 meq/L; Cl⁻, 95 meq/L; CO₂, 22 mmol/L; BUN, 57 mg/dL; Creatinine, 6.0 mg/dL; Ca²⁺, 9.2 mg/dL; Phosphorous, 3.5; Mg²⁺, 2.0 mg/dL; SGOT, 24 U/l; SGPT, 78 U/l; total bilirubin, 0.6 mg/dL. Complete blood cell count revealed WBC, 18.0 K/mcL; hemoglobin, 11.7 g/dL; hematocrit, 33.5; platelets, 162 K/mcL. A chest radiograph showed diffuse patchy infiltrates bilaterally, worse on the right than left. An arterial blood gas on room air revealed: pH, 7.47; PCO₂ 36 mmHg, PO₂ 56 mmHg; HCO₃, 25 mmol/L. A serum paraquat concentration performed by National Medical Services, Inc. four days after the ingestion was 0.08 mcg/mL (normal limit < 0.06 mcg/mL) by spectrophotometry (SP). A urine paraquat concentration also 4 days post-ingestion and by SP was 0.76 mcg/mL (asymptomatic sprayers up to 0.3 mcg/mL, urine).

Upon arrival to the tertiary care center, the patient was started on methylprednisolone, 1 g IV every day for 3 days and dexamethasone, 6 mg IV every 6 hours. He was also started on a cycle of cyclophosphamide, 1.7 g IV every day for 2 consecutive days. An infusion of acetylcysteine (Acetadote®) at a rate of 685 mg/hr was administered for 7 days as well as vitamin C and vitamin E supplementation throughout the hospitalization. He required continuous veno-venous hemodialysis for 3 days followed by intermittent hemodialysis for 3 more days until his creatinine normalized to 1.4 mg/dL on HD #6 and did not require any further hemodialysis. The patient's respiratory status worsened requiring oxygen supplementation and at 2 L nasal cannula had a resting pulse oximetry of 80%. On hospital day #8, as he was moving himself to the lavatory, his pulse oximetry decreased to 70% which prompted a computed tomographic scan of the chest which revealed diffuse pulmonary fibrosis with a ground glass appearance and pneumomediastinum. An esophagram was performed and revealed no signs of perforation. Rapamycin therapy was initiated to limit any further pulmonary fibrosis on HD #12 and continued for 15 days. The patient became neutropenic with a WBC of 0.2 K/mcL prompting treatment with neupogen causing the WBC to peak at 29.6 K/mcL but returned to normal limits at 10.2 K/mcL. During his neutropenia secondary to the cyclophosphamide, the patient was covered empirically with piperacillin/tazobactam and vancomycin despite never mounting a fever or identifying a source of infection. On HD #14, the patient developed an iliofemoral deep venous thrombosis and had lovenox and coumadin therapy initiated. After HD #39, the patient's resting pulse oximetry was 90% on 2L NC, was able to perform basic activities of daily living and was stable for transfer to the inpatient psychiatric ward.

ATTACHMENT C

Fatal Unintentional Incidents Involving Non-Inteon Paraquat Formulations

September 2005. Apparently a paraquat-containing product was poured into a soft drink bottle and given to a neighbor, and the patient consumed an unknown amount. The family apparently reported the ingestion was accidental, however other reports indicated the product was intentionally ingested along with an organophosphate insecticide. The caller did not know name of two products nor the concentrations or amounts ingested. Paraquat was detected in the patients urine. The patient died as a result of ingesting paraquat.

June 2005. On 06/06/05, Syngenta was notified that a 48 year-old man accidentally consumed the pesticide through misuse of the product on June 3, 2005. The patient initially thought the glass containing paraquat contained tobacco spit, and he did not immediately seek medical attention. He subsequently developed symptoms that were consistent with paraquat ingestion. The patient eventually expired on June 15, 2005.

December 2004. Syngenta was notified that a homeless man moved in with his ex-wife and her new husband and then became ill. He presented to VA hospital on 12/14/04 and was diagnosed with atypical pneumonia and hypoxia. Symptoms did not respond to standard therapy and he had deteriorating condition required intubation. The patient's lung was biopsied and honeycomb effects were noted. Poison Center Toxicologists were involved as of 12/28/05 and suspicion of paraquat ingestion was raised, although no oral or GI lesions or corrosive injuries were present. The patient expired on 12/31/04, and no plasma or urine samples were retained; therefore, paraquat analysis was not possible. It is unclear whether or not the individual was actually exposed to paraquat or how the exposure occurred, if at all.

September 2004. A chemist in the clinical lab at Presbyterian Hospital in Dallas, Texas, called regarding a patient that the treating physician suspected was exposed to Paraquat. The chemist did not have any details of how the patient was exposed; he only knew that it was an adult patient, and the treating physician requested a test for paraquat. Very little information was obtained about this case because the treating physician would not return the calls. Based on the sparse information obtained, it appears that the patient was a cattle rancher, and his family denied that this was a suicide attempt. He presented to emergency room seriously ill and expired in hospital due to pulmonary fibrosis and pulmonary emboli. A specific cause for these complications has not been identified. A 2 1/2 ml sample of post mortem whole blood was submitted for analysis however this may not be a sufficient volume for paraquat analysis. Furthermore, the blood sample was collected post-mortem, and, considering the rapid half-life of paraquat in blood, it is unlikely paraquat concentrations will be below the level of detection.

March 2003. A 49 year-old male apparently worked in the agricultural business and obtained a small volume of the Gramoxone from a farmer to use around his yard at home. He reported that he was cleaning out his garage, found the container containing Gramoxone, and proceeded to pour Gramoxone into a coffee cup; it is not clear why he decanted the Gramoxone. He reported that he mistakenly drank from the cup containing the Gramoxone instead of his coffee, which was apparently nearby. He indicated that he ingested one to two swallows (up to 1/2 cup) and immediately rinsed and spit with water after he discovered his mistake. Within an hour of exposure, he developed abdominal pain and vomiting prompting him to go to the local emergency room.

The patient was treated with activated charcoal and started on IV fluids. He did not receive any supplemental oxygen. Physical exam did not reveal any evidence of corrosive injury to lips or mucosal surfaces in mouth and throat. The patient had multiple episodes of vomiting and initial tests reported serum creatinine of 1.0, BUN of 10, and normal lung function. The following morning kidney function decreased (serum creatinine of 3.0 and BUN of 19) but the Chest XRAY was unremarkable. The patient was in no respiratory distress, but continued to complain of abdominal pain and dizziness. On 03/05/2003, a nurse indicated that the patient's kidney function continued to decline. On 3/12/03, it was reported that the patient died.

ATTACHMENT C (Cont.)

November 2002. Reportedly, an individual purchased two 20-ounce bottles (plastic bottles with screw-caps) of Pepsi from a local convenience store, and she placed them in her refrigerator at her residence. Her brother opened one of the two bottles, and took one sip (exact amount ingested unknown). He immediately noted that it didn't taste like Pepsi. The patient had several subsequent bouts of vomiting and was taken to Appalachian Medical Center that evening or the following morning. He was in "critical condition" in the emergency room until he died.

FDA criminal investigator shared a few of the facts of the incident. It appears that the Pepsi bottles containing the paraquat were not purchased at the local convenience store as previously suggested. Apparently, the nephew of the patient owned a local farm, which is located near the convenience store where the Pepsi's were allegedly purchased. One of the farm hands at the nephew's farm apparently reported that he filled two Pepsi bottles with Gramoxone Max and gave them to the patient's brother-in-law. It is surmised that the brother-in-law brought the Pepsi bottles home where the patient accidentally ingested the product. FDA classified the incident as an isolated event involving the use of an inappropriate container for storing an herbicide.

October 2002. A 66 year-old female operated her own greenhouse, and a neighbor needed help with weed control. She retrieved an old container of paraquat (29.9% Ortho Paraquat) from storage and put on her counter to give to the neighbor the next day. During the night the patient allegedly woke up to get some cough medicine, which was next to product. On 10/02/02 (1 a.m.), the patient allegedly drank a couple sips of paraquat by accident as she reached for her coffee. She was seen at the emergency room approximately 20 hours after ingesting the product. The treating physician reported that she had oral and esophageal burns, had WBC of 20,000, was hypokalemic, in renal failure and acidotic. The patient died on 10/04/02.

April 2000. On 04/10/00, a paraquat-containing herbicide was stolen from the workplace, decanted into a sports drink container, and placed in the back seat of a car. A 15 month-old child picked up the container and ingested an unknown quantity. The child was put in the intensive care unit and had evidence of oral ulcerations. The child died after 11 days in the hospital.

McDonald Mary USGR

Subject: FW: Agenda/Draft Study Protocol-Meeting on August 30th

Attachments: Agenda EPA Mtg Aug 30, 2006.doc; Example Paraquat PK Protocol in Dogs.pdf

From: Abbott John USGR
Sent: Friday, August 25, 2006 3:52 PM
To: tompkins.jim@epa.gov; kenny.dan@epa.gov; scarano.louis@epa.gov; herndon.george@epa.gov; protzel.alberto@epa.gov; Johnson.Hope@epamail.epa.gov
Cc: Elliott Barry GBAP; Pastoor Tim USGR; Akins Jonathan USGR
Subject: Agenda/Draft Study Protocol-Meeting on August 30th

To all,

On behalf of Syngenta, I want to thank you for your willingness to meet with us, particularly with your busy schedules and the short notice. In Hope Johnson's absence today (thanks for your coordination), she asked that I send these documents to you directly. Attached below is the proposed agenda for the meeting which we have scheduled for August 30th from 1-2:30 in Rm. 7671.



Agenda EPA Mtg
Aug 30, 2006.do...

We view this as a working meeting with the goal to get your critical thoughts and inputs prior to conducting the proposed acute tox study. Attached below is a draft protocol provided as an example of what could be done and to facilitate our joint discussion and thinking. Our hope is that the details of the study design, including dose levels, etc. will be discussed and agreed to during our meeting. Please note that the first two pages of the draft protocol also contains a summary of the main study elements.



Example Paraquat
PK Protocol i...

Again, thanks in advance for meeting with us and we look forward to our discussion and getting your input.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
336-632-7074
336-253-9666 (mobile)
john.abbott@syngenta.com

Agenda
Meeting with EPA/HED to Discuss Inteon Technology

- **Background/Introduction**
 - The objective of this development project has been to create a formulation that would increase the likelihood of survival after ingestion of a paraquat formulation.
 - EPA's standard:

"This product is to be used only for formulation into herbicides with an acute oral toxicity to dogs (lethal effects) that exceeds 128 mg paraquat ion/kg body weight (602 mg of formulation/kg body weight for a 240 g paraquat ion/l formulation) and that contain an effective emetic that meets FAO specifications, a dye, and an olfactory alerting agent that have been cleared under FIFRA for use in pesticides registered for food use."
 - Data thus far have indicated safening, but need to verify the degree between various PQ formulations in a contemporaneous study in dogs.
- **Proposed Study to Determine Degree of Inteon Safening**
 - **Range of Paraquat Formulations**
 - Gramoxone Extra (360 g/L)
 - Gramoxone (ROW-200 g/L)
 - Inteon (US) (240g/L)
 - Inteon (ROW) (200 g/L)
 - **What is the basis?**
 - Lethality in dogs: no mortalities at 128 mg PQ/kg BW.
 - Area under the curve (AUC) for plasma paraquat: This is an indicator of absorption and is a predictor of mortality. AUC will be related to the minimally lethal dose for each formulation.
 - **What study would best indicate the degree of safening?**
 - A protocol is included.
 - Dogs will be given capsules containing formulation.
 - The proposed dose levels would span the range of from no mortalities to minimally lethal doses.
 - AUC, clinical signs, mortality, and lung, kidney, and GI tract pathology will be recorded.
 - **What is the timeline for doing such a study?** The study would start September/October, with raw results known within a month of termination.
- **Sri Lankan Monitoring**
 - Preliminary findings
 - Timeline for report preparation
- **Discussion**

Agenda EPA Mtg Aug 30 2006

23.8

MAIN STUDY ELEMENTS TO THE PROPOSED BASELINE GRAMOXONE AND INTEON DOG STUDIES

Objective for single oral dose studies over a range of formulation doses

Study to determine kinetic data on paraquat absorption gaining minimum lethal dose

Formulation type for non-Inteon formulation currently on sale

Two studies needed

Gramoxone Max (360g/l PQ) for the USA

Gramoxone 200 (200g/l PQ with BIW) for ROW

Inclusion of Inteon formulation or not

Two studies needed

Inteon K (240 g/l PQ NBIW) for comparison to Max

Inteon EN (200g/l NBIW) for comparison to ROW

Both sexes required?

Use a single sex; use males

Aim of study: LD50 number or minimal lethal dose

Determine the shape of the kinetic curve together with the minimum lethal dose.

Numbers of animals per dose level

Proposed to use 4. Based on 2 being too few and 4 giving added clarity over a group size of 3 in the event of an observation of 2 terminations.

Rising doses or concurrent group dosing

Use rising doses, moving up when reasonable confirmation of the tox of the first dose is available (likely 48 hours)

Dose levels: number and actual levels

Non-Inteon (Max): Plan for 8, 16, 32 as initial doses.

Will progress downwards if 8 does not define the bottom of the kinetics dose response, and upwards if 32 does not incur terminations. These dose levels to be decided based on the kinetic (AUC) parameters.

Non-Inteon (ROW): Plan for 4, 8, 16 as initial doses

Will progress downwards if 4 does not define the bottom of the kinetics dose response, and upwards if 16 does not incur terminations. These dose levels to be decided based on the kinetic (AUC) parameters.

Inteon US and ROW: Plan for 64, 128 as initial doses

Will progress downwards if 64 does not define the bottom of the kinetics dose response. Will progress upwards with a dose space depending on the kinetics seen at 64, and the kinetics and termination data from the Gramoxone Max study

Means of oral dosing

Dose by capsule

Endpoints to measure

As currently done in CTL - Plasma paraquat kinetics (peak/AUC); clinobs; bodyweight; full gross macropathology; histopathology (lungs, kidneys, GI tract)

Endpoint thresholds for requiring termination

Clinobs or bodyweight thresholds exceeded (detailed limits to be confirmed)

Measurement of paraquat absorption (assess accuracy needed) to be done in real time to advise clinobs frequency

Measure emetic levels in plasma?

Include measurement. No need for real time measurement.

Source of dogs - parity to existing Inteon data

Beagles of similar weight range to CTL studies (10-12kg). Control potential stress and GI tract factors such as worming, diet

Analysis - parity to existing sensitivity/specificity

Method validation for PQ analysis in advance on spiked plasma and confirmation the same as results obtained in CTL

Histopathology

Return tissues as wet tissues or blocks to CTL for CTL histopathology analysis

Laboratory for conducting study

Tim and NAFTA to recommend

Monitoring of study

Study monitors with first-hand experience of these studies are essential for a significant portion of the studies (ie low dose right through to final high dose) for at least one formulation.

PARAQUAT 240G/L SL FORMULATION (A7813K)

EXAMPLE PROTOCOL

ASSESSMENT OF TOXICOKINETICS AND ACUTE TOXICITY IN DOGS

DRAFT

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DRAFT

SUMMARY OF STUDY DESIGN

Groups:	A minimum of 3 groups.
Number of animals:	4 Males per group.
Dose administration:	Single oral dose (via gelatine capsule) on 1 occasion.
Clinical observations:	<p>On each day of dosing: continuous cageside observations (including gastro-intestinal abnormalities) for up to 4 hours post dosing; clinical observations recorded at hourly intervals for up to 7 hours post dosing. Time to first emesis and times of subsequent emesis (up to 4 hours) to be recorded.</p> <p>Pre-study and throughout the study: detailed observations recorded weekly; cageside observations and gastro-intestinal abnormalities recorded daily.</p>
Veterinary examinations:	Detailed clinical examination (including cardiac and pulmonary auscultation) of all dogs prior to dosing and prior to termination.
Bodyweights:	Weekly (pre-study and throughout the study) and on day of dosing and daily thereafter.
Food consumption:	Daily (pre-study and throughout the study).
Toxicokinetics:	Blood samples taken from all animals prior to dosing and at 15 and 30 minutes, 1, 2, 4, 7, 12 and 24 hour post dosing for analysis of paraquat and emetic agent (PP796).
Clinical chemistry	Blood samples taken from all animals prior to and at 24 hours after each dose and prior to termination, for analysis of clinical chemistry parameters.
Pathology:	Limited range of organs to be processed and examined from all animals, including lungs and kidneys.
Report:	Full report

1. INTRODUCTION

1.1 Purpose

The 240g/L paraquat formulation A7813K is a Manutex triggered gel formulation (a new acid-triggered gelling approach based on water-soluble alginate technology) intended for use in the United States of America. The toxicokinetics of an alginate-based formulation of paraquat (240g/l) will be determined in the dog to assess the systemic profile of paraquat over a series of increasing doses until the minimum lethal dose is determined.

The formulation A37813K contains an emetic agent (PP796) and a purgative (magnesium sulphate) as well as stenching agents (cis-hexanol). Vomiting and diarrhoea are expected following dosing.

1.2 Regulatory guidelines

This is a specially designed investigative study which is not intended to comply with any Regulatory Guidelines.

1.3 Testing facility

To be conducted at a contract lab within the US, details to be confirmed

1.4 Justification for selection of the test system

The dog is the preferred non-rodent species for this type of study since emesis is an essential part of the proposed safening action of the new formulation and because substantial data are available at CTL relating to the toxicokinetics of paraquat following oral doses. The oral route has been chosen for the administration of the test substance as it is the major route of exposure in humans in cases of poisoning.

1.5 Dose selection

The dose levels of the A7813K formulation have been selected as 64 and 128mg paraquat ion/kg, initially, as these dose levels were used in the previous toxicokinetic study with A7813K (CTL Study No. XD7355).

1.6 Standard operating procedures

Reference to Standard Operating Procedures (SOPs) should be taken to imply the version current at the time the procedures are performed.

2. GOOD LABORATORY PRACTICE AND QUALITY ASSURANCE

This study will be conducted according to the Principles of Good Laboratory.

The protocol, study procedures and report will be audited by the Quality Assurance Unit.

3. TEST AND CONTROL SUBSTANCES

3.1 Safety

3.2 Test substance

Name:	Paraquat 240g/l SL formulation (A7813K)
Source:	Jealotts Hill, Syngenta Ltd
Colour:	Green
Physical state:	Liquid
Batch reference:	
CTL test substance reference number:	
Purity (% w/w):	
Specific gravity:	
Storage conditions:	Ambient temperature in the dark
Stability:	
Intended Use	Agriculture

4. EXPERIMENTAL PROCEDURES

4.1 Dose preparations

Dogs will be dosed with the appropriate volume of A7813K, to achieve the required oral dose, based on the most recent bodyweight. Capsules will be prepared locally immediately prior to dosing, using a positive displacement pipette (SOP CT90-772). **The test substance must be shaken vigorously prior to dispensing.** The capsules will be enclosed in a second capsule. Details of dose preparation will be recorded in the raw data.

Dose Level of A7813K (mg Paraquat ion/kg)	Dose Volume of A7813K (ml/kg)
64	0.267
128	0.533

4.2 Analysis of dose preparations

The A7813K formulations will be analysed and a copy of the Certificate of Analysis archived with the raw data.

4.3 Experimental design

A schedule of events and a correlation of unique ear number, experimental number and pen number are given in Appendices A and B, respectively.

4.3.1 Animals

Species:	Dog
Breed:	Beagle
Source:	
Sex:	4 Males per group.
Specification:	9-12 months of age on delivery, weight range – 9-12kg Vaccinated against canine viral hepatitis, distemper, leptospirosis, canine influenza and canine parvovirus (prior to delivery). Regularly treated for possible nematode infestation (prior to delivery - records supplied)
Selection:	On the basis of normal:- clinical parameters, health status and bodyweight.

4.3.2 Accommodation and husbandry

On arrival, the dogs will be housed as 'stock dogs' and assessments will be made independently of the study in order to determine their suitability for the study. The dogs will be selected for this study on the basis of normal health and clinical parameters (determined prior to delivery) and will be assigned experimental numbers in pen number order, based on the random order of housing on delivery.

The dogs will be housed together in pens in the Dog Facility, ~~except on the day of dosing when they will be individually housed for up to 6 hours after dosing.~~ The pens have a sleeping platform (with heated floor underneath) and interlinking gates which enable the dogs to be separated for feeding (SOP CT90-643).

Wood flakes (supplied by WTL International Ltd, Macclesfield, Cheshire, UK) are provided as bedding material. Toys/chews are also provided daily. The dogs will receive lead exercise for all routine procedures (e.g. weighing) and will be allowed free exercise, as a group, daily in the central corridor and weekly in the exercise area.

The animal room provides the following nominal environmental conditions:

Temperature:	19 ± 2°C
Relative humidity:	45-65%
Air:	Approximately 15 changes/hour
Light cycle:	Artificial giving 12 hours light, 12 hours dark

Temperature and relative humidity will be monitored and recorded daily throughout the study (SOP CT90-845).

Each morning, male dogs will receive 350g of LABORATORY DIET A (supplied by SDS Limited, Witham, Essex, UK) an expanded dry diet. Each batch of diet is routinely analysed for composition and for the presence of contaminants. Mains water, supplied by an automatic system will be available *ad libitum*; water is also periodically analysed for the presence of contaminants. Details of analyses are retained in the CTL Archives.

The dogs will be separated for feeding for approximately 3 hours. After this time the food bowls will be removed and the dogs will be group housed until the following day. During the

acclimatisation period, food bowls will be removed after 2 hours in order to encourage the dogs to eat up quickly.

4.3.3 Acclimatisation

The dogs will be acclimatised for 4 weeks before the start of the study.

4.3.4 Animal randomisation and identification

The dogs will be uniquely identified (whilst at the breeding unit) with implanted ear numbers. Prior to the start of the study, the dogs will be randomly allocated to individual pens in the dog Unit as they come to hand. Experimental numbers will be allocated in pen order and these numbers will be cross-referenced to the appropriate individual ear numbers. Thereafter, dogs will be identified by their experimental number in all procedures and the unique ear number will be checked each day and whenever a dog is removed from its pen (Appendix B).

On the front of each pen will be a card identifying the contained animals by dose level, group number, unique ear number, experimental number, sex and study.

All procedures and analyses will be performed in pen order.

4.3.5 Dose levels and treatment groups

The study will consist of a minimum of two groups with 4 males per group, with 1 dose per group:

Group	Dose Level of A7813K (mg Paraquat ion/kg)	Experimental Numbers
		Males
1	64	1 - 4
2	128	5 - 8

Additional dose levels will be added as necessary in order to provide definition of the toxicokinetic dose response and to determine the minimum lethal dose relevant for the test material.

4.3.6 Dose administration

Dogs will receive a single oral dose of the appropriate dose of A7813K formulation on 1 occasion during the study. All dogs will be dosed orally with gelatine capsules (SOP CT50-184) containing the appropriate volume of the test substance (see Section 4.1). Dogs will be fed approximately 4 hours after dosing.

4.3.7 Duration of dose administration

The animals will receive the appropriate volume of test substance, on 1 occasion.

4.4 Clinical observations

On the day of dosing, all dogs will be singly housed (see 4.3.2) in order to eliminate any possibility of cross contamination of dogs with test substance present in vomit or faeces and to assist in observation of individual clinical signs. All dogs will be observed cage-side continuously for the first 4 hours after dosing, particularly for the timing of emesis and the volume, colour and consistency of vomit and faeces; these findings will be recorded on data sheets. *Vomit and faeces will be cleared away immediately to prevent re-ingestion.*

The dogs will also be observed continuously for the first 4 hours after dosing and then at hourly intervals from 4-7 hours post dose and at 12 hours post dose, for gross clinical or behavioural abnormalities (SOP CT50-199). Observations will be recorded on pre-printed forms.

Detailed clinical observations will be made once a week in the procedure room (SOP CT50-199) from week -1 (pre-study), throughout the study and prior to termination.

Gastro-intestinal findings (e.g. regurgitation, faecal abnormalities) will be assessed daily (SOP CT90-338) and a record of abnormal findings will be made for at least two weeks pre-study and then throughout the study period.

Details of worming or other health treatment will be recorded.

4.5 Veterinary examination

A detailed clinical examination (SOP CT50-199) including cardiac and pulmonary auscultation will be made by a veterinarian on all dogs prior to dosing and prior to termination.

4.6 Bodyweights

All dogs will be weighed weekly (before feeding), for at least 1 week pre-study and then at weekly intervals throughout the study and prior to termination (SOP CT60-068), as a health check. Weights will be recorded on the day of dosing (for dose calculation) and daily thereafter.

4.7 Food consumption

Food residues will be recorded daily, (SOP CT60-079) approximately three hours after feeding to enable food consumption to be calculated. Any residual food will be discarded. These measurements will be made for at least 1 week pre-study and throughout the study.

4.8 Clinical pathology

Jugular blood samples (1.3ml in lithium heparin) will be taken from each dog, to assess toxicity, on the day prior to each dose, 24 hours after each dose and prior to termination (SOP CT50-051). Samples will be submitted to the Clinical Pathology Unit for analysis. Details of SOPs used will be recorded in the raw data.

The following parameters will be determined in plasma:-

urea
creatinine
glucose
albumin
total protein
cholesterol
triglycerides
total bilirubin
albumin/globulin ratio

alkaline phosphatase activity
aspartate aminotransferase activity
alanine aminotransferase activity
glutamate dehydrogenase activity
calcium
phosphorus (as phosphate)
sodium
potassium
chloride
creatinine kinase

4.8.1 Toxicokinetics

Blood samples will be taken on each day of dosing to determine a toxicokinetic profile following the dose of A7813K. Jugular blood samples (in lithium heparin) will be taken from each dog on the day prior to dosing and then at 15 and 30 minutes and 1, 2, 4, 7, 12 and 24 hours after dosing (SOP CT50-051). Approximately 2ml blood will be taken at 15 and 30 minutes and 1, 2, and 4 hours after dosing and approximately 5ml blood will be taken pre-dose and at 7, 12 and 24 hours after dosing. Details will be recorded in the raw data.

All blood samples will be separated by centrifugation (at 1500g for 10 minutes) and plasma samples will be submitted for analysis of paraquat ion, residual plasma will be sent to Syngenta CTL for analysis of the emetic PP796 in plasma. For the 12 hour samples only, the plasma will be stored at 4°C overnight prior to analysis. Details will be recorded in the raw data.

The mean plasma concentration-time profiles and AUC_{0-24} , calculated using the linear trapezoidal rule will be calculated for each group of 4 dogs and plasma paraquat and emetic concentrations presented for individual animals and as mean \pm SEM.

The toxicokineticist will provide a data report including detailed methodology and the results of the toxicokinetic analyses.

4.9 Investigations *post mortem*

4.9.1 Termination

At the end of the study (14 days following the final dose) all dogs will be killed by an overdose of anaesthetic (induced by intravenous injection of sodium pentobarbitone) followed by exsanguination (SOP CT35-003).

Dogs will be killed intercurrently according to the termination criteria specified in the provided document. One objective of the study is to determine the minimum lethal dose for the test material, that is to say a dose that is lethal to one or more dogs. However, the termination criteria set out are intended to recognise that this is the probable outcome as a result of ingestion of the test material, and so meet the study objective, but to avoid unnecessary pain, suffering or distress to the dogs. The following criteria may be used to assist in decision making:

1. Peak plasma paraquat ion concentration of $\geq 10\mu\text{g/ml}$ and / or 24 hour plasma paraquat AUC value of $> 40\mu\text{g/ml.h}$.
2. Clinical pathology changes indicative of renal or lung toxicity (e.g. significantly increased plasma creatinine).

4.9.2 Macroscopic examination

All animals will be examined *post mortem* (SOP CT45-023). This will involve an external observation and a careful examination of all internal organs and structures.

4.9.3 Tissue submission

The following will be taken from all animals and stored in appropriate fixatives.

abnormal tissues
duodenum
heart
ileum
jejunum
colon
adrenals

Kidney
Liver
Lung
Oesophagus
Stomach
caecum

4.9.4 Tissue Processing

Lung, kidney and abnormalities will be trimmed, embedded in paraffin wax, 5µm sections cut and stained with haematoxylin and eosin (SOP CT45-041, CT45-053, CT45-057 and CT45-059). Other submitted tissues will be stored in fixative.

4.9.5 Microscopic examination

Lung, kidney and abnormalities will be examined by light microscopy.

5. DATA EVALUATION

Toxicokinetic data will be analysed by relevant methods. Other data will be evaluated by inspection only because of the small number of animals per group.

The minimum lethal dose will be determined from the lethality profile over the time period of the study, based on acute toxicity parameters.

6. ARCHIVING AND REPORTING

APPENDIX A - SCHEDULE OF EVENTS

Study Phase.	Procedures	Proposed Date
Pre-Study	Arrival of animals Start pre-study recording of clinical observations, bodyweights & food	
Dose 1 64mg/kg Pq ion	Veterinary examination & blood samples (clin path & TK) <u>Day of dosing</u> House individually, record bodyweights Dose and observe continuously for 4 hours; hourly observations recorded (4 - 7hrs) & 12hrs p.d. Blood samples @ 15 & 30 minutes and 1, 2, 4, and 12 hour post dosing Feed 4 hours post dose. Group house 6 hrs after dosing. Blood samples @ 24 hour post dosing.	
Dose 2 128mg/kg Pq ion	Veterinary examination & blood samples (clin path) Termination <u>Day of dosing</u> House individually, record bodyweights Dose and observe continuously for 4 hours; hourly observations recorded (4 - 7hrs) & 12hrs p.d. Blood samples @ 15 & 30 minutes and 1, 2, 4, 7 and 12 hour post dosing Feed 4 hours post dose. Group house 6 hrs after dosing. Blood samples @ 24 hour post dosing.	
	Veterinary examination & blood samples (clin path) Termination	

Bodyweights will be measured weekly (from week -1), food consumption will be measured daily (from week -1).

**APPENDIX B - CORRELATION OF UNIQUE EAR NUMBER AND EXPERIMENTAL
NUMBER AND PEN NUMBER**

Group	Males		
	Experimental Number	Ear Number	Pen Number

DRAFT

McDonald Mary USGR

Subject: FW: Agenda for Tox Meeting
Attachments: Agenda EPA Mtg Aug 2006 v2.doc

From: Abbott John USGR
Sent: Thursday, August 24, 2006 4:18 PM
To: Johnson.Hope@epamail.epa.gov
Subject: Agenda for Tox Meeting

Hope,

Thanks again for coordinating our meeting with the toxicologists next week. It is much appreciated. Attached is the proposed agenda. Again, I expect to have the protocol to you by Friday at the latest.



Agenda EPA Mtg
Aug 2006 v2.doc...

Please contact me if you have any questions.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
336-632-7074
336-253-9666 (mobile)
john.abbott@syngenta.com

Agenda
Meeting with EPA/HED to Discuss Inteon Technology

- **Background/Introduction**
 - The objective of this development project has been to create a formulation that would increase the likelihood of survival after ingestion of a paraquat formulation.
 - EPA's standard:

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 - Inteon (ROW) (200 g/L)
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 - Area under the curve (AUC) for plasma paraquat: This is an indicator of absorption and is a predictor of mortality. AUC will be related to the minimally lethal dose for each formulation.
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 - The proposed dose levels would span the range of from no mortalities to minimally lethal doses.
 - AUC, clinical signs, mortality, and lung, kidney, and GI tract pathology will be recorded.
 - **What is the timeline for doing such a study?** The study would start September/October, with raw results known within a month of termination.
- **Sri Lankan Monitoring**
 - Preliminary findings
 - Timeline for report preparation
- **Discussion**

McDonald Mary USGR

From: Rudolph Tiffany USGR
Sent: Thursday, September 14, 2006 11:23 AM
To: McDonald Mary USGR
Subject: FW: Meeting Follow-up and Submission Items

Attachments: EPA PQT Presentation 8-30-06.pdf; ParaquatreportBarrueto.pdf; 060724 APAMT Inteon Presentation (comp).pdf

From: Abbott John USGR
Sent: Friday, September 01, 2006 2:59 PM
To: Rudolph Tiffany USGR
Subject: FW: Meeting Follow-up and Submission Items

Tiffany,
I forgot to include you as a bcc. This should be included in our records, please coordinate with Kim. We will need to submit this via the front end screen as well so can you please help me with that? I should get the Cockrill study on Tuesday and that can accompany this along with any corrections that you assisted me with on the emetic. Have a great weekend but I guess we better be ready to work on Tuesday. Thanks.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
336-632-7074
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john.abbott@syngenta.com

From: Abbott John USGR
Sent: Friday, September 01, 2006 2:54 PM
To: 'Johnson.Hope@epamail.epa.gov'
Cc: 'Tompkins.Jim@epamail.epa.gov'; 'kenny.dan@epa.gov'; Elliott Barry GBAP; Pastoor Tim USGR; Akins Jonathan USGR
Subject: Meeting Follow-up and Submission Items

Hope,
First, I want to thank you again for pulling the meeting together yesterday under a difficult timeline. We found the meeting helpful to this project and hope you and your colleagues did as well. Attached are a few of the items that we had committed to provide to you during our meeting. I am providing them by email but will also discuss with you regarding submission through the front-end screen. Please distribute to the other participants from our meeting.

First, below is our slide presentation from yesterday's meeting. Please note that we have added 5 information slides to reflect the details of our discussion during the meeting and presented on flip charts. We believe these additional slides will be useful as you review our proposed study design and goal in more detail. As we discussed, we are committed to conducting the acute tox dog study and look to initiate this study as soon as possible. We welcome any feedback/input that you can provide and we are glad to accept the input by email or otherwise to facilitate this short timeframe. Thanks in advance for your assistance.



EPA PQT
Presentation 8-30-06.p

Next, I am providing the updated statement from Dr. Barueto, the physician who treated the patient in Maryland who intentionally ingested Gramoxone Inteon and has survived. This update includes confirmation that it was Gramoxone

Inteon that was ingested and not an older paraquat formulation. Please use this statement in conjunction with the original statement provided by Dr. Barreto and submitted to the Agency.



ParaquatreportBar
reto.pdf (58...

Lastly, I am providing the slide presentation entitled "Improvement in survival following paraquat ingestion after introduction of a new formulation with INTEON® technology in Sri Lanka" that was presented at the APAMT Conference held in August, 2006. As we discussed, Dr. Dawson from the Science Advisory Panel has extended the offer to meet with you to present more details of the survey and answer any questions the Agency has regarding the results.



060724 APAMT
Inteon Presentati...

I will plan to call you next week to follow-up but please call me if you have any questions. Have a great weekend.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
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john.abbott@syngenta.com

Agenda

- Introductions
- Brief Meeting Introduction – John Abbott
 - Submission Plans
- Study Design Proposal – Barry Elliott
- Sri Lanka Survey Information & Plans – Barry Elliott
- Conclusions and Future Plans



Baseline studies in the dog for evaluation of the toxicity of Inteon and non-Inteon Gramoxone formulations

Proposals



Main study elements

Objective

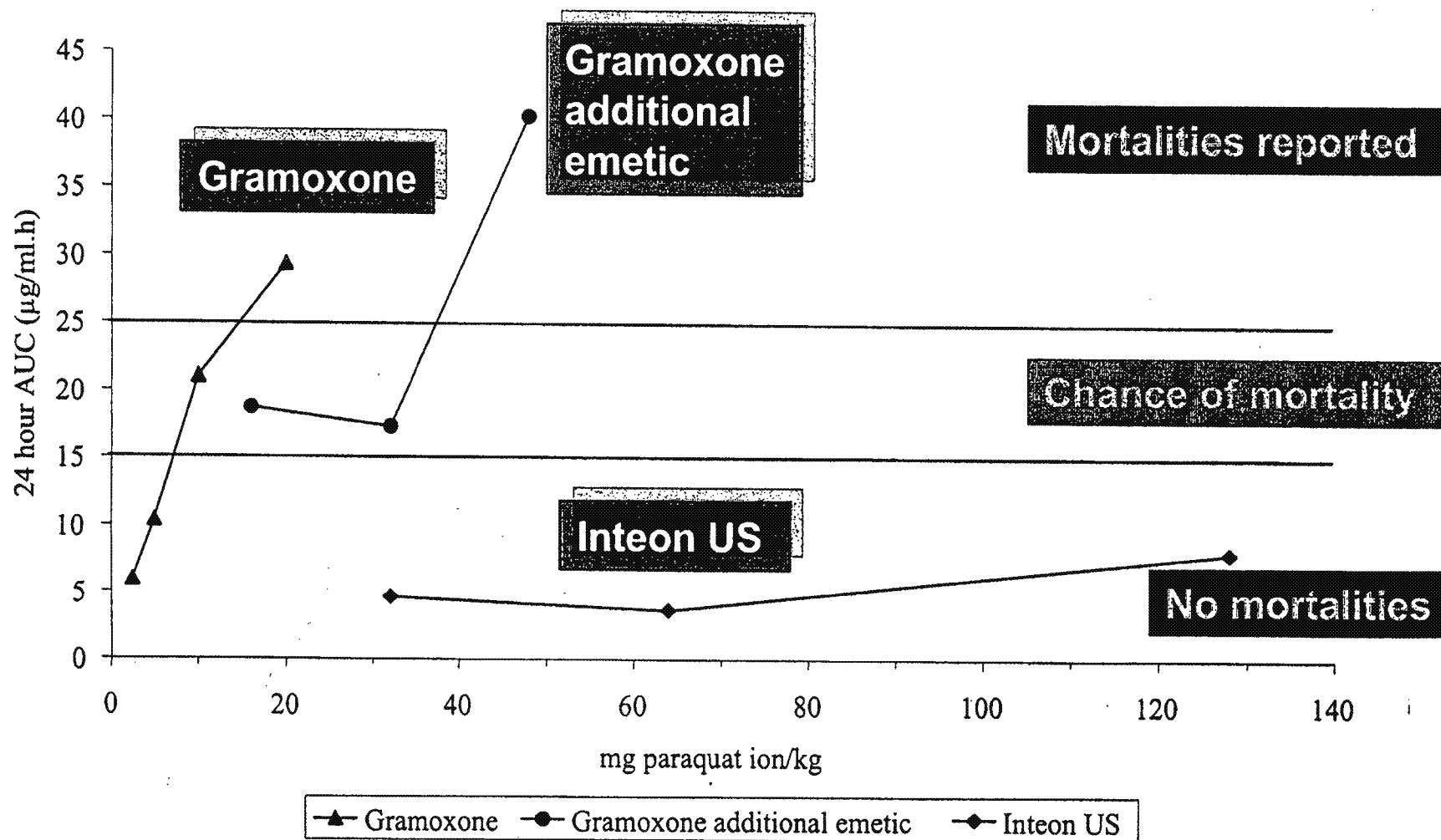
Formulations to evaluate

Study details

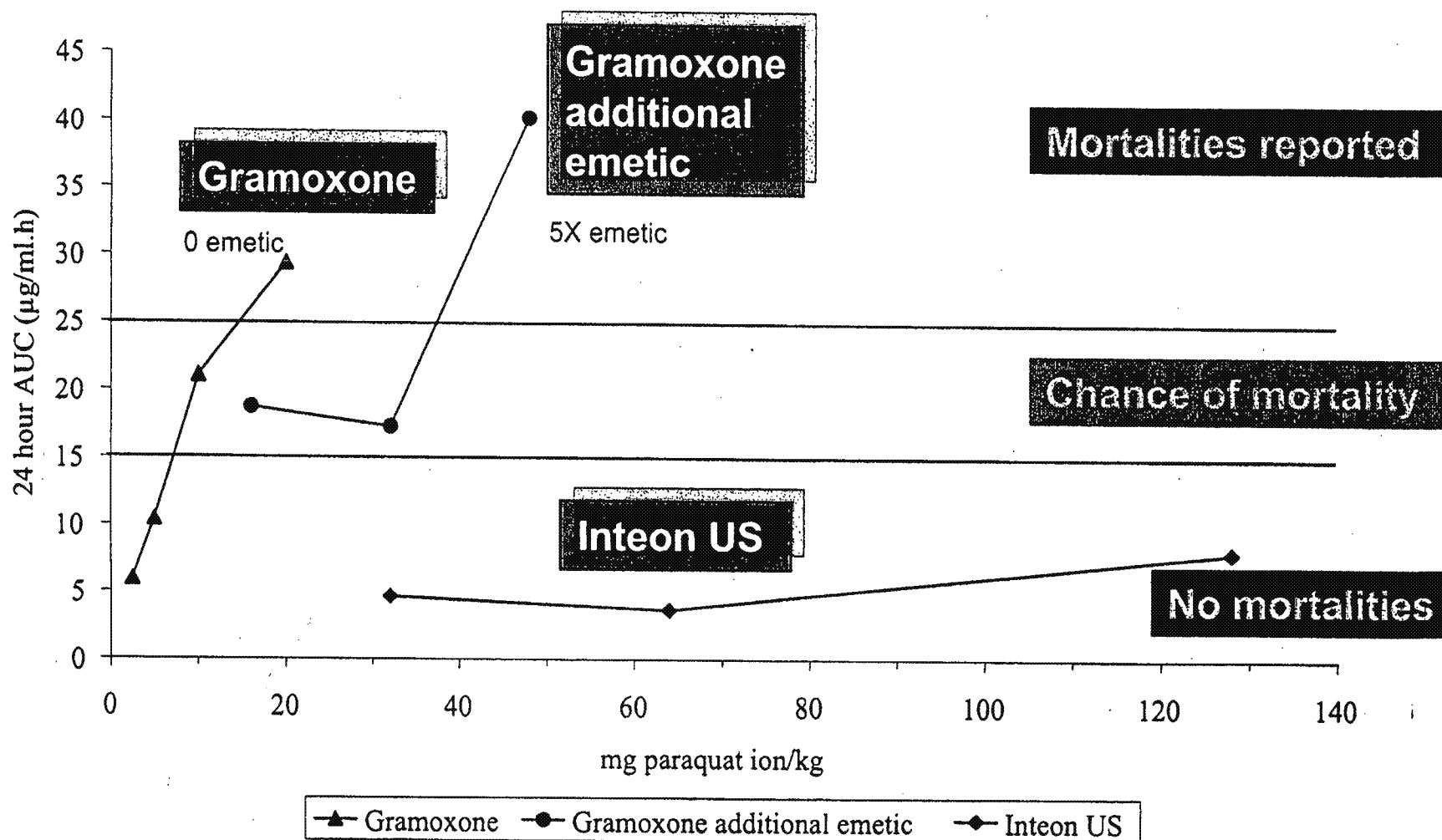
Study placement

Timing

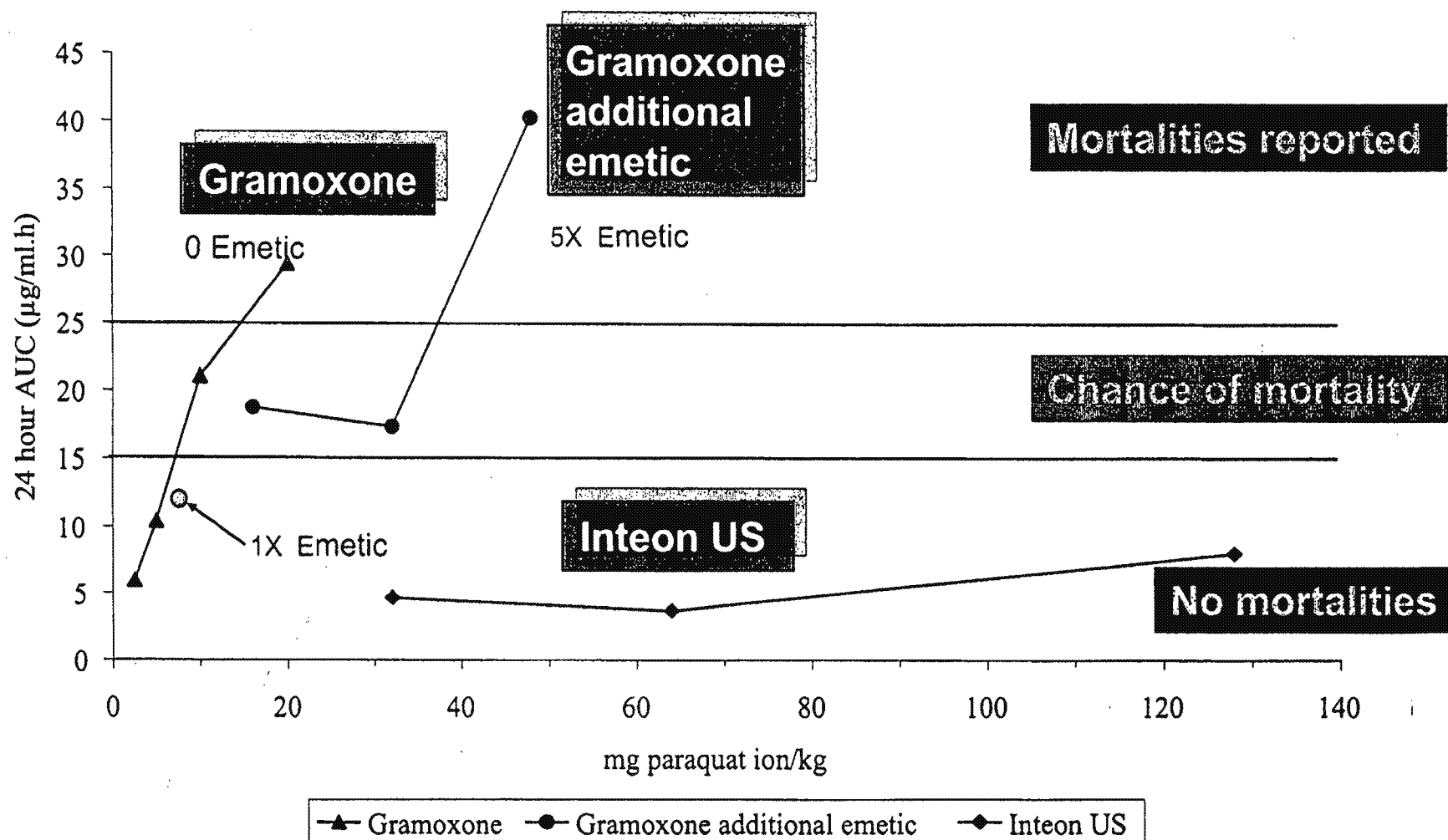
Comparison of 24h plasma paraquat AUC levels in dog



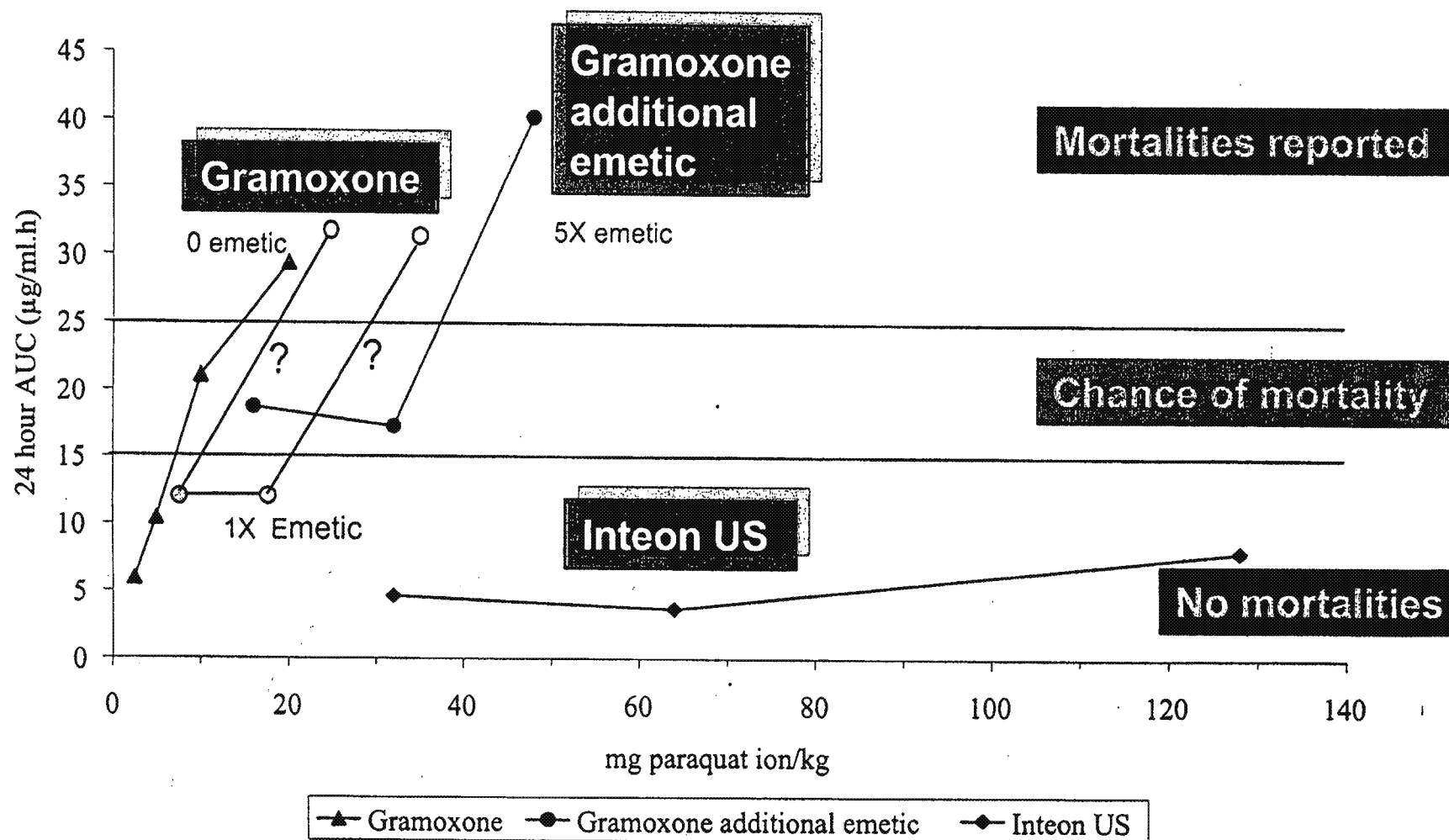
Comparison of 24h plasma paraquat AUC levels in dog



Comparison of 24h plasma paraquat AUC levels in dog



Comparison of 24h plasma paraquat AUC levels in dog



Main study elements

Objective

Objective for single oral dose studies over a range of formulation doses

- Determine kinetic data on paraquat absorption
- Determine acute toxicity (lethality) - minimum lethal dose

Formulation Comparison

	Non-Inteon		Inteon	
	US Gramoxone Max	Global Gramoxone	US Gramoxone Inteon	Global Gramoxone Inteon
Paraquat Concentration	360g/l	200g/l	240 g/l	200g/l
Emetic Concentration	0.5g/L	0.5g/L	1.5g/L	1.5g/L
Built In Wetters	No	Yes	No	No

Main study elements

Study details

Both sexes required?

- Use a single sex; use males

Aim of study: LD50 number or minimal lethal dose

- Determine the shape of the kinetic curve for paraquat absorption together with the minimum lethal dose.

Numbers of animals per dose level

- Proposed to use 4.

Rising doses or concurrent group dosing

- Use rising doses, moving up when reasonable confirmation of the toxicity of the first dose is available (likely 48 hours). Fresh animals per dose level

Main study elements

Study details

Dose levels: number and actual levels

Non-Inteon (Max): Plan for 8, 16, 32 mg/kg as initial doses

Non-Inteon (ROW): Plan for 4, 8, 16 mg/kg as initial doses

Inteon US and ROW: Plan for 64, 128 mg/kg as initial doses

Main study elements

Study details

Means of oral dosing

- Dose by capsule

Endpoints to measure

- As currently done in CTL - Plasma paraquat kinetics (peak/AUC); clinobs; bodyweight; full gross macropathology; histopathology (incl lungs, kidneys, GI tract)

Endpoint thresholds for requiring termination

- Clinobs or bodyweight thresholds exceeded (detailed limits to be confirmed)
- Measurement of paraquat absorption to be done in real time to advise clinobs frequency

Source of dogs - parity to existing Inteon data

- Beagles of similar weight range to CTL studies (10-12kg). Control potential stress and GI tract factors such as worming, diet, housing

Analysis - parity to existing sensitivity/specificity

- Method validation for PQ analysis in advance on spiked plasma and confirmation the same as results obtained in CTL

Histopathology

- Return tissues as wet tissues or blocks to CTL for histopathology analysis

Main study elements

Study placement

Laboratory for conducting study

- To be determined

Monitoring of study

- Study monitors with first-hand experience of these studies are essential for a significant portion of the studies (ie low dose right through to final high dose) for at least one formulation.

Main study elements

Timing

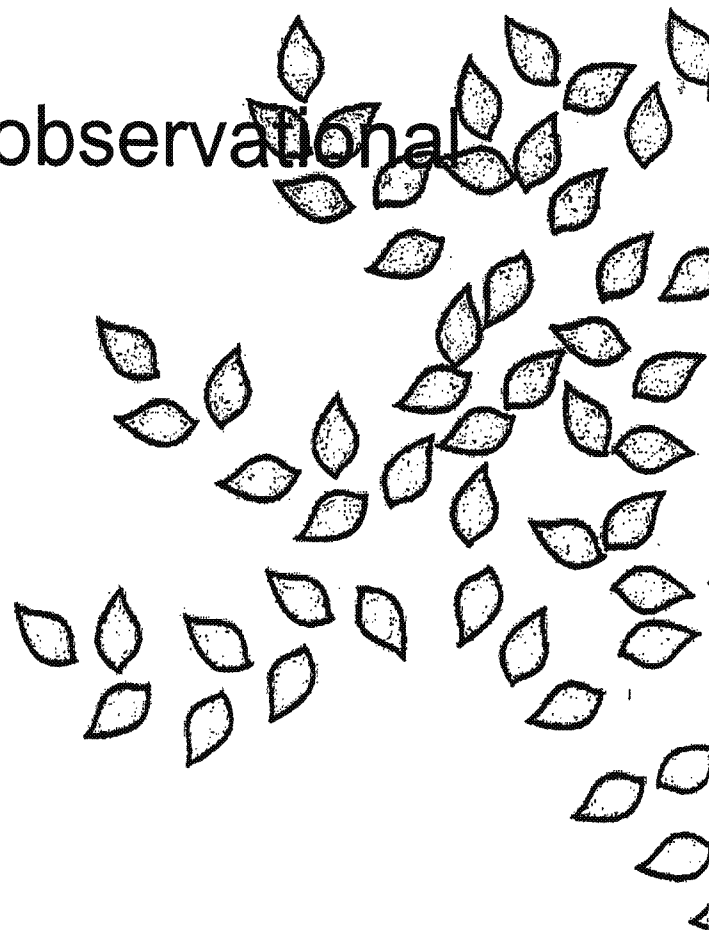
Planning on study start
end September / beg October

Main study elements: Humane termination criteria

- Excessive weight loss and/or extreme emaciation
- Prolonged absence of voluntary responses to external stimuli
- Prolonged anorexia
- Severe dehydration
- Evidence to suggest irreversible organ failure
- Persistent, difficult, laboured breathing
- Prolonged diarrhoea
- Significant and sustained decrease in body temperature
- Other treatment related effects judged to be indicative of impending death



Reporting of the Sri Lankan observational monitoring survey



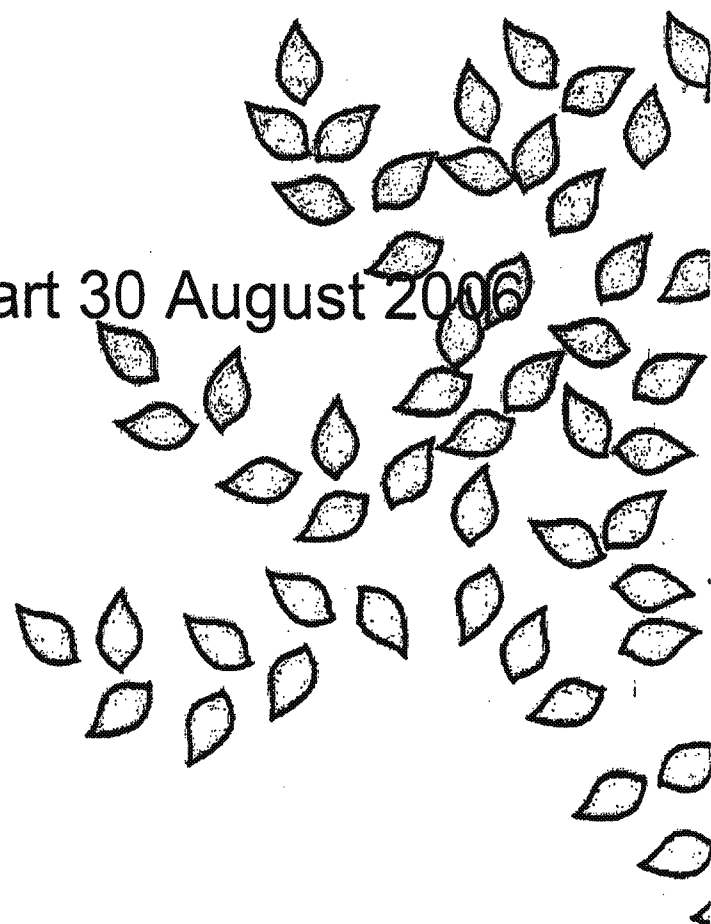
Current status

- Presentation to Conference in Sri Lanka August 2006
- Draft publication in progress
 - Expected draft for end September, then review by SAP
 - Approval for release by SAP earliest in October but depending on agreement and any additional data manipulation required

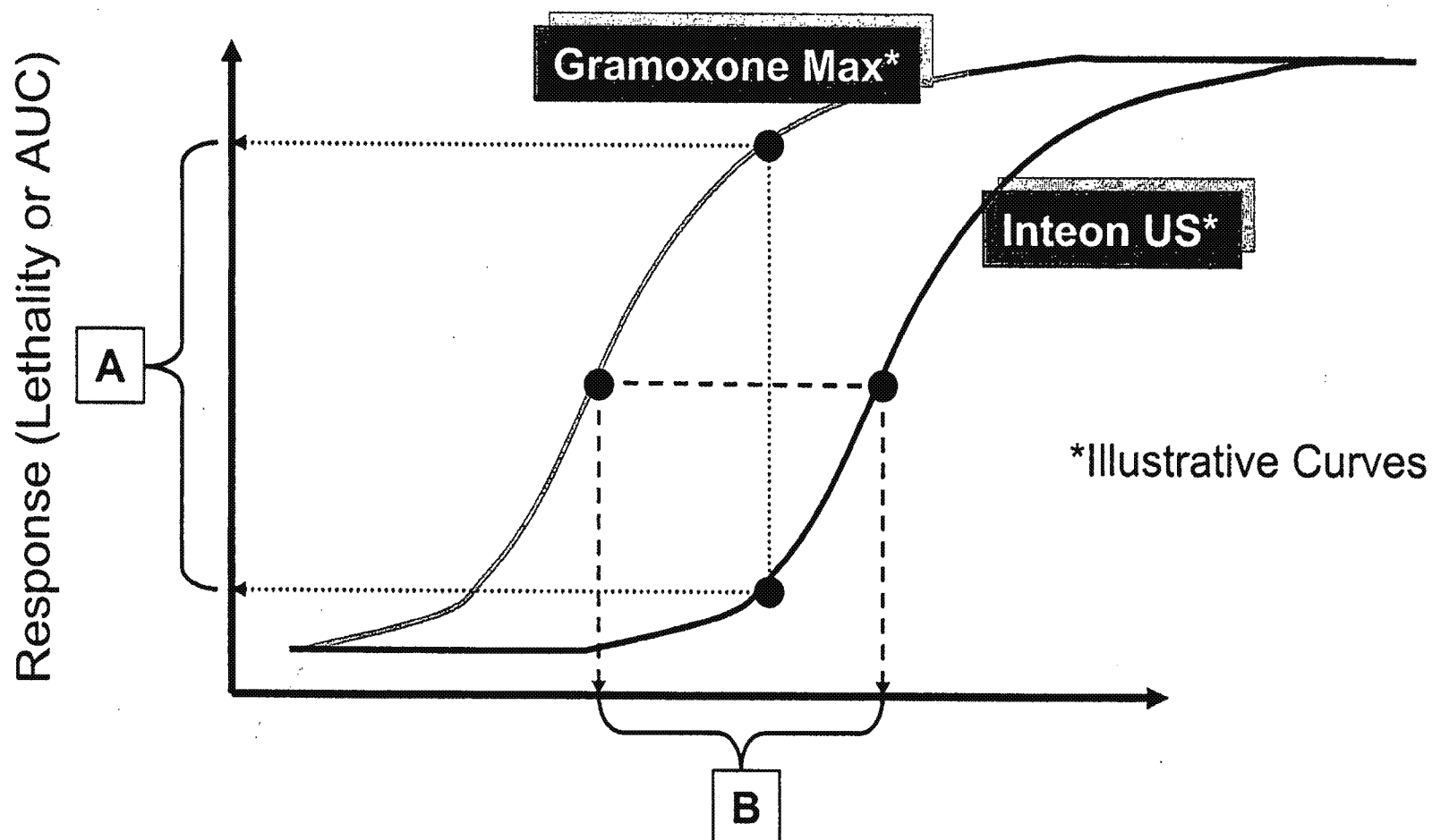


Additional Slides

Based on graphics drawn on flipchart 30 August 2006



Theoretical Dose-Response Comparisons

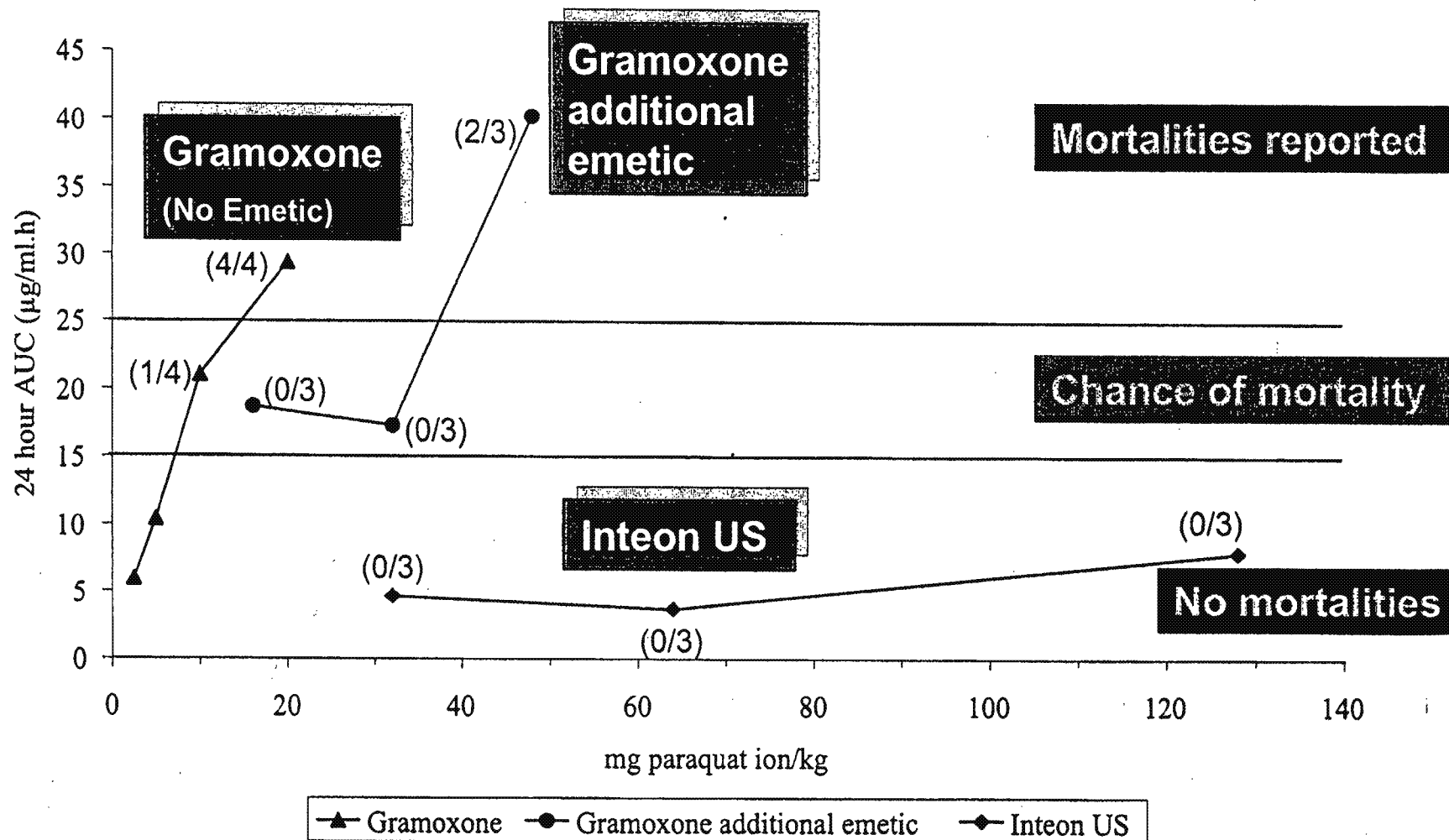


A= The difference in degree of response at the same unit dose

B= The difference in dose to achieve the same degree of response

syngenta

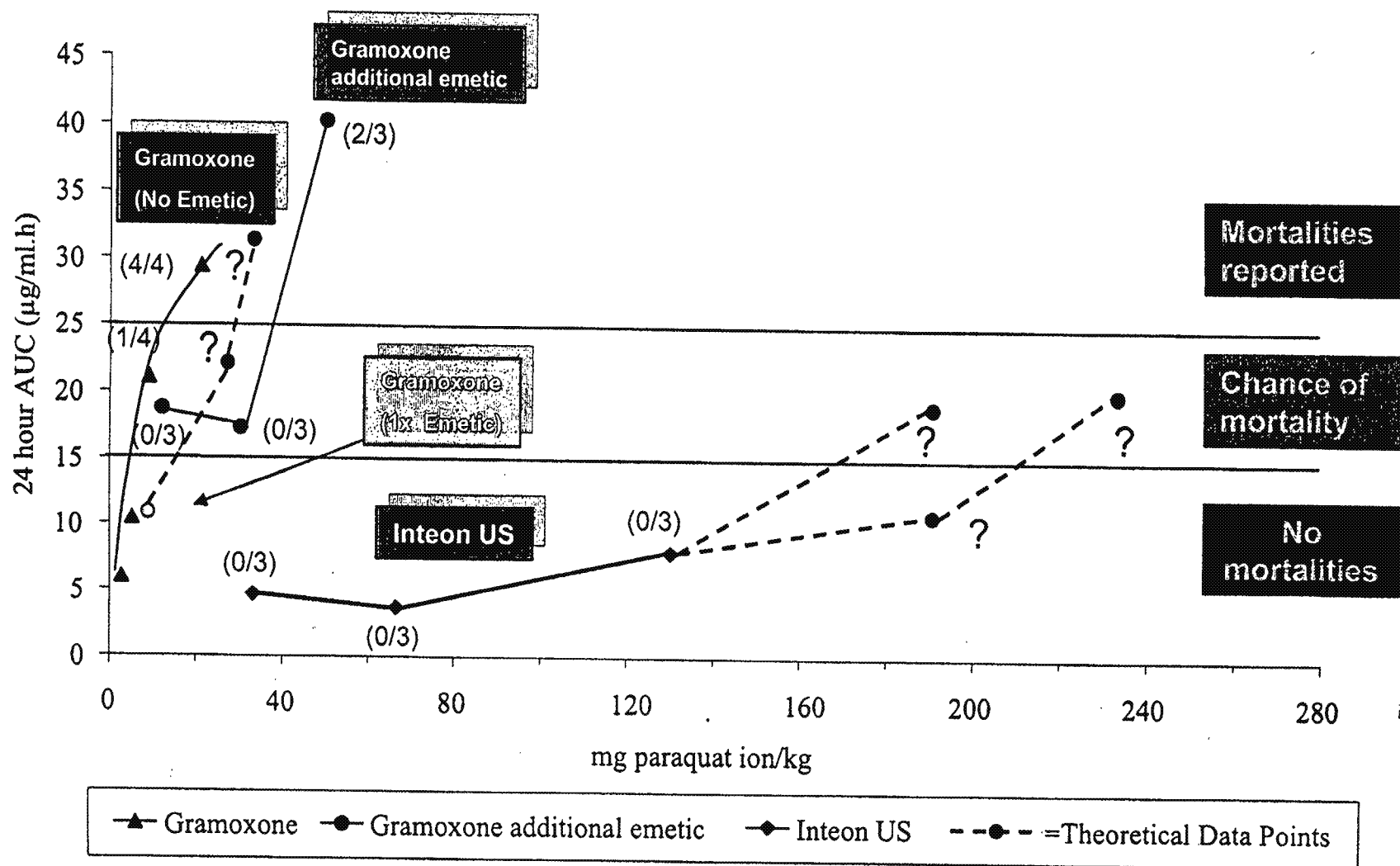
Comparison of 24h plasma paraquat AUC levels in dog



Comparison of 24h plasma paraquat AUC levels in dog (Comments for Previous Slide)

This is from actual dosing data in dogs, showing an increase in AUC and lethality for Gramoxone with and without emetic and a lack of mortalities in Inteon-dosed dogs, with AUC values remaining low.

Comparison of 24h plasma paraquat AUC levels in dog (illustrative)



Comparison of 24h plasma paraquat AUC levels in dog (illustrative) (Comments for Previous Slide)

This builds from the previous slide, which shows an increase in AUC and lethality for Gramoxone with and without emetic and a lack of mortalities in Inteon-dosed dogs, with AUC values remaining low. This slide extends the X-axis (dose) and schematically represents potential outcomes.



UNIVERSITY OF MARYLAND
SCHOOL OF MEDICINE

To Whom It May Concern:

I am reporting a case of a patient I treated who ingested Gramoxone INTEON® and had resulting severe pulmonary fibrosis. The case is summarized here.

A Severe Paraquat Ingestion that Survived

A 27 year old man, in a suicide attempt, ingested ½ a cup (4 ounces) of Gramoxone INTEON® (Syngenta), a 30% solution of paraquat, that was in his landscaping truck. Forty-five minutes after the ingestion, the patient vomited several times and went to the Emergency Department(ED). He complained of burning in his chest and mouth. He was admitted and had an esophagogastroduodenoscopy (EGD) performed which showed gastritis and superficial ulcerations of the esophagus, stomach and proximal duodenum. The patient was discharged after 24 hours of observation and returned to the ED 4 days later with hemoptysis and shortness of breath. He was immediately transferred to a tertiary care facility. He has no past medical or surgical history. He takes no prescription or herbal medications. Social history revealed he drinks alcohol 2-3 days a week and has used marijuana and cocaine in the past. Vital signs at the tertiary care facility were: temperature, 102.3°F; pulse, 108/minute; blood pressure, 132/71 mmHg; respiratory rate 31/minute; pulse oximetry, 90% on room air. This is a well nourished male in moderate respiratory distress. Head and neck exam revealed no oropharyngeal burns or ulcerations. Lung examination revealed diffuse rhonchi and tachypnea but no accessory muscle use. Cardiovascular examination revealed tachycardia but no murmur, rub or gallop. Abdominal examination was benign and neurologic examination revealed an alert and oriented man with no focal deficits.

Laboratory investigation included a comprehensive metabolic panel that revealed: Na⁺, 132 meq/L; K⁺, 3.0 meq/L; Cl⁻, 95 meq/L; CO₂, 22 mmol/L; BUN, 57 mg/dL; Creatinine, 6.0 mg/dL; Ca²⁺, 9.2 mg/dL; Phosphorous, 3.5; Mg²⁺, 2.0 mg/dL; SGOT, 24 U/L; SGPT, 78 U/L; total bilirubin, 0.6 mg/dL. Complete blood cell count revealed WBC, 18.0 K/mcL; hemoglobin, 11.7 g/dL; hematocrit, 33.5; platelets, 162 K/mcL. A chest radiograph showed diffuse patchy infiltrates bilaterally, worse on the right than left. An arterial blood gas on room air revealed: pH, 7.47; PCO₂ 36 mmHg, PO₂, 56 mmHg; HCO₃, 25 mmol/L. A serum paraquat concentration performed by National Medical Services, Inc. four days after the ingestion was 0.08 mcg/mL (normal limit < 0.06 mcg/mL) by spectrophotometry (SP). A urine paraquat concentration also 4 days post-ingestion and by SP was 0.76 mcg/mL (asymptomatic sprayers up to 0.3 mcg/mL, urine).

Upon arrival to the tertiary care center, the patient was started on methylprednisolone, 1 g IV every day for 3 days and dexamethasone, 6 mg IV every 6 hours. He was also started on a cycle of cyclophosphamide, 1.7 g IV every day for 2 consecutive days. An infusion of acetylcysteine (Acetadote®) at a rate of 685 mg/hr was administered for 7 days as well as vitamin C and vitamin E supplementation





**UNIVERSITY OF MARYLAND
SCHOOL OF MEDICINE**

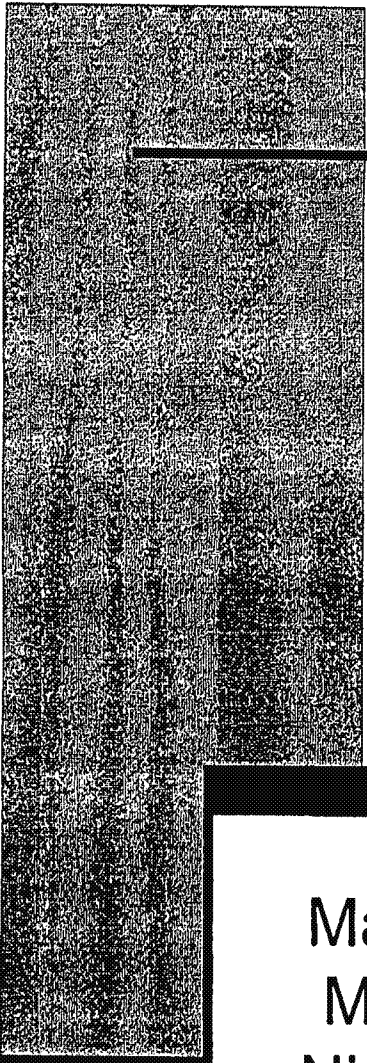
throughout the hospitalization. He required continuous veno-venous hemodialysis for 3 days followed by intermittent hemodialysis for 3 more days until his creatinine normalized to 1.4 mg/dL on HD #6 and did not require any further hemodialysis. The patient's respiratory status worsened requiring oxygen supplementation and at 2 L nasal cannula had a resting pulse oximetry of 80%. On hospital day #8, as he was moving himself to the lavatory, his pulse oximetry decreased to 70% which prompted a computed tomographic scan of the chest which revealed diffuse pulmonary fibrosis with a ground glass appearance and pneumomediastinum. An esophagram was performed and revealed no signs of perforation. Rapamycin therapy was initiated to limit any further pulmonary fibrosis on HD #12 and continued for 15 days. The patient became neutropenic with a WBC of 0.2 K/mcL prompting treatment with neupogen causing the WBC to peak at 29.6 K/mcL but returned to normal limits at 10.2 K/mcL. During his neutropenia secondary to the cyclophosphamide, the patient was covered empirically with piperacillin/tazobactam and vancomycin despite never mounting a fever or identifying a source of infection. On HD #14, the patient developed an iliofemoral deep venous thrombosis and had lovenox and coumadin therapy initiated. After HD #39, the patient's resting pulse oximetry was 90% on 2L NC, was able to perform basic activities of daily living and was stable for transfer to the inpatient psychiatric ward.

If there are any further questions about this case please feel free to contact me at 443 465 4289. Thank you.

Sincerely,

Fermin Barrueto Jr., MD
Assistant Professor
University of Maryland School of Medicine
Department of Emergency Medicine
Medical Toxicologist





Improvement in survival following paraquat ingestion after introduction of a new formulation with INTEON[®] technology in Sri Lanka

Martin Wilks, Ravindra Fernando, P L Ariyananda,
Michael Eddleston, Dave Berry, John Tomenson,
Nick Buckley, Shaluka Jayamanne, David Gunnell,
Andrew Dawson

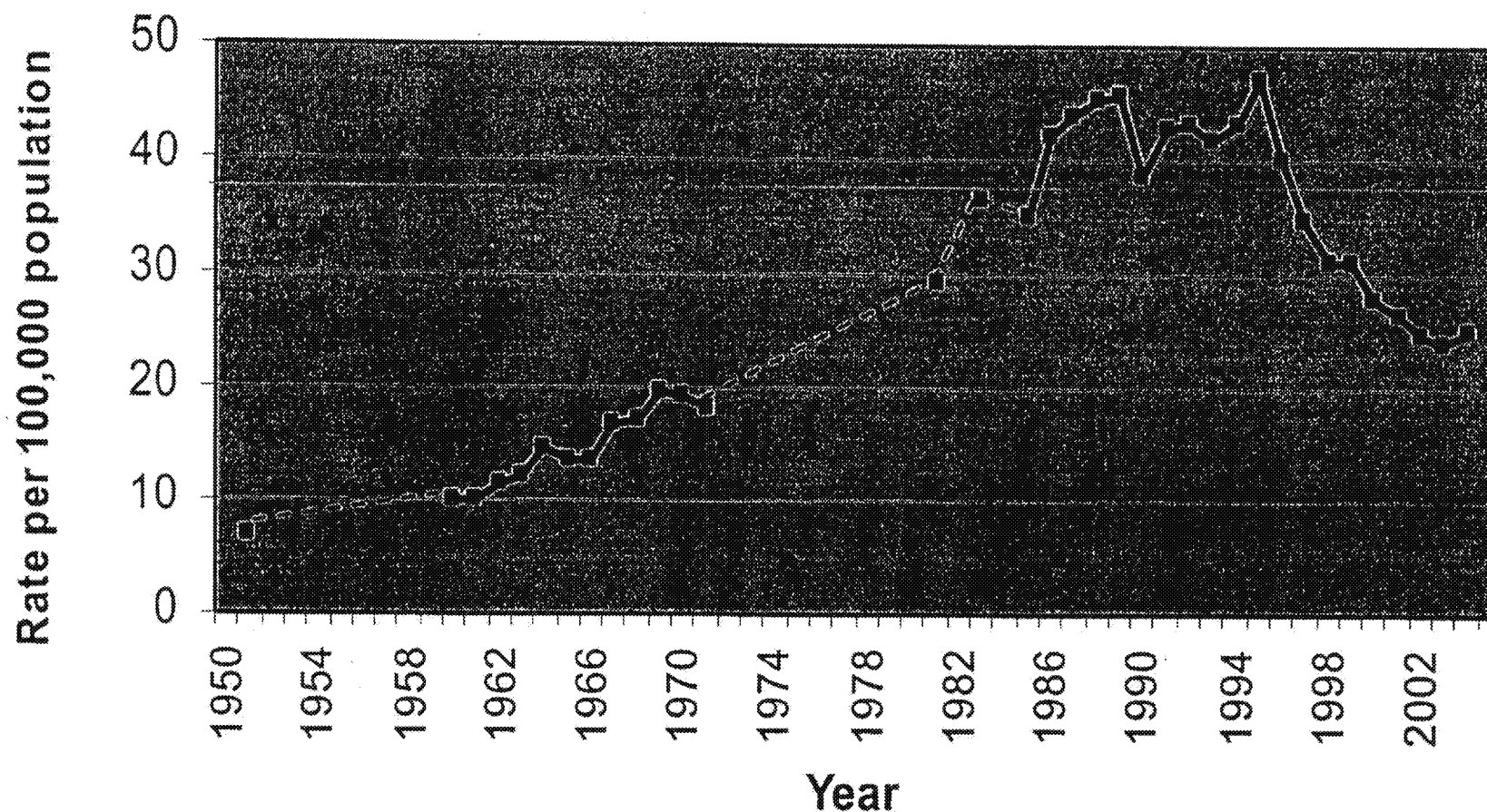
Background

- Self harm with pesticides is a significant public health concern in many developing countries.
- Recent studies estimate that as many as 300,000 deaths from pesticide self poisoning may occur in the Asia-Pacific region – accounting for up to one quarter of the world's suicides.

Phillips, Lancet, 2002, Eddleston, BMJ, 2004

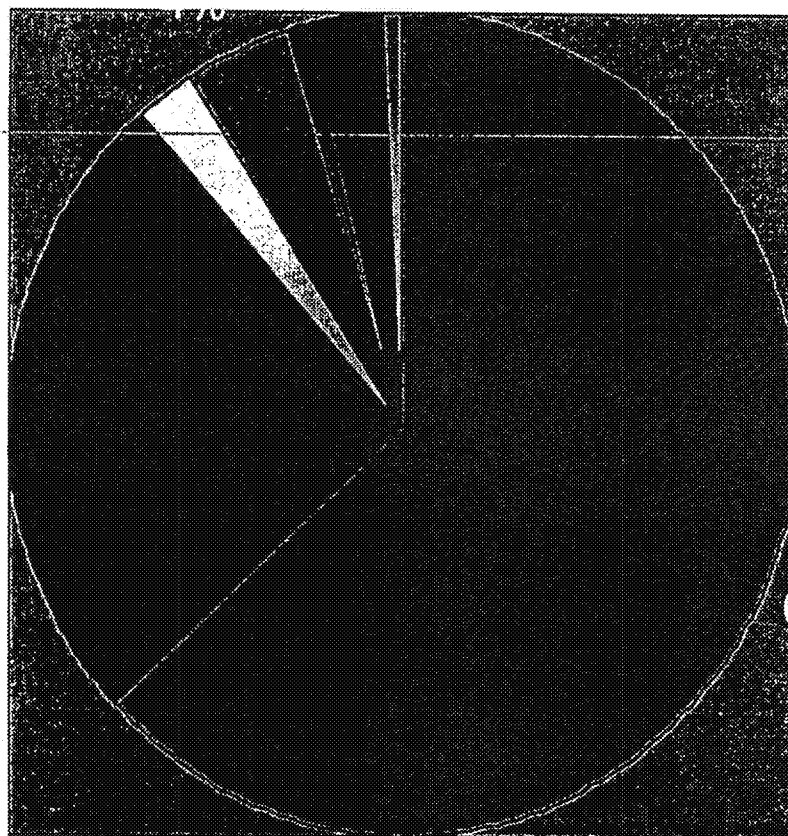
- Strategies to address this problem include
 - Limiting availability of products for self harm
 - Improving medical management of poisoning
 - Reducing the hazard of pesticide formulations

Suicide rates in Sri Lanka from 1950 - 2004



Source: National Poisons Information Centre

Methods used to commit suicide in Sri Lanka (2004)



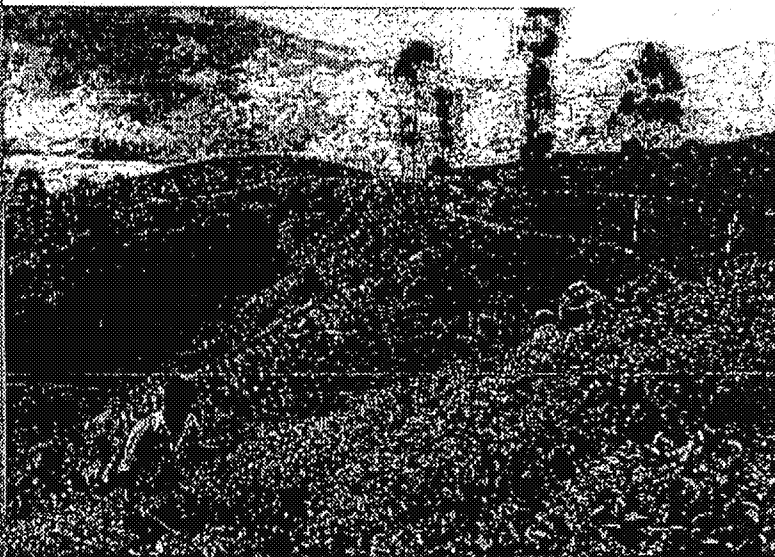
- Self poisoning
- Hanging
- Drowning
- Self immolation
- Firearm use
- Explosives
- Sharp weapons
- Jumping in front of trains/motor vehicles
- Jumping from a height
- Over dosage of drugs
- Others

Source: National Poisons Information Centre

Mortality rates of poison admissions at Anuradhapura General Hospital, Sri Lanka (2.4.02 – 13.1.03)

	# Admissions	# Deaths	Mortality Rates (%)
Oleander	350	25	7.1
Organophosphate	277	39	14.1
Other Pesticides	141	6	4.3
Medicines	101	1	1.0
Carbamates	57	4	7.0
Hydrocarbons	44	0	0
Paraquat	45	21	46.7
Unknown	56	3	5.4
Unknown Pesticides	93	9	9.7
Organochlorines	5	3	60.0
Acid	3	0	0
Alkali	4	0	0
TOTAL	1176	111	9.4

Paraquat in Sri Lankan agriculture

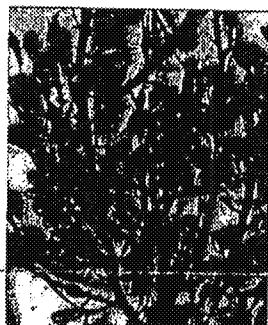


- No damage to surrounding crops
- Broad spectrum, low weed resistance
- Key crops in Sri Lanka are tea, rice and vegetables

- Non-systemic, fast acting
- Rain-fast, quickly deactivated in soil
- No tillage preserves soil structure



Paraquat INTEON[®] technology - what is it?



Acid triggered gel

Emetic

MgSO₄

Benefits:

Acid Triggered Gel: Alginate, *Ascophyllum*
Seaweed extract: coats skin, reduces
irritancy and reduces g.i. tract absorption

Emetic: more productive emesis

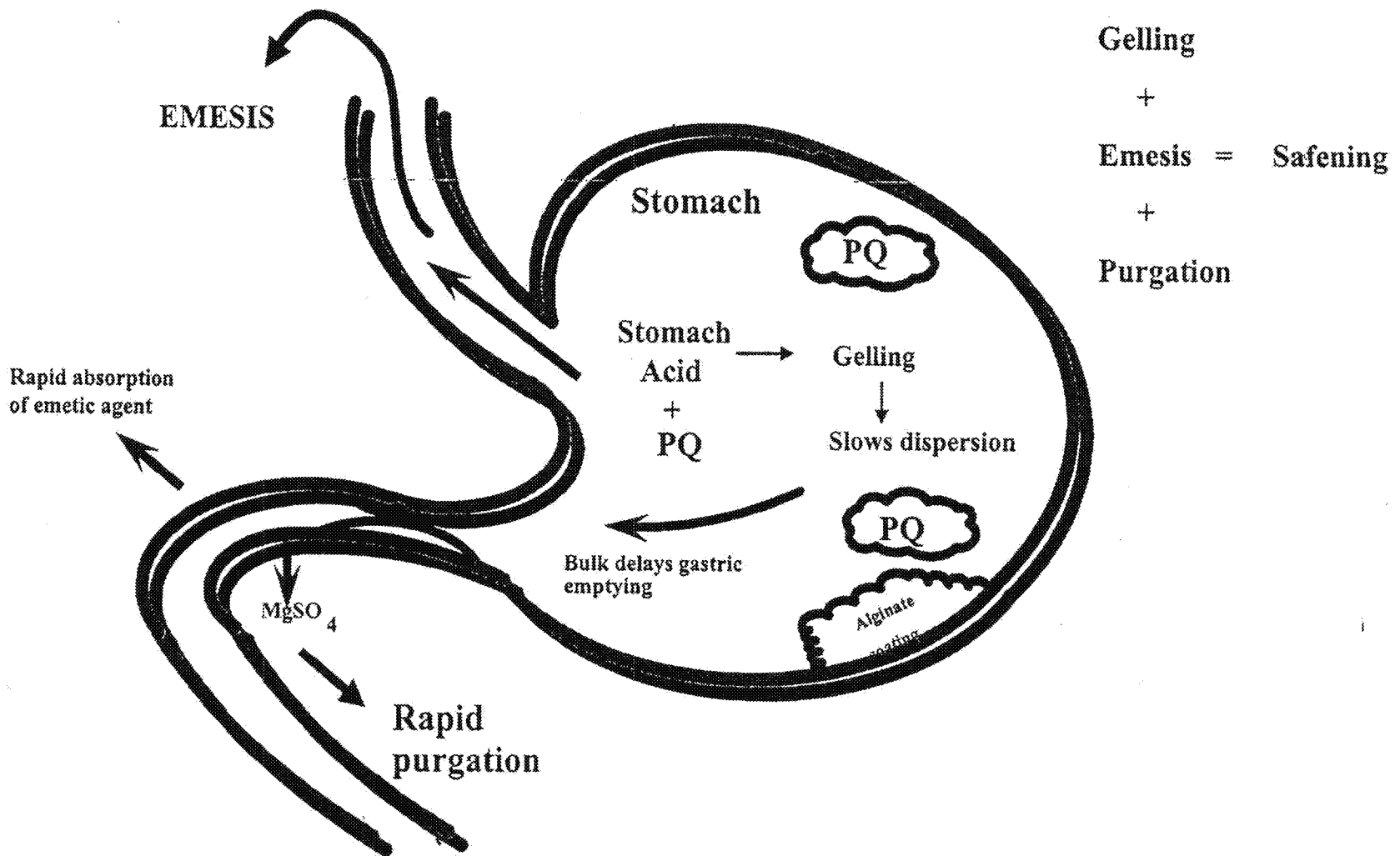
MgSO₄: purgative

slightly thicker, less odour

**Complex technology, based on
optimized package of factors**

- Efficacy
- Skin / Eye irritation improvements
- Lowering Ingestion toxicity

How does INTEON[®] work in the G.I. tract?



Survey outline

■ Objective

- Initially, set up to investigate circumstances of paraquat self-harm incidents.
- Objective modified to compare the outcome of poisoning cases following the introduction of INTEON® with the standard paraquat formulation.
 - Analytical marker was added to INTEON® to differentiate between old and new formulations

Governance

■ Legal

- New formulation registered in Sri Lanka following review by PETAC

■ Ethical

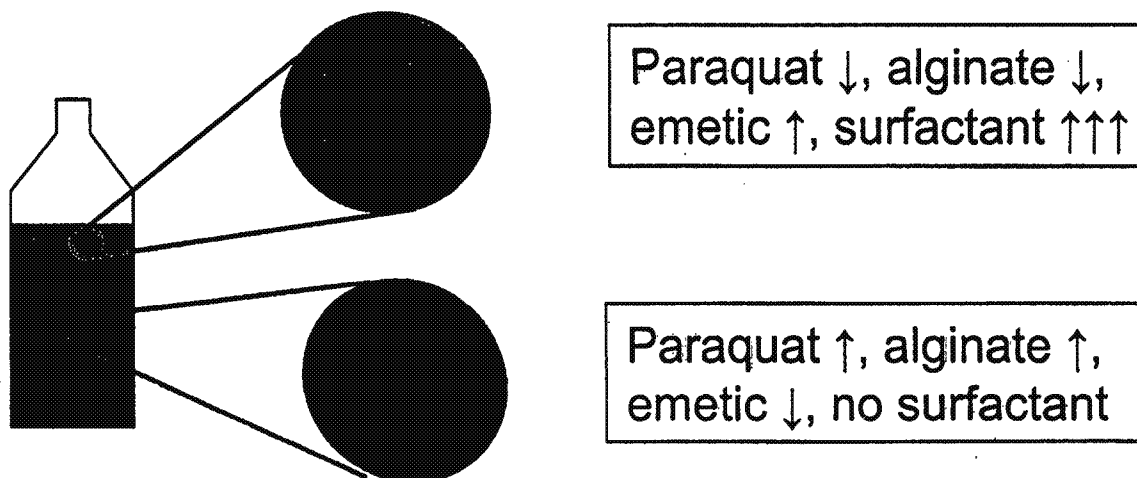
- Review and approval of the survey by Ethics Committees covering all participating hospitals

■ Scientific

- Establishment of a Steering Committee and independent Science Advisory Panel
- Commitment to publish results

Introduction of INTEON®

- INTEON® introduced into Sri Lanka Sept 2004. Standard product actively removed from distributors and wholesalers.
- Challenges with quality of formulated product – separation of ingredients into two phases



- Quality control of batches to ensure product meets minimum criteria to deliver a safening benefit.

Survey methodology

Data collected from 9 hospitals

- ACCESS questionnaire
- Key Parameters
 - Amount ingested; time of exposure, time to treatment. Outcome and treatment. Use of FE/charcoal
 - Differentiation between Gramoxone and INTEON® formulation
 - Plasma paraquat concentration
 - Vomiting data
 - Body weight, sex, age.
 - Follow-up of survivors
- Power calculation: 210 cases with ingestion of standard product and 210 with INTEON® would give 90% power to detect a x2-fold reduction in toxicity.

Statistical methodology

- Non-parametric analysis methods (Kaplan-Meier survival curve estimates and log rank tests)
- Cox's proportional hazards regression to identify prognostic factors and adjust for possible confounding factors. Covariates included:
 - estimate of ingested paraquat concentrate;
 - sex, age and body weight of subject;
 - treatments received; adsorbent use;
 - time between ingestion and start of medical care.
- Stratification by treatment centre (9 hospitals) used to account for variability in survival characteristics

Survey subjects

Total cases (1.12.2003 to 26.1.2006)	774*
Exclusions non-oral/refusals (38); Kassipu incident (36); sample with no patient record (4); inadequate information (1)	79
Cases not included during "washout"	62
Cases with standard product excluded since introduction of Inteon, post washout	47
Incidents included with standard product	297
Incidents included with Inteon (195 confirmed with plasma/urine analysis; 94 classified as 'probable' post washout period)	289

*includes 5 patients with records at 2 hospitals

Demographic details

	Standard product (n = 297)		Confirmed or probable Inteon (n = 289)	
	Mean (SD)	unknown	Mean (SD)	unknown
Age (year)	31.0 (13.7)	-	29.4 (12.5)	1
Weight (kg)	55.0 (8.1)	65	56.4 (9.0)	50
	N (%)		N (%)	
Sex: male	230 (77.4%)	-	233 (80.6%)	-

No statistically significant differences between the two groups

Clinical details

	Standard product (n=297)		Confirmed or probable Inteon (n=289)	
	N (%)	n.k.	N (%)	n.k.
Vomiting 15 min	113 (38.0%)	38	158 (54.7%)***	37
Treated 4 h	174 (58.6%)	29	157 (54.3%)	26
Fullers Earth	233 (78.5%)	1	209 (72.3%)	17
Charcoal	11 (3.7%)	1	5 (1.7%)	17
Anti-emetic	38 (12.8%)	22	50 (17.3%)	11
Cyclophos.	34 (11.4%)	27	38 (13.1%)	19
IV fluids	277 (93.3%)	3	257 (88.9%)	10
Diuretics	22 (7.4%)	12	28 (9.7%)	20
Prednisolone	50 (16.8%)	23	27 (9.3%)**	19
Lavage	162 (54.5%)	11	115 (39.8%)***	19

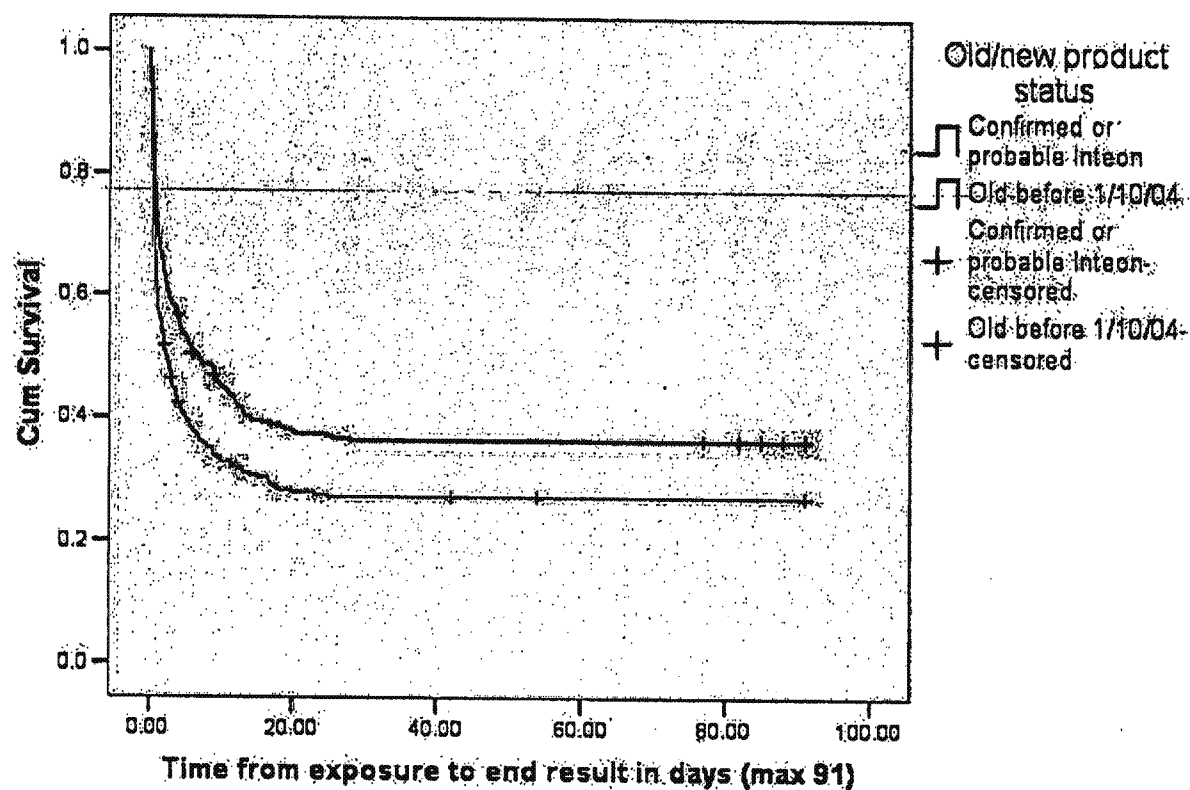
p < 0.01 vs standard product; *p < 0.001 vs standard product

Survival by Group

		Outcome 3 months after ingestion			
		Dead	Alive	Lost to follow-up	Total
Standard product before 1/10/04	Cases	215	76	6	297
	%	72.4%	25.6%	2.0%	100.0%
Confirmed or probable Inteon	Cases	183	102	4	289
	%	63.3%	35.3%	1.4%	100.0%
Total	Cases	398	178	10	586
	%	67.9%	30.4%	1.7%	100.0%

INTEON[®] and standard product survival curves

Survival Functions



Overall Comparisons

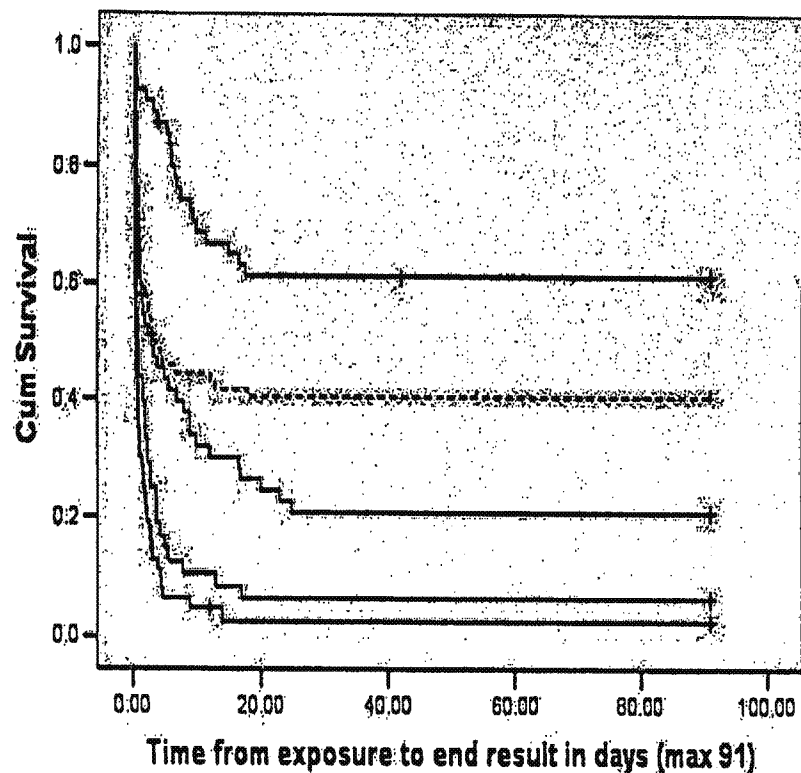
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	9.187	1	.002

Test of equality of survival distributions for the different levels group Old/new product status.

Survival by estimated ingestion amount

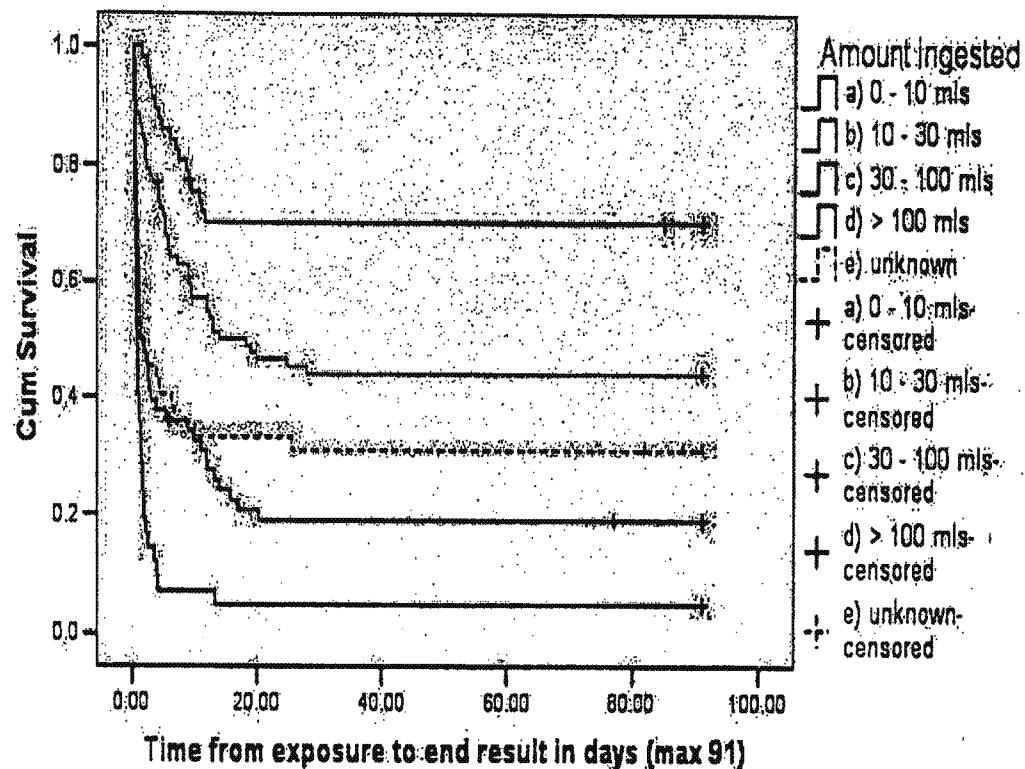
Survival Functions

group = Old before 1/10/04



Survival Functions

group = Confirmed or probable Inteon



Median survival time

	Standard product (n = 215*)		Confirmed or prob. Inteon (n = 183*)	
	Median survival (days)	IQR**	Median survival (days)	IQR**
All patients	0.9	0.5 – 3.1	1.5	0.5 – 5.4
Ingestion 0 - 30 ml	2.8	0.7 – 8.7	5.0	2.0 – 9.5

*Basis for calculation is the number of patients who died.

**IQR = Inter-quartile range

Cox PH regression – Log Dose Stratification by Centre

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	90% CI for Exp(B)	
							Lower	Upper
group	-.366	.129	8.018	1	.005	.694	.538	.893
age50	.911	.183	24.757	1	.000	2.487	1.737	3.561
sex	.334	.160	4.384	1	.036	1.397	1.022	1.910
weight	.019	.009	4.778	1	.029	1.019	1.002	1.036
absorb	.137	.180	.576	1	.448	1.146	.806	1.631
rx4hrs	.068	.132	.266	1	.606	1.070	.827	1.385
lavage	.143	.148	.937	1	.333	1.154	.863	1.543
Indose	.649	.053	50.613	1	.000	1.913	1.725	2.122

Potency estimate = $\text{Exp}(-0.366/0.649) = 0.57$ i.e. an individual would need to ingest 1.8 times more Inteon than standard product to have the same effect.

Sensitivity Analysis

Cox PH Comparison of Confirmed INTEON® (201) and all Old cases (382) - Stratification by Centre

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
groups2	-.426	.127	11.232	1	.001	.653	.509	.838
age50	.857	.182	22.145	1	.000	2.357	1.649	3.368
sex	.286	.155	3.424	1	.064	1.331	.983	1.803
weightm	.016	.008	3.736	1	.053	1.016	1.000	1.033
absorb2	.115	.179	.413	1	.521	1.122	.790	1.594
rx4hrs	.394	.127	9.597	1	.002	1.483	1.156	1.904
lavagey	.020	.147	.019	1	.890	1.021	.766	1.361
Indose	.595	.050	139.892	1	.000	1.813	1.643	2.001

Potency estimate = $\text{Exp}(-0.426/0.595) = 0.49$ i.e. an individual would need to ingest 2.0 times more Inteon than standard product to have the same effect.

Summary

- The overall survival rate is increased from 25.6% to 35.3% which is considered to be clinically significant
- All statistical analyses indicate that this was due to a real difference between the two products
- The correlation between amount ingested and survival was strong; in all ingestion sub-groups, INTEON[®] showed increased survival
- Patients who have ingested a lethal amount of product survive longer with INTEON[®], raising the prospect of more opportunities for intervention medicine

Conclusion

- The survey has shown that INTEON® technology significantly improves the survival of patients following paraquat ingestion

Next steps

- A fully homogenous INTEON® formulation has been submitted for registration in Sri Lanka
- It is proposed that monitoring will continue. (Protocol to be submitted to Ethics Committees)
- It is anticipated that the fully homogenous INTEON® formulation will lead to a further reduction in toxicity

Acknowledgements

- Mr Justin Perera (CIC Ltd)
- Mr Bruce Woollen (Syngenta)
- Miss Nilupa Herath (SACTRC)
- Dr Fahim Mohamed (SACTRC)
- Professor Keith Hawton (Oxford)

- Dr Sasanka Gunaratne
- Dr Hasantha Ranganath
- Dr Lumbini de Silva Harris
- Dr K Chathurika

Plus the many consultants, interns and pre-interns who have aided us in the data collection across Sri Lanka over the past few years.

The survey was funded by Syngenta Crop Protection AG, Switzerland

McDonald Mary USGR

From: Rudolph Tiffany USGR
Sent: Tuesday, September 26, 2006 11:03 AM
To: McDonald Mary USGR
Subject: FW: Follow-up to question from August 30th Meeting with Syngenta

From: Abbott John USGR
Sent: Monday, September 25, 2006 3:36 PM
To: herndon.george@epa.gov
Cc: Johnson.Hope@epamail.epa.gov; Tompkins.Jim@epamail.epa.gov
Subject: Follow-up to question from August 30th Meeting with Syngenta

Dear Jeff,

First, on behalf of Syngenta I want to take this opportunity to thank you and the others for your time and willingness to meet with us regarding our proposed paraquat study. During our discussion, you asked a question seeking clarity regarding use of capsules as the proposed method for animal dosing in this study. Below is some additional information that explains our rationale and support for this methodology. Upon review of the information below, please contact me if you have any additional follow-up questions. As noted during our meeting, we are on an accelerated timeframe to initiate this acute tox study. Therefore, we welcome and look forward to any timely input that you could provide with regards to our proposed study design.

Thanks in advance for your assistance.

Rationale for use of capsule dosing in proposed dog studies with Inteon and non-Inteon paraquat formulations

The objective of the studies is to evaluate paraquat absorption and consequent toxicity following oral ingestion across a range of dose levels. The main site of absorption of paraquat is the small intestine (Heylings 1991). When human ingestion occurs by drinking a paraquat product, the paraquat formulation is quickly transferred to the stomach. The canine studies should therefore provide accurate doses of paraquat to the stomach, thereby allowing for appropriate evaluation of systemic paraquat absorption and consequent toxicity. In practical terms, oral administration to the dog could be by gavage or capsule, and the two methods have been shown to provide similar kinetics of paraquat absorption into the blood in dogs (Heylings et al 2004). However, in the proposed studies, capsule administration is protocolled since:

- Small doses will be required (some <0.5ml formulation) and these can be more accurately dispensed into a capsule. The more viscous nature of the Inteon formulations will make this even more appropriate
- The reproducibility of dosing small volumes across animals is considered greater with capsule
- There is a reduced risk of misdosing or inadvertent inspiration of small quantity into lungs
- This will give consistency with data from recent CTL studies, which have used capsule dosing
- It is important to minimize stress to the animals, and capsule dosing is a less stressful procedure

References

Heylings JR (1991) Gastrointestinal absorption of paraquat in the isolated mucosa of the rat. *Toxicol Appl Pharmacol* **107** 482-493.

Heylings J, Swain C and Brammer A (2004). Paraquat: Gramoxone 200 g/L SL formulation – Toxicokinetics in the dog. CTL Report no. CTL/026118/RESEARCH REPORT.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
336-632-7074

336-253-9666 (mobile)
john.abbott@syngenta.com



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

OCT 5 2006

CERTIFIED MAIL – RETURN RECEIPT REQUESTED

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Jerry Wells
Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, North Carolina 27419-8300

Re: Freedom of Information Act Request HQ RIN 0862-06

Dear Mr. Wells:

The EPA Office of Pesticide Programs (OPP) has received a request under the Freedom of Information Act (FOIA) for a copy of correspondence, including emails, on or after January 1, 2004, between EPA and Syngenta Crop Protection, Inc. that relate to Paraquat Dichloride. In accordance with 40 CFR 2.204(e)(1), we are asking you to substantiate your claim of confidentiality for the enclosed record.

The EPA Office of General Counsel will be making a final determination concerning this information. If you believe that some or all of the information is entitled to confidential treatment, please specify which portions of the information you consider confidential. Please be specific when identifying the information subject to your claim. Any information not specifically identified as subject to a confidentiality claim will be disclosed to the requester without further notice to you. For each item or class of information that you identify as being subject to your claim, please answer the following questions:

1. For what period of time do you request that the information be maintained as confidential? If the occurrence of a specific event will eliminate the need for confidentiality, please specify that event.
2. Information submitted to the EPA becomes stale over time. Why should the information you claim as confidential be protected for the time period specified in your answer to question 1?
3. What measures have you taken to protect the information claimed as confidential? Have you disclosed the information to anyone other than a governmental body or someone who is bound by an agreement not to disclose the information further?

If so, why should the information still be considered confidential?

OCT 12 2006
x

Internet Address (URL) • <http://www.epa.gov>
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4. Has any governmental body made a determination as to the confidentiality of the information? If so, please attach a copy of the determination.

5. Is the information contained in any publicly available material such as promotional publications, annual reports, articles, etc.? Is there any means by which a member of the public could obtain access to the information?

6. For each category of information claimed as confidential, discuss with specificity why release of the information is likely to cause substantial harm to your competitive position. Explain the nature of those harmful effects, why they should be viewed as substantial, and the causal relationship between disclosure and such harmful effects. How could your competitors make use of this information to your detriment?

7. Do you assert that the information is voluntarily submitted as defined at 40 CFR Section 2.201(i)? If so, explain why, and how disclosure would tend to lessen EPA's ability to obtain similar information in the future.

8. Any other issue you deem relevant.

Please note that you bear the burden of substantiating your confidentiality claim pursuant to 40 CFR 2.208(e). Conclusory allegations will be given little or no weight in the determination. Be advised that the information described by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Section 10(d)(1) (A), (B), and (C) is not automatically entitled to confidential treatment. Disclosure of such information would only be prohibited, by FIFRA Section 10(b), if the information is eligible for confidential treatment as described by 40 CFR 2.208.

If you wish to claim any information in your response to this letter as confidential, you must mark the response CONFIDENTIAL or with a similar designation, and must bracket all text so claimed. Information so designated will be disclosed by EPA only to the extent allowed by, and by means of the procedures set forth in 40 CFR Part 2. If you fail to claim the information as confidential upon submission, it may be made available to the public without further notice to you.

Your reply can be mailed to the following address:

Sherri Y. Street, Chief
Public Information and Records Integrity Branch (7502P)
Information Resources and Services Division
Office of Pesticide Programs
Environmental Protection Agency
Washington, D.C. 20460

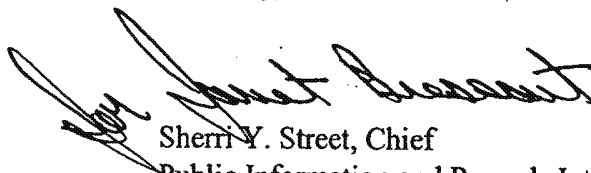
Or your reply can be delivered to the following address:

Document Processing Desk (7504P)
Office of Pesticide Programs
U.S.. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, Virginia 22202-4501

Your comments must be postmarked or hand-delivered by the 15th working day after your receipt of this letter. **If you intend to submit timely comments, please notify Janet Bressant by phone at (703) 305-6445, by email at bressant.janet@epa.gov or by mail at the address above. EPA will only inquire into the whereabouts of comments not received if notice of your intention to submit them was provided. Failure to submit timely comments will be regarded as a waiver of your confidentiality claim and EPA will release the information.**

You may request an extension of the 15-day deadline. Except in extraordinary circumstances, no extension will be granted without the permission of the requestor. Should you have any questions in this matter, please contact Janet Bressant at (703) 305-6445.

Sincerely,



Sherri Y. Street, Chief
Public Information and Records Integrity Branch
Information Technology and Resources Management
Division
Office of Pesticide Programs

Enclosure

Freedom of Information Act Request – HQ RIN 0862-06

Record enclosed for substantiation:

January 12, 2005, email from Jerry Wells, Syngenta to Jim Tompson and Hope Johnson, EPA,
with attachment:

Inteon Presentation



jerry.wells@syngenta.com
01/12/2005 01:49 PM

To tompson.jim@epamail.epa.gov, Hope
Johnson/DC/USEPA/US@EPA
cc
bcc
Subject Inteon Presentation.pdf

<<Inteon Presentation.pdf>>

Jim and Hope,

Attached are the slides that Dr. Clapp presented the other day. A copy was
also sent to HED.

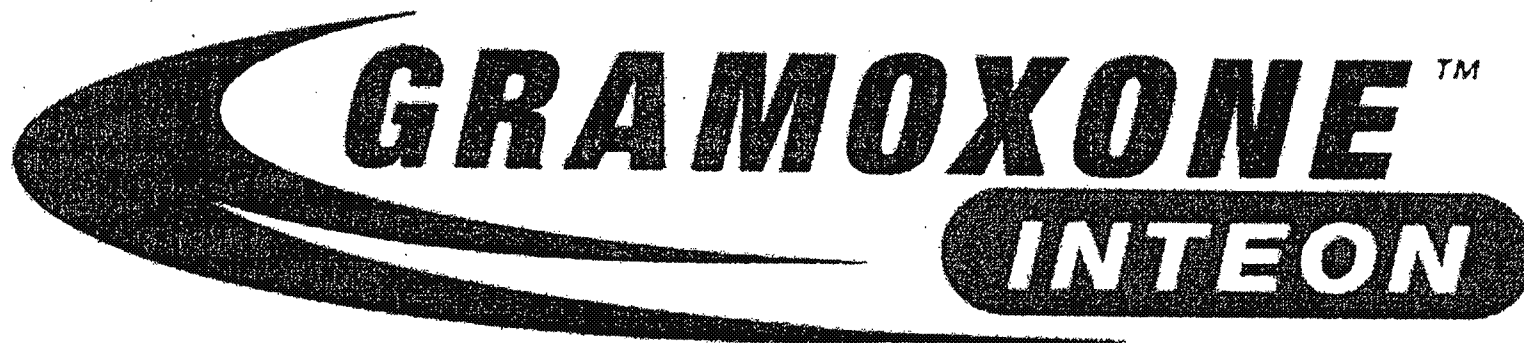
Regards,

Jerry



Inteon Presentation.pdf

1



A new Paraquat formulation

Dr Mike Clapp
Senior Product Toxicologist



CONFIDENTIAL BUSINESS INFORMATION



Paraquat INTEON Technology

- **Existing paraquat formulations**
 - offer outstanding weed control in a broad range of crops
 - Does not pose unacceptable risk when used according to the label.
- **From toxicology studies**
 - they show toxicity by oral route
 - they show irritancy to skin and eye
- **Syngenta has therefore been conducting an extensive programme of research with the aim of reducing this toxicity**



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Paraquat INTEON Technology

- **Existing paraquat formulations**
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 - they show irritancy to skin and eye
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4

Paraquat INTEON Technology

Site of absorption of paraquat from the gastrointestinal tract

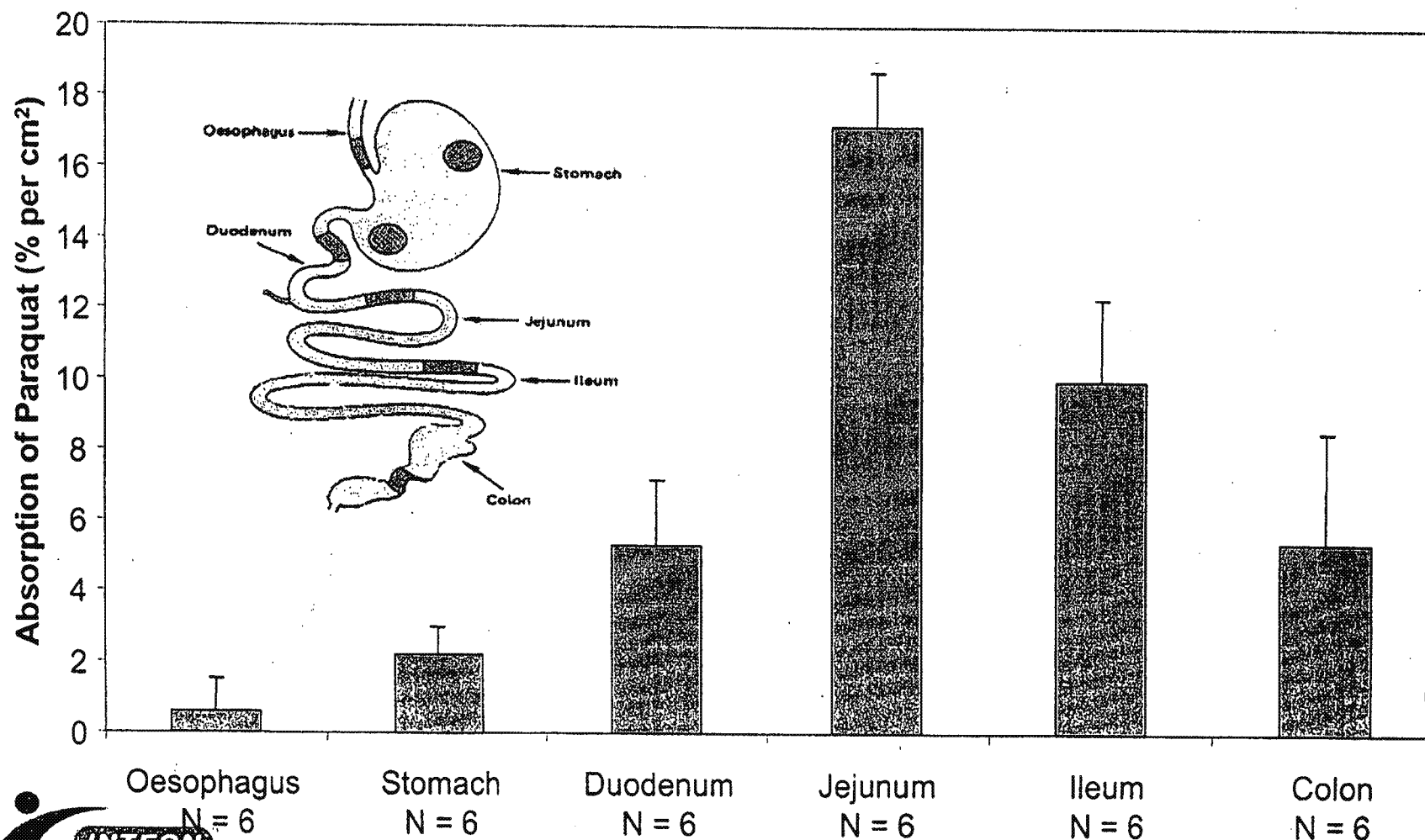


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Paraquat Absorption from the Gastrointestinal Tract

CONFIDENTIAL BUSINESS INFORMATION



Heylings JR *Toxicol. Appl. Pharmacol.* 107, 482-493, 1991

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6

INTEON Technology

- Syngenta have been evaluating a wide range of soluble polymers in the quest to identify safer formulations.
- Gelling agents have known protective effects in pharmaceutical preparations for alleviating irritation in stomach and skin.
- Following an extensive research programme over several years, inclusion of alginates in the formulations has been shown to offer benefits without interfering with herbicidal action.



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INTEON Technology

- Alginates are carbohydrates of polymannuronic and polyguluronic acid
- They are non toxic and extensively used in the food and pharmaceutical industries
- Gramoxone INTEON contains:
 - 200 or 240g/l paraquat ion
 - an alerting blue/green dye, an olfactory alert and the effective emetic as stipulated in the FAO specification for paraquat products
 - INTEON technology

Ascophyllum Seaweed extract



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Paraquat INTEON technology

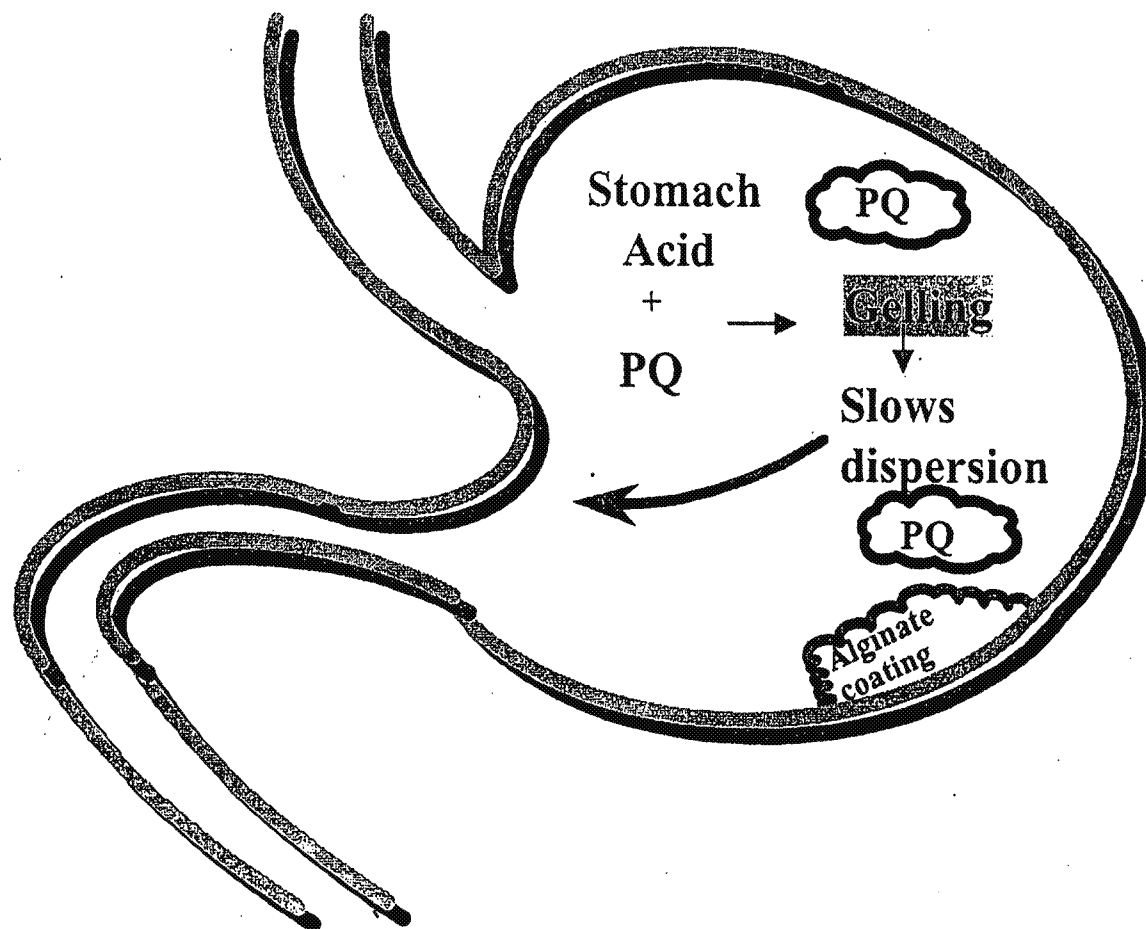
Theoretical mechanism for oral safening (gelling, emesis and purgation)



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Gastrointestinal physiology

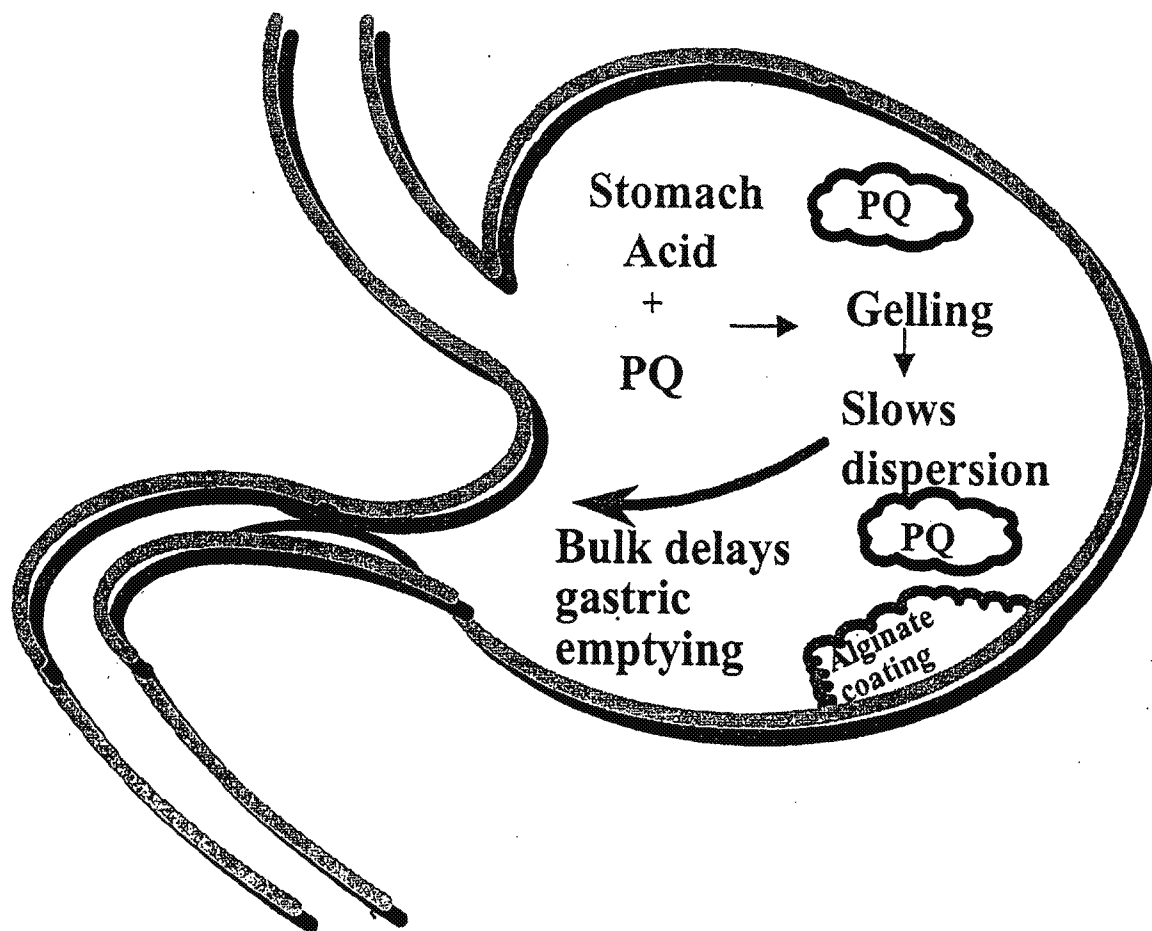


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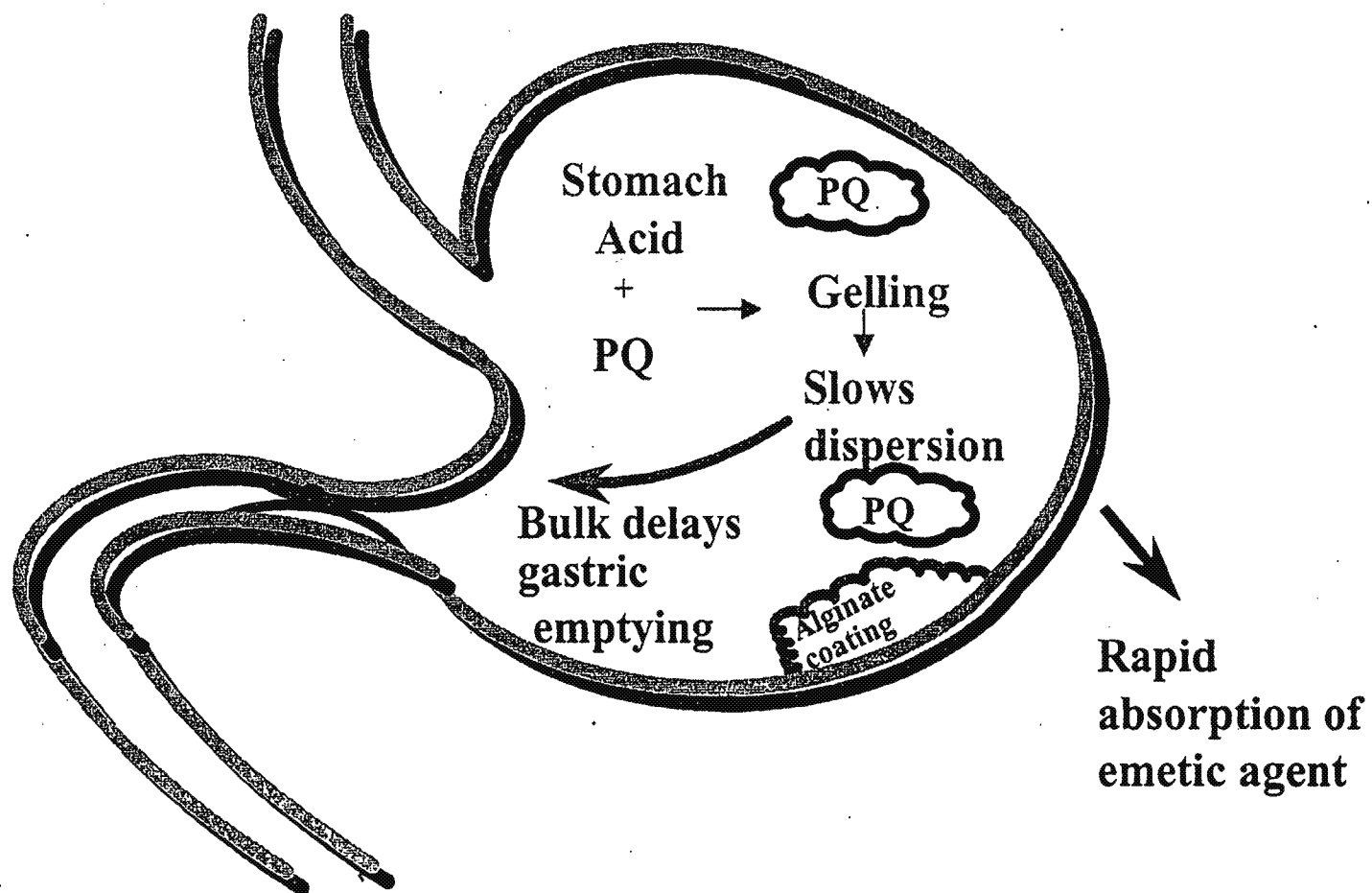
Gastrointestinal physiology



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Gastrointestinal physiology

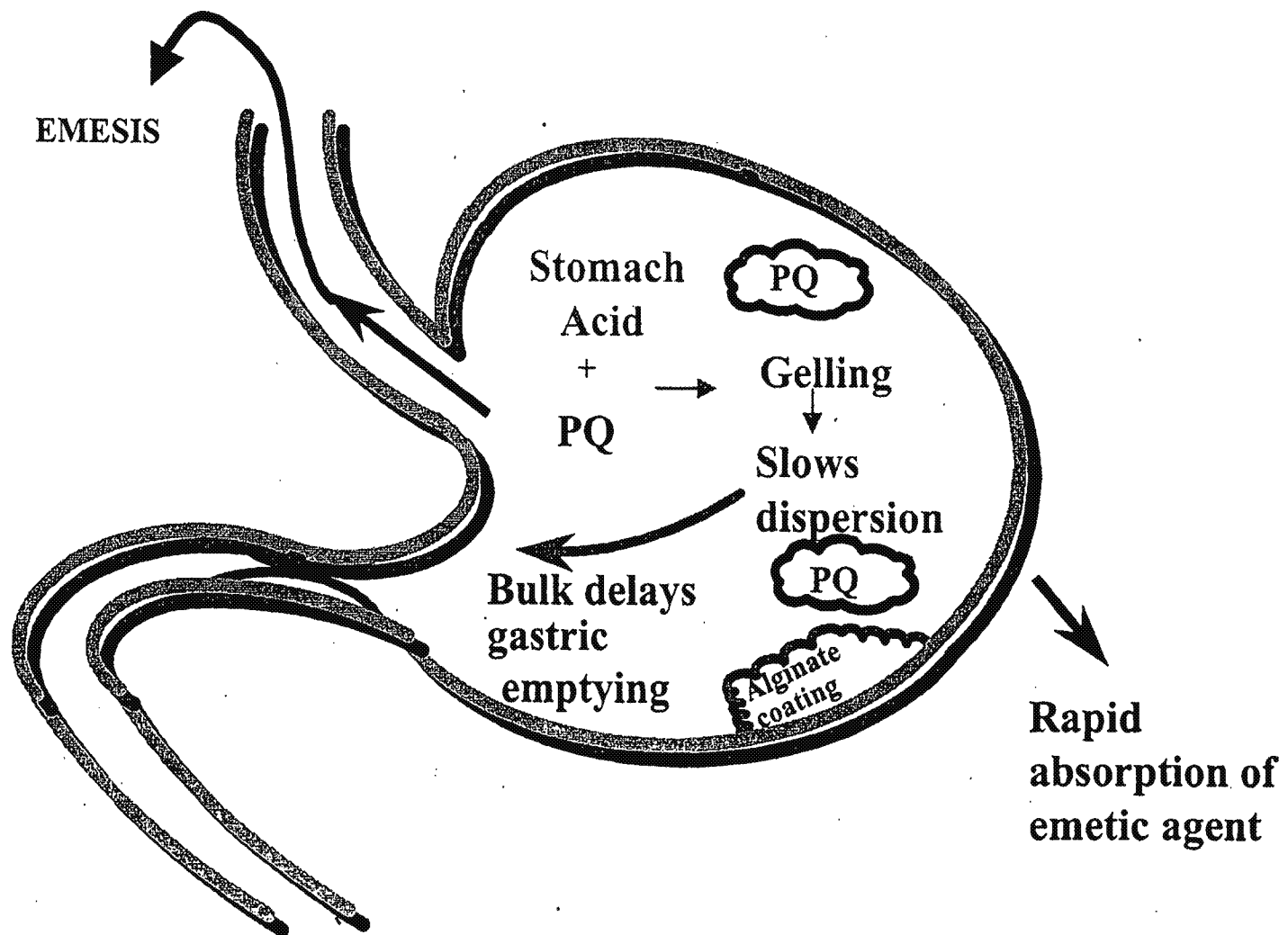


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Gastrointestinal physiology

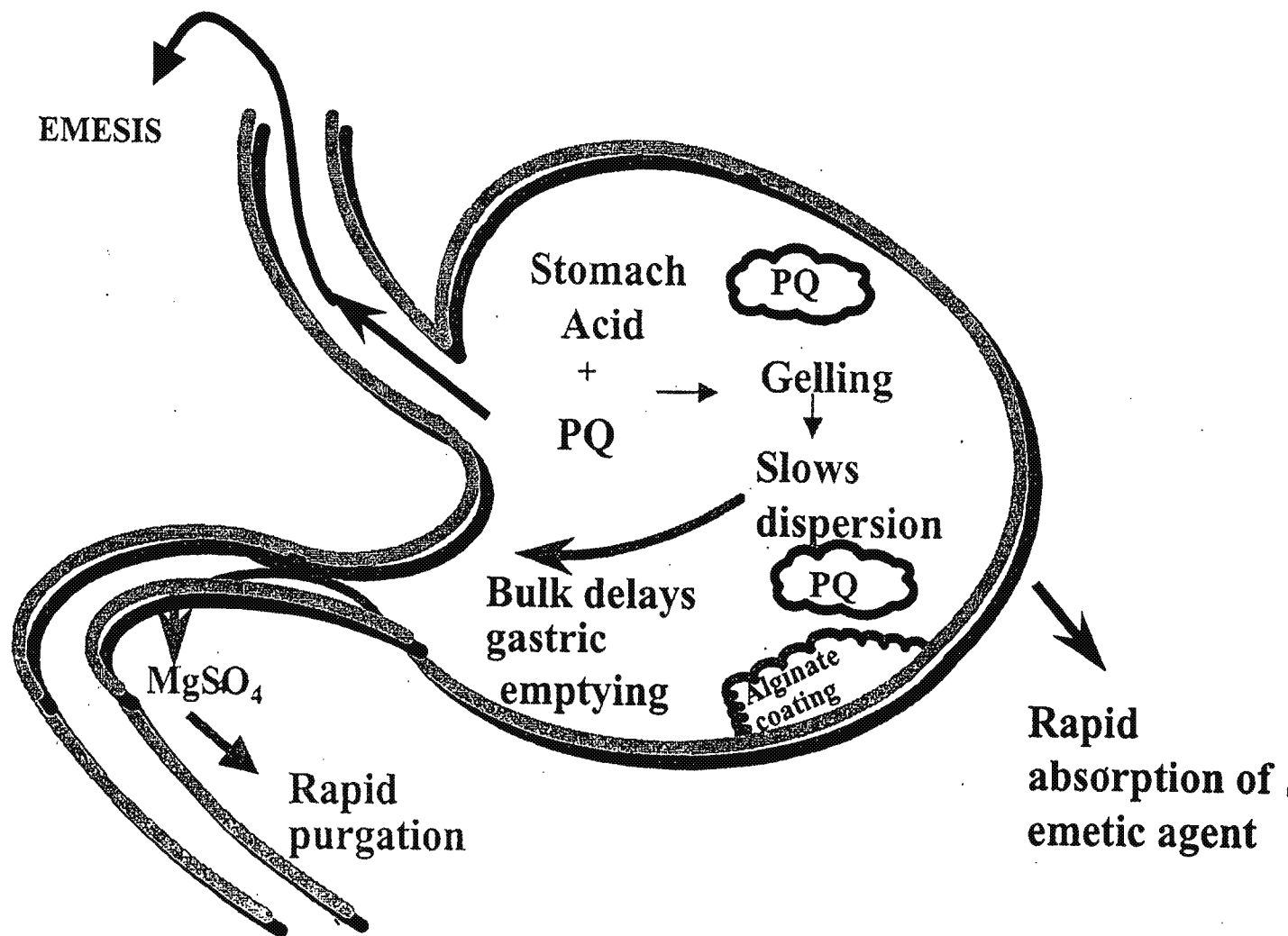


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Gastrointestinal physiology

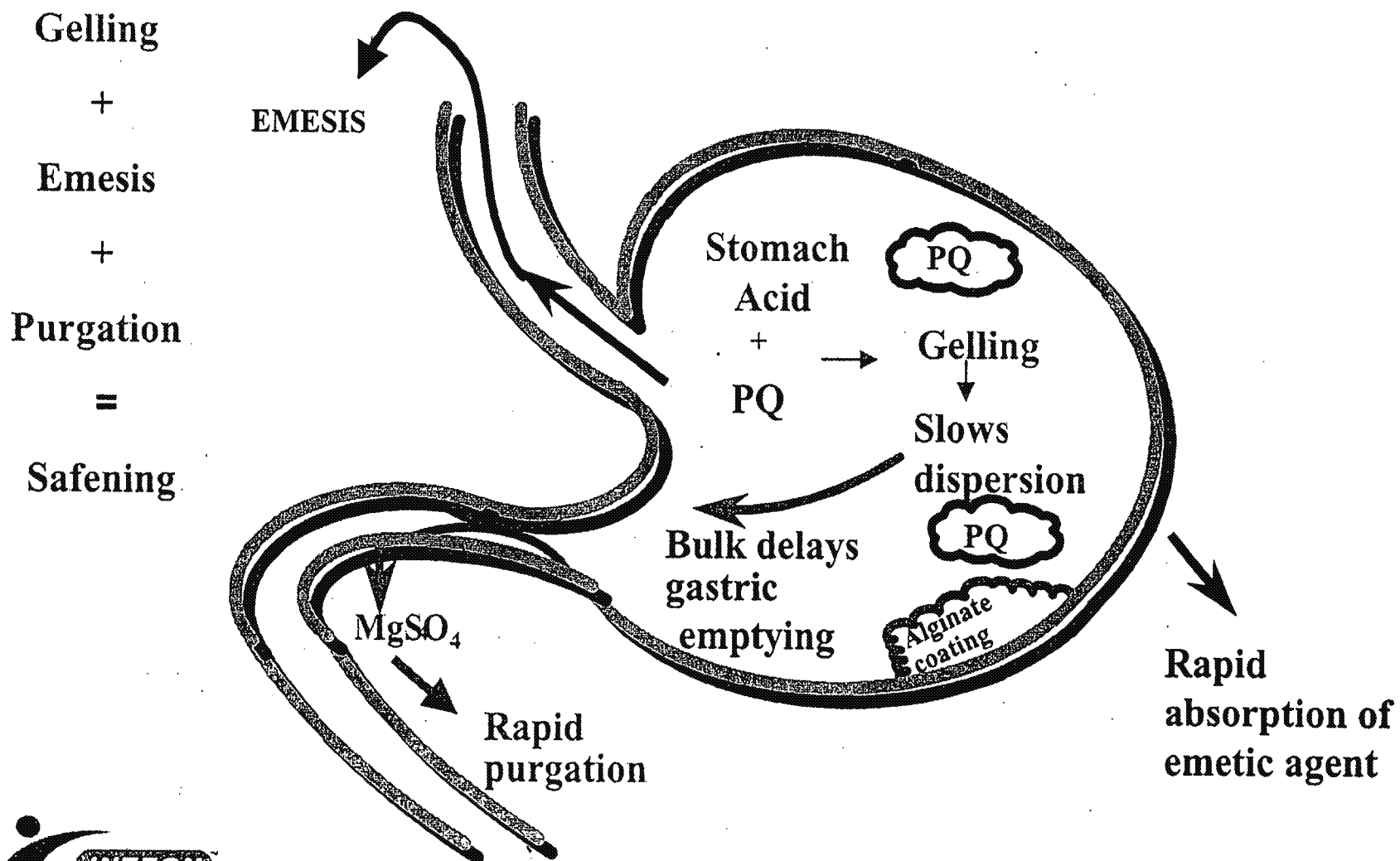


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Gastrointestinal physiology



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Studies undertaken

1. Toxicokinetic study on a Gramoxone INTEON 200g/l formulation - A3879BU
 - Subsequently compared to historic data on a Gramoxone 200g/l formulation A3879D
2. Toxicokinetic study on a Gramoxone INTEON 240g/l formulation – A7813K
 - Comparison with a contemporaneous Gramoxone 200g/l formulation A3879D



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Toxicokinetic: Study design

- A group of three male beagle dogs
- Gramoxone Inteon 200g/l SL formulation (A3879BU)
- Oral doses by capsule
- On 5 occasions at monthly intervals
- The nominal dose levels used were 8, 16, 32, 64 and 128mg paraquat ion/kg bw.
- Achieved dose levels of 46, 92, 184, 368 and 736mg A3879BU formulation/kg bw.
- General clinical observations, bodyweights and food consumption were measured frequently throughout the study.



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Toxicokinetic: Study design

- **Following each dose dogs were:**
 - observed continuously for 4 hours and frequently during the remainder of the day.
 - incidences of emesis were recorded and vomit and faeces were removed immediately to prevent possible re-ingestion
 - Blood samples were taken at intervals (0.5, 1, 2, 4, 7, 12 and 24h) following each dose to enable a plasma profile of paraquat and PP796 (the emetic) to be determined
 - Veterinary examinations (including cardiac and pulmonary auscultation) were made prior to each dose, during the observation period, and prior to termination
 - Clinical pathology parameters were measured from blood samples taken prior to and then 24 hours after each dose.
 - At the end of the study period, the animals were killed and examined *post mortem*. Kidney and lung samples were taken for subsequent histopathological examination.



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Results

- All of the animals were clinically normal and remained in excellent clinical condition throughout the studies
- However following the highest dose of 736mg A3879BU formulation, clinical signs including prolonged retching, abdominal discomfort and decreased activity were observed for up to 3 hours after dosing.
- One animal, which had the highest peak plasma paraquat level, showed additional signs of inappetance, weight loss and decreased activity for several days following this dose.
- Kidney and liver function tests and veterinary examination have shown no adverse effects in any dog over this dose range (46 - 736mg A3879BU formulation/kg)
- At termination one animal had some pathology of the lung (slight focal interstitial fibrosis, slight alveolar macrophage infiltration and slight focal pneumonocyte hypertrophy) consistent with signs of paraquat toxicity.
- The other 2 dogs had no pathology of the lung.



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Paraquat INTEON Technology

Evidence for reduced oral toxicity in the dog



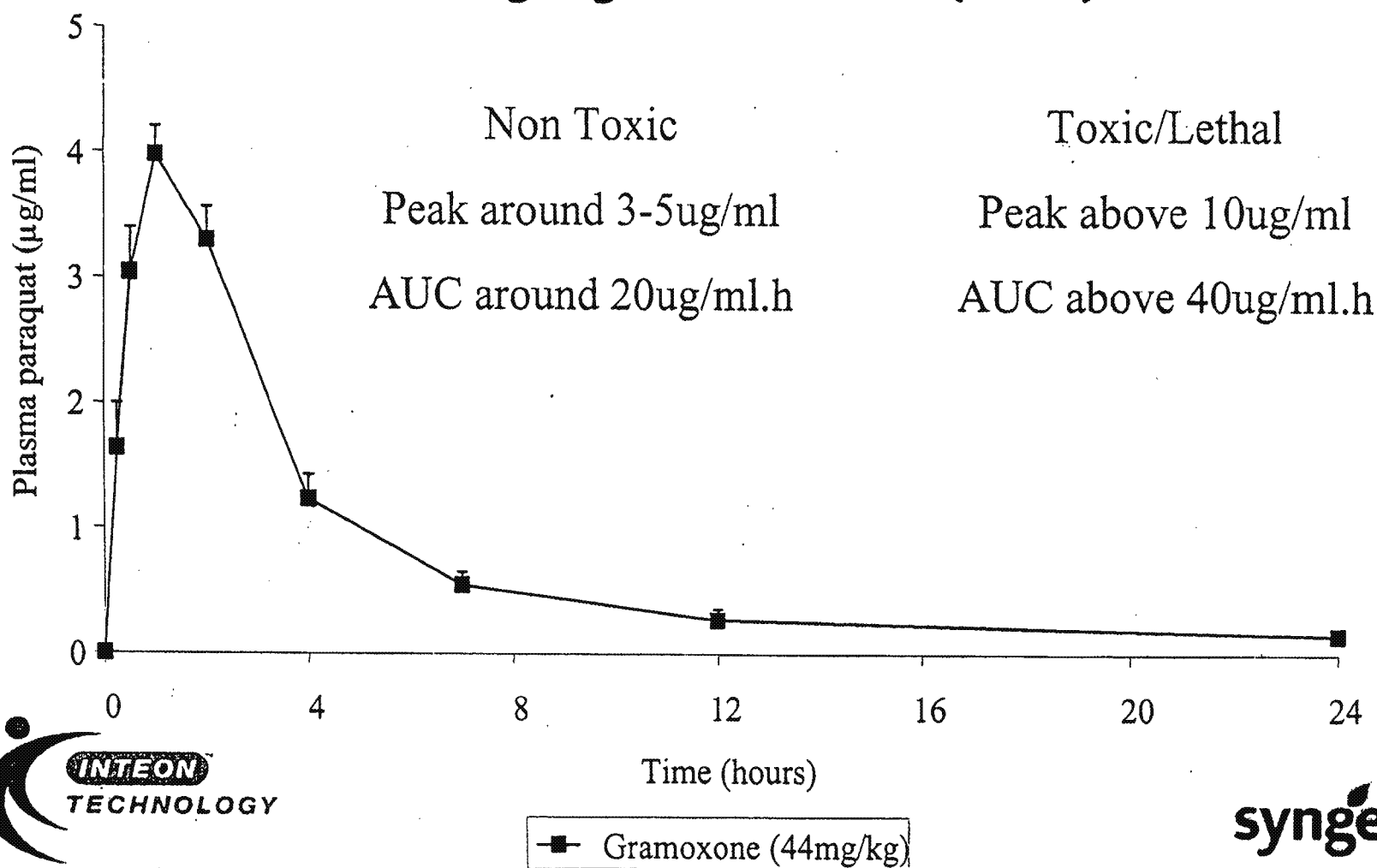
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Paraquat Absorption in the Dog

Plasma paraquat following a non-toxic oral dose of Gramoxone 44mg/kg formulation (n=21)



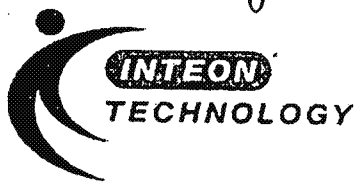
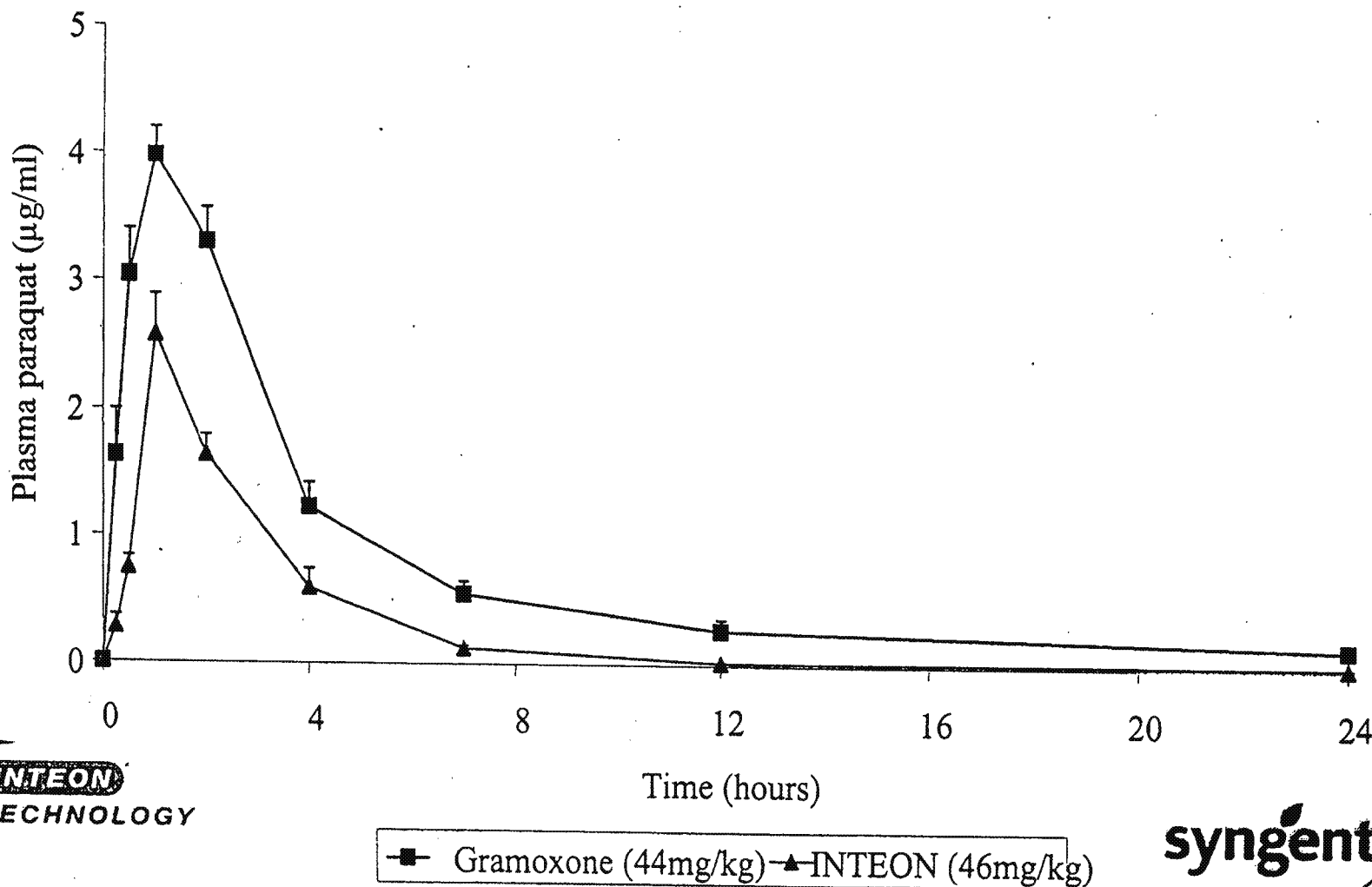
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Paraquat Absorption in the Dog

Plasma paraquat following the same oral dose of paraquat as Gramoxone or Gramoxone INTEON



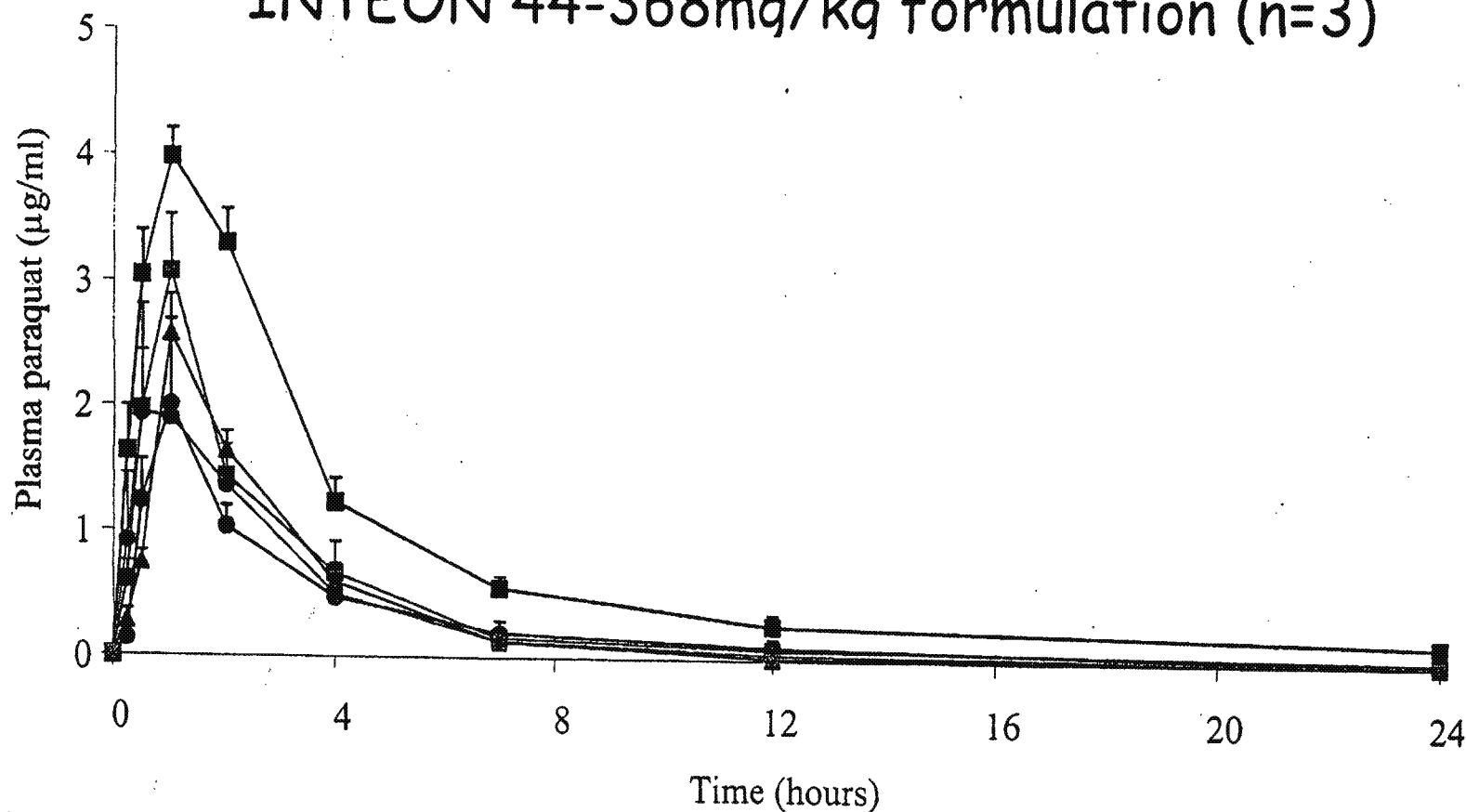
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22

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Paraquat Absorption in the Dog

Plasma paraquat following an oral dose of Gramoxone
INTEON 44-368mg/kg formulation (n=3)



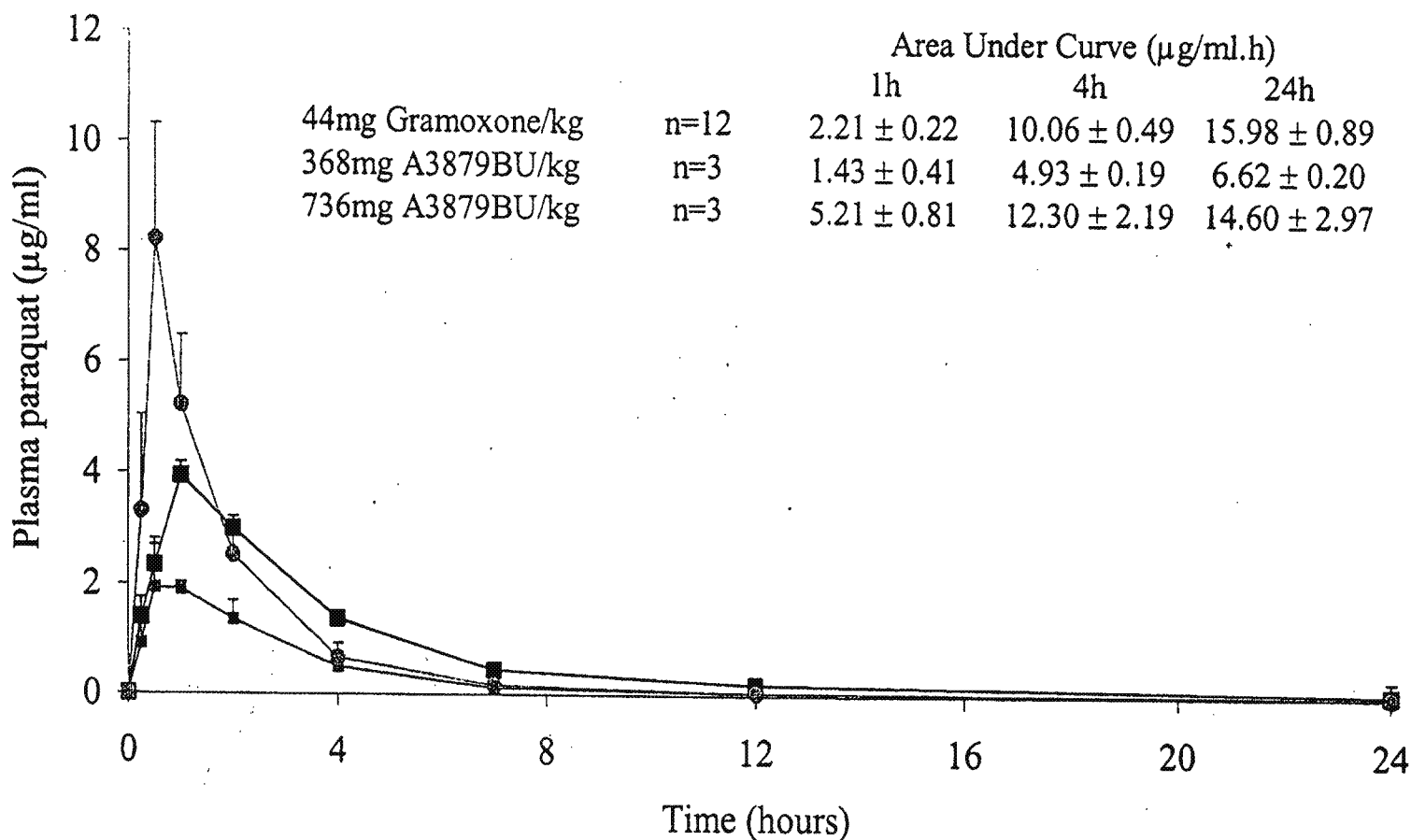
Gramoxone (44mg/kg) INTEON (46mg/kg) INTEON (92mg/kg)
INTEON (184mg/kg) INTEON (368mg/kg)

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Plasma paraquat following an oral dose of Gramoxone or 200g/l INTEON (44-736mg formulation/kg) in male dogs



■ 44mg Gramoxone/kg ▣ 368mg A3879BU/kg ● 736mg A3879BU/kg

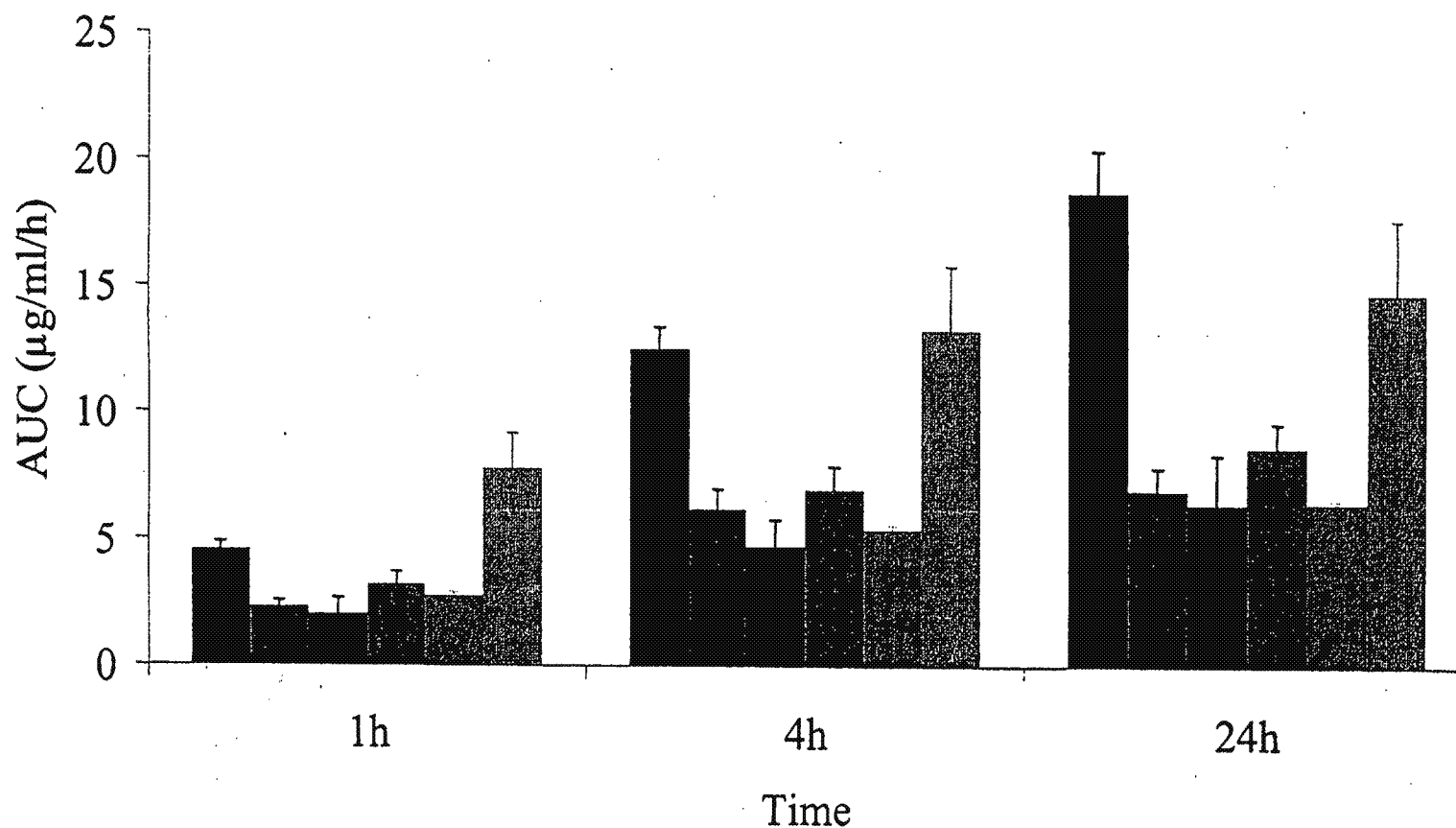


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Plasma paraquat AUC values following an oral dose of 200g/l INTEON (46 - 736mg formulation/kg b wt.) in dogs (n = 3)



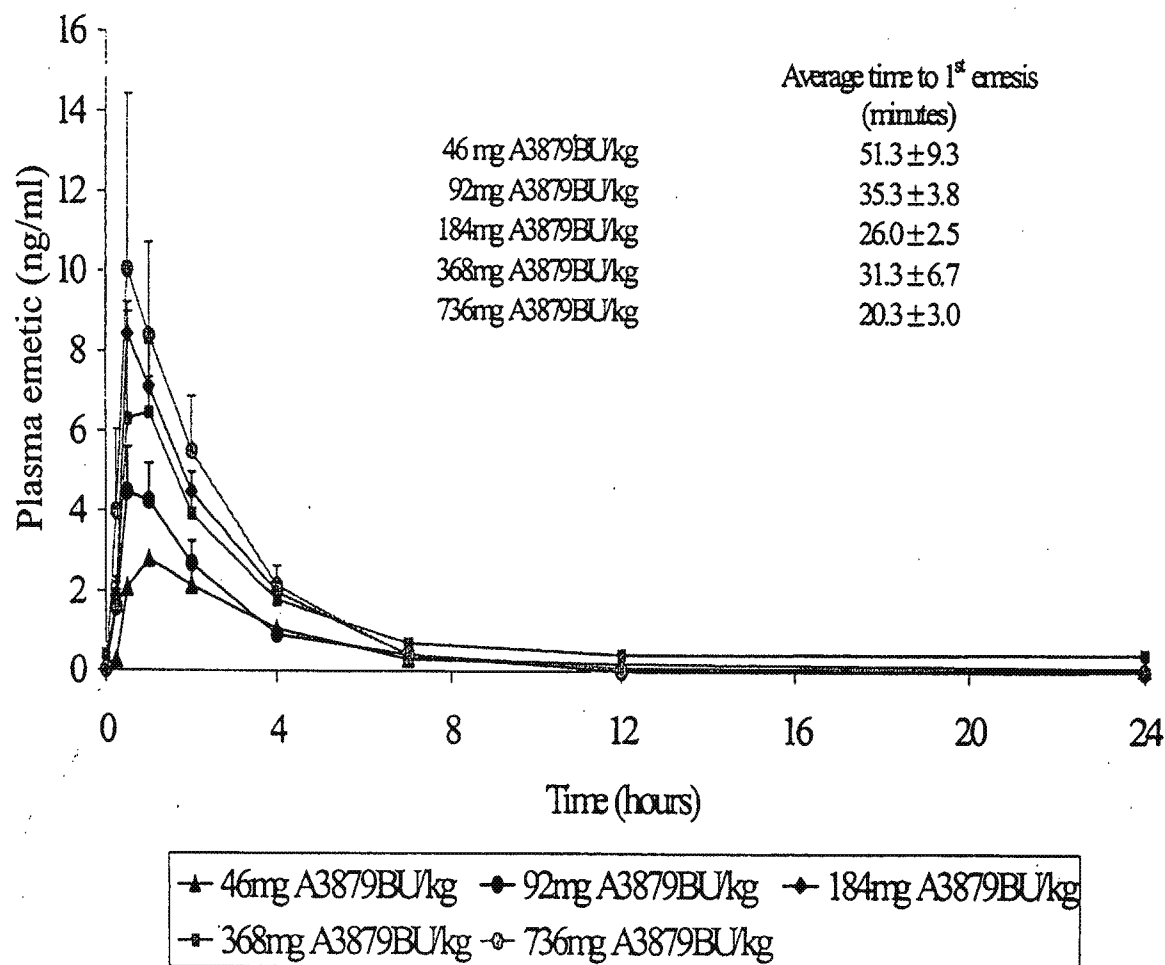
■ Gramoxone (44mg/kg) ■ A3879BU (46mg/kg) ■ A3879BU (92mg/kg)
 ■ A3879BU (184mg/kg) ■ A3879BU (368mg/kg) ■ A3879BU (736mg/kg)

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Plasma emetic values following an oral dose of 200g/l INTEON (46 - 736mg formulation/kg b wt.) in dogs (n = 3)



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Second study

2. Toxicokinetic study on a Gramoxone INTEON 240g/l formulation – A7813K

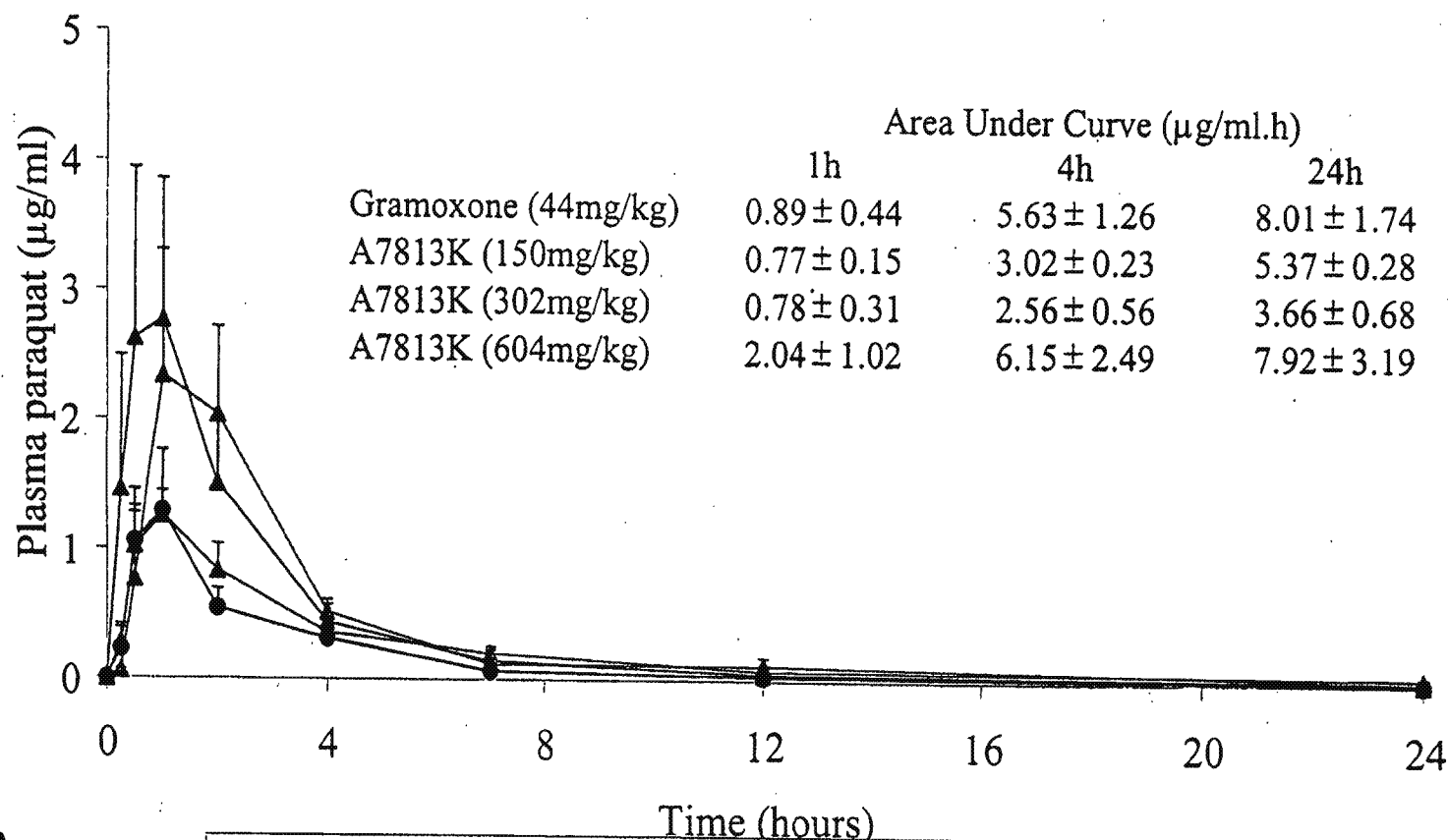
- **Comparison with a contemporaneous
Gramoxone 200g/l formulation A3879D**



CONFIDENTIAL BUSINESS INFORMATION



Plasma paraquat levels following an oral dose of Gramoxone or 240 g/l INTEON (150-604mg formulation/kg) in male dogs



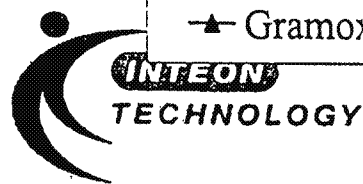
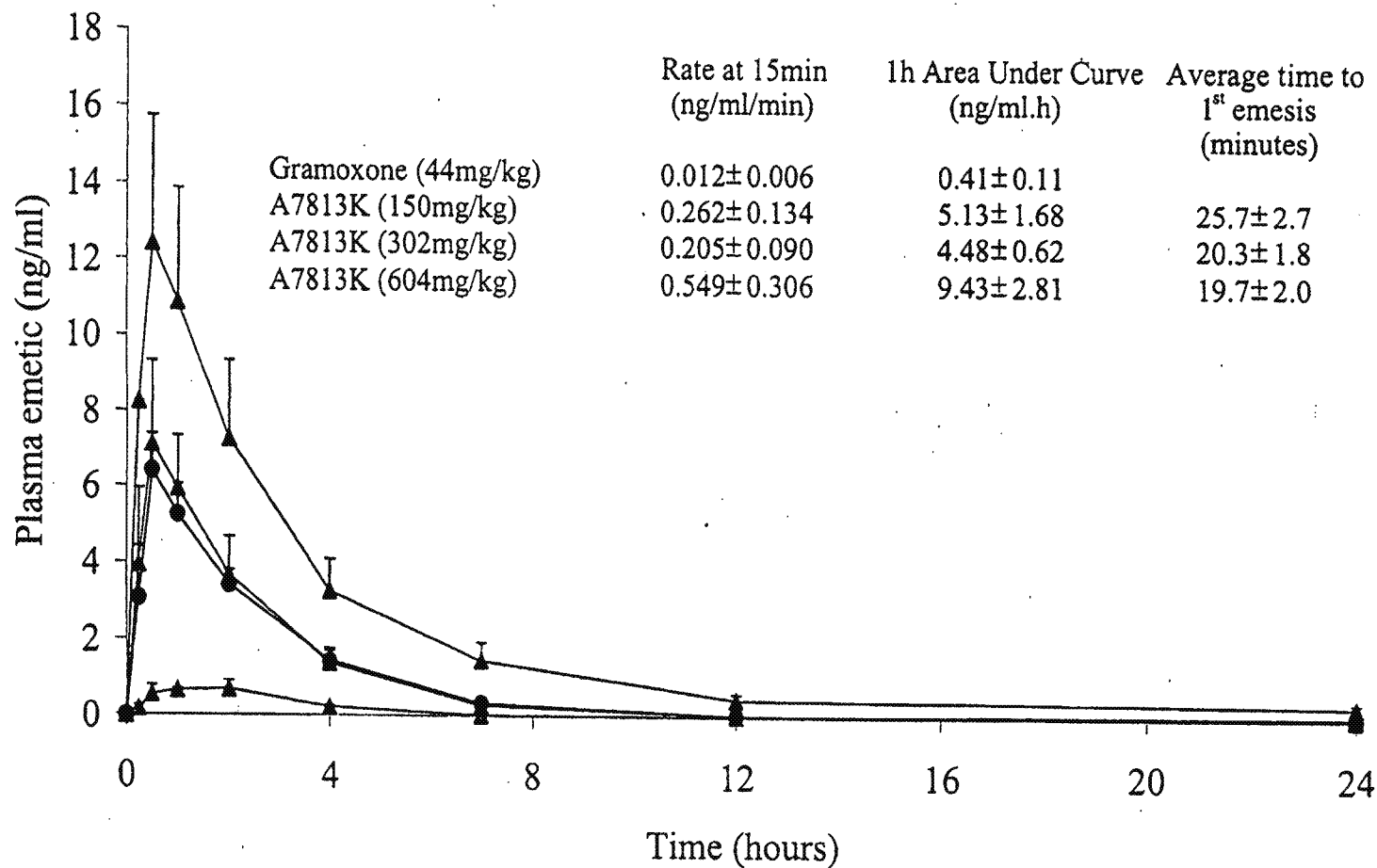
▲ Gramoxone (44mg paraquat ion/kg) ▲ A7813K (150mg paraquat ion/kg)
 ● A7813K (302mg paraquat ion/kg) ▲ A7813K (604mg paraquat/kg)

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Plasma Emetic following an oral dose of Gramoxone or Gramoxone INTEON (A7813K) to male dogs



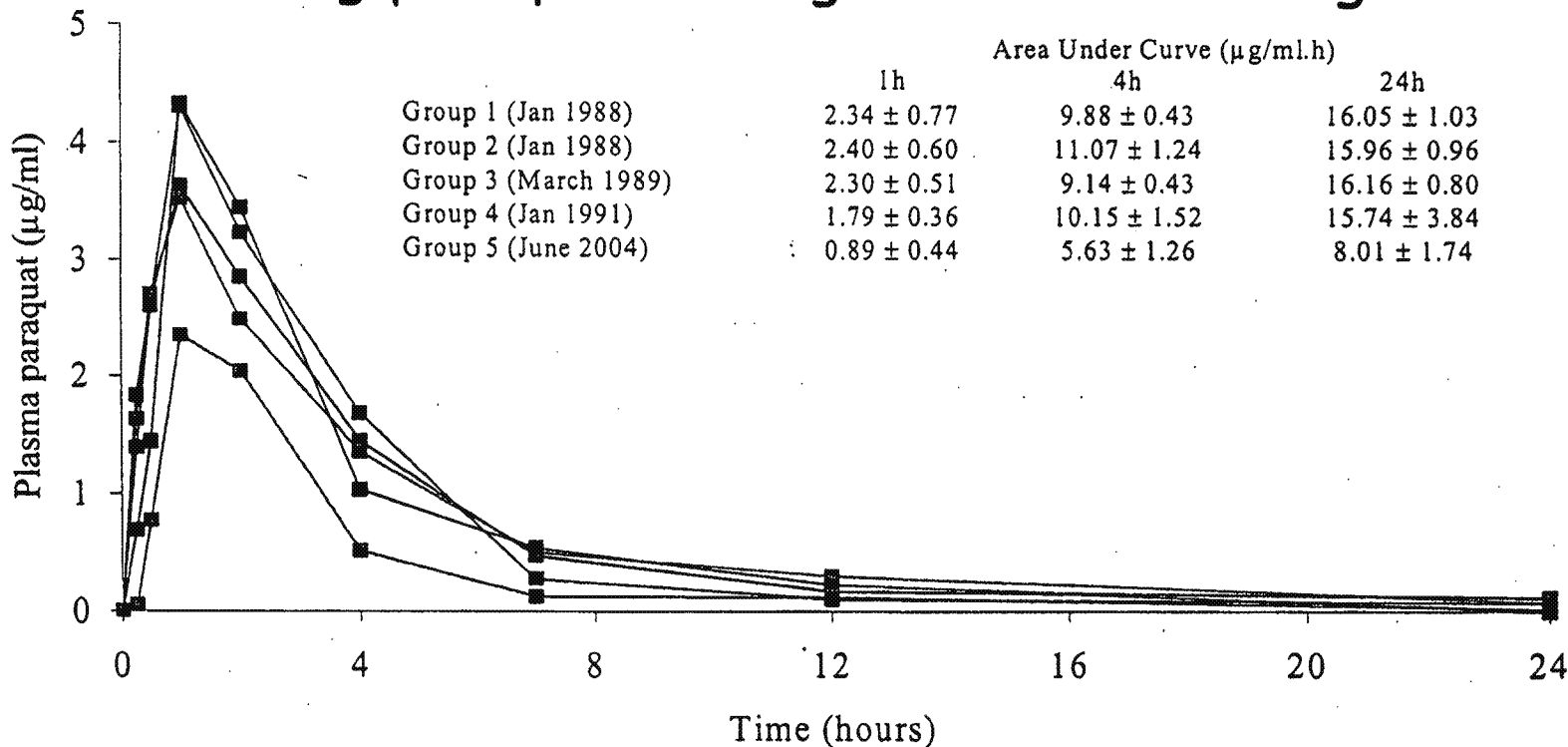
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Gramoxone 200g/l (A3879D) NON-INTEON

Plasma paraquat concentration following an oral dose of 8mg paraquat ion/kg to adult male dogs



■ Group 1 (Jan 1998) ■ Group 2 (Jan 1998) ■ Group 3 (March 1989)
 ■ Group 4 (Jan 1991) ■ Group 5 (June 2004)



All dogs received APE-containing Gramoxone 200g/l (YF7697A= A3879D).

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Conclusions in the dog

- These data are consistent with acid triggered gelling in the stomach and productive emesis prior to any movement into the small intestines.
 - Earlier emesis occurs with increasing dose
- Shown reduced absorption with Gramoxone INTEON (200 g/l and 240 g/l) formulation across a 16 fold dose range
- Lethal dose of Gramoxone (Non-INTEON) in dogs is just above dose used in toxicokinetic study - approximately 55 to 66 mg formulation/kg
- Therefore Gramoxone INTEON (200 g/l and 240 g/l) formulations have shown a 10x safening in the dog



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Comparison of the acute toxicity to the Dog

Estimated median lethal dose in dog 12mg paraquat ion/kg

Formulation	Estimated lethal dose mg formulation/kg	New INTEON data mg formulation/kg
Gramoxone Max 360g/l	36	-
240g/l	55	> 602 > (10.9x)
200g/l	66	> 736 > (11x)



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Extrapolation to likely outcome in man

- Scientific rationale for INTEON technology reducing the oral toxicity of paraquat formulations
- Recent experimental data in dogs, a vomiting species, have shown a reduction in the gastrointestinal absorption of paraquat from an INTEON formulation compared with Gramoxone
- Anticipate that the INTEON formulation will eliminate fatal accidents of mistaken ingestion
- Anticipate that the INTEON formulation will significantly increase the survival rate following intentional ingestion



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Clark Kimberly USGR

From: Abbott John USGR
Sent: Tuesday, November 07, 2006 11:27 AM
To: Rudolph Tiffany USGR; Clark Kimberly USGR
Subject: FW: Any feedback on Tox Study?

Email exchange for our records. Thanks.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
336-632-7074
336-253-9666 (mobile)
john.abbott@syngenta.com

-----Original Message-----

From: Johnson.Hope@epamail.epa.gov [mailto:Johnson.Hope@epamail.epa.gov]
Sent: Tuesday, November 07, 2006 7:21 AM
To: Abbott John USGR
Subject: Re: Any feedback on Tox Study?

Mr. Abbott,

HED expects to have a response ready within a couple of weeks. I will contact you when I receive something.

Thank you,

Hope A. Johnson
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Herbicide Branch
Phone: 703-305-5410
Mail Code 7505P

john.abbott@syng
enta.com

11/03/2006 10:33
AM

Hope Johnson/DC/USEPA/US@EPA

monty.dixon@syngenta.com

Any feedback on Tox Study?

To

cc

Subject

Hope,
Thanks again for meeting with us last week to work through the concerns on the harvest-aid use. Our discussion was very helpful.

I am contacting you regarding the acute toxicology study in dogs with paraquat that we had discussed in our August 30th meeting. During that meeting we presented as well as provided a copy of our planned study protocol. I was contacted by our toxicologists to see if EPA had any comments/revisions concerning the protocol that we should consider prior to initiating the study. Have you received or should we anticipate getting any response or feedback?

Have a great weekend.

Regards,
John D. Abbott, Ph.D., CPH
Syngenta Crop Protection, Inc.
NAFTA Herbicide Team Leader
Regulatory Affairs
336-632-7074
336-253-9666 (mobile)
john.abbott@syngenta.com



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

DEC 19 2006

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Mr. John Abbott
Syngenta Crop Protection, Inc.
PO Box 18300
Greensboro, NC 27419-8300

Subject: Gramoxone Inteon
EPA Registration Number 100-1217
Protocol Response

Dear Mr. Abbott:

The U.S. EPA OPP Health Effects Division has reviewed the protocol for an acute toxicity study in dogs as provided in your PowerPoint presentation sent to us on September 1, 2006 (e-mail from John Abbott to Hope Johnson, EPA). Given this information and our review of the Inteon™/Non-Inteon™ issue over the past year, we have the following comments:

1. Again, as we stated at the August 30, 2006 meeting in which you first presented the protocol for this study, we are not asking for or requiring this study. In fact, it is not entirely clear how the study will add value to the current database. In a previous study, you have shown that the protection afforded by Inteon™ is being breached at 128 mg paraquat ion/kg (lung effects seen). Based on the relatively steep dose response curve [change from non-lethalities to lethalities with an increase of less than 10 mg paraquat ion/kg] the non lethal dose (or the minimum lethal dose as may be determined in the new study) will not be much greater than the 128 mg paraquat ion/kg observed in the initial study. Thus the protective non-lethal value is around 64 mg paraquat ion/kg. As pointed out in our calculations using a range of volumes ingested, this value does not guarantee survival in many cases of accidental ingestion (63 to 250 mg paraquat ion/kg bw, assuming a 60 kg person, from previous comments) and clearly not in cases of suicidal intention where the ingestion is much higher.
2. Our biggest concern is that the formulations proposed for the study (Slide 9) show that, in addition to the gel and purgative that are both present in Inteon™ compared to non-Inteon™, there is 3X more emetic in the Inteon™ formulations vs. the non-Inteon™ formulations. Thus, this may not answer the question as to what may be more protective: the presence of the gel, the purgative, or the additional emetic - or any combination of these three.
3. While we don't think this study is necessary, if you elect to do it, we note that you plan to use fresh animals as you increase the dose in the rising dose level process (Slide 10). This would be useful since earlier studies/protocols used the same dogs for multiple dose levels. In addition, it would be worthwhile to follow all dosed animals for a period of time to assess possible delayed/persistent effects following a acute exposure to paraquat.

DEC 27 2006

Rt

Page 2

4. Again, if you still plan to do the study, it would be useful to get the details for determining "minimum lethal dose". You allude to them on Slide 12 ("endpoint thresholds for requiring termination"), but don't provide the necessary details.

We apologize for the delay in our response. If you have any questions, please contact Hope Johnson at 703-305-5410.

Sincerely,



James A. Tompkins

Product Manager 25

Herbicide Branch

Registration Division (7505P)



February 6, 2007

Mr. Jim Tompkins
Document Processing Desk
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

**SUBJECT: SUBMISSION OF ADDITIONAL INFORMATION RELATED TO SAFETY
IMPROVEMENT OF GRAMOXONE INTEON, EPA REG. NO. 100-1217**

Dear Mr. Tompkins:

Syngenta Crop Protection is herein submitting additional information related to the safety improvement of Gramoxone Inteon. This submission is intended to ensure the completeness of the Gramoxone Inteon data records. The information being submitted herein includes 3 study supplements and a corrected graphic from an earlier submission. This corrected graphic is intended to replace Figure 2 in a document entitled: *Gramoxone Inteon and Improved Safety, A Document Reviewing The Information Presented At The Meeting By Dr. Mike Clapp* that was submitted to the EPA on June 19, 2006.

Specifically, the included documents are:

- Attachment A: Supplement to Effects of Increased Emetic Levels on Toxicokinetics in the Dog (MRID 46865501), Swain C., Heylings J., October 5, 2006
- Attachment B: Supplement to Toxicokinetic Study in Dogs (MRID 46364517), Brammer A., October 5, 2006
- Attachment C: Supplement to Toxicokinetic Study in Dogs (MRID 46364510), Brammer A., October 5, 2006
- Attachment D: Corrected Figure 2: *Gramoxone Inteon and Improved Safety, A Document Reviewing The Information Presented At The Meeting By Dr. Mike Clapp*.

This information is submitted for informational purposes. This submission is outside the scope of PRIA. If you have any questions regarding this submission, please contact me at (336) 632-7055.

Kind regards,

Montague Dixon
Regulatory Product Manager
Enclosure

**VOLUME 1 OF 4 OF SUBMISSION
(TRANSMITTAL DOCUMENT)**

1. Name and Address of Submitter

Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419

2. Regulatory Action in Support of which this Package is Submitted

Submission of Additional Information Related to Safety Improvement of
Gramoxone Inteon, EPA Reg. No. 100-1217

3. Transmittal Date

2/6/2007

4. List of Submitted Studies

MRID NUMBER	VOLUME NUMBER	STUDY TITLE	EPA GUIDELINE NUMBER
	1 OF 4	Transmittal document	NA
	2 OF 4	Paraquat 240g/l SL Formulation (A7813K) -Supplement to Toxicokinetic Study in Dogs -MRID 46364510; (T011144-06),(450844),	NA
	3 OF 4	Paraquat 200g/l SL Formulation (A3879BU) -Supplement to Toxicokinetic Study in Dogs -MRID 46364517;(T011142-06),(450843)	NA
	4 OF 4	Gramoxone -Supplement to Effects of Increased Emetic Levels on Toxicokinetics in the Dog-MRID 46865501; (T003396-06),(451270)	NA

COMPANY OFFICIAL:

MONTAGUE DIXON
(NAME)

Montague Dixon
(SIGNATURE)

COMPANY NAME:

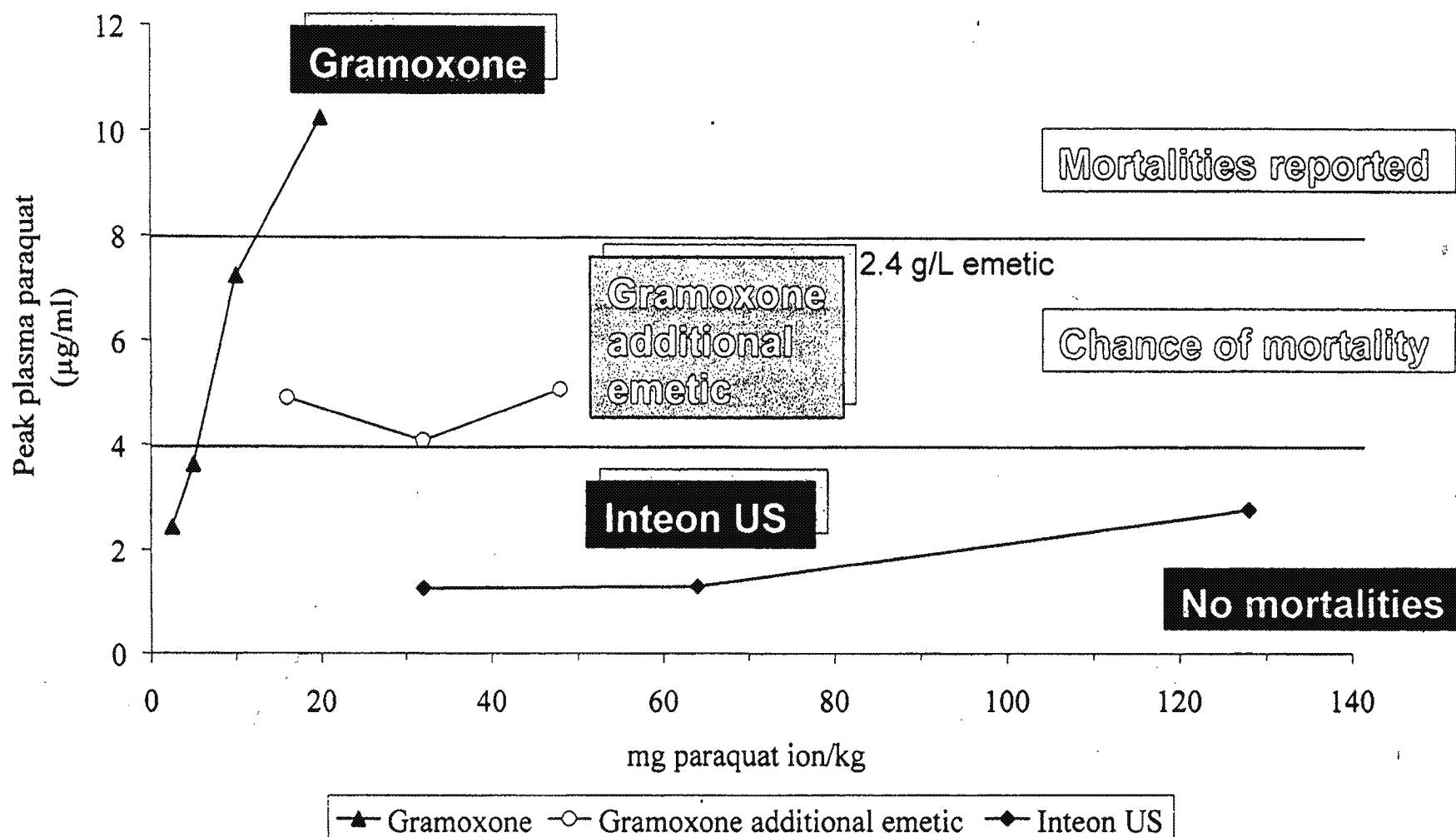
SYNGENTA CROP PROTECTION, INC.

COMPANY CONTACT:

MONTAGUE DIXON
(NAME)

(336) 632-7055
(PHONE)

Gramoxone: influence of increased emetic on peak plasma paraquat levels in dog





R.E.D. FACTS

Pesticide Reregistration

Paraquat Dichloride

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered before November 1, 1984, be reregistered to ensure that they meet today's more stringent standards.

Under the Food Quality Protection Act of 1996, EPA must consider the increased susceptibility of infants and children to pesticide residues in food, as well as aggregate exposure of the public to pesticide residues from all sources, and the cumulative effects of pesticides and other compounds with a common mechanism of toxicity in establishing and reassessing tolerances.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then reregisters pesticides that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case 0262, paraquat dichloride (commonly referred to as paraquat).

Use Profile

Paraquat dichloride is a herbicide currently registered to control weeds and grasses in many agricultural and non-agricultural areas. It is used preplant or preemergence on vegetables, grains, cotton, grasses, sugar cane, peanuts, potatoes, and tree plantation areas; postemergence around fruit crops, vegetables, trees, vines, grains, soybeans, and sugar cane; during the dormant season on clover and other legumes; as a desiccant or harvest aid on cotton, dry beans, soybeans, potatoes, sunflowers, and sugar cane; and as a post harvest desiccant on staked tomatoes. It also is applied to pine trees to induce resin soaking. Paraquat dichloride is also used on non-crop areas such as public airports, electric transformer stations and around commercial buildings to control weeds.

Paraquat dichloride is applied aerially, by groundboom, backpack sprayer, and low pressure handwand.

A soluble concentrate/liquid (SC/L) is the sole paraquat formulation type registered for all uses. This formulation may be applied to crops pre-plant, at planting, pre-emergence (broadcast or band), post-emergence (broadcast, band, split, directed, or spot), post-harvest (as a pre-harvest desiccant or harvest aid), and for suckering and stripping of hops.

Regulatory History

Paraquat dichloride was first registered as a pesticide in the U.S. in 1964. EPA issued a Registration Standard for paraquat dichloride in June 1987 (NTIS# PB88-217005). A December 1991 Data Call-In (DCI) required additional ecological effects, environmental fate and residue chemistry data.

Currently, 7 pesticide products are registered which contain the active ingredient paraquat dichloride. All paraquat products are classified as Restricted Use Pesticides.

Human Health Assessment

Toxicity

In acute toxicity studies using laboratory animals, paraquat has been shown to be highly toxic by the inhalation route and has been placed in Toxicity Category I (the highest of four levels) for acute inhalation effects. However, the Agency has determined that particles used in agricultural practices (400 to 800um) are well beyond the respirable range and therefore inhalation toxicity is not a toxicological endpoint of concern. Paraquat is moderately toxic (Category II) by the oral route and slightly toxic (Category III) by the dermal route. Paraquat will cause moderate to severe eye irritation and minimal dermal irritation, and has been placed in Toxicity Categories II and IV for these effects.

In a subchronic toxicity study using rats, paraquat caused changes in the lungs. A dermal toxicity study using rabbits resulted in scabbing and inflammation when tested at the two highest doses (2.6 mg cation/kg group and 6.0 mg cation/kg group). In an inhalation toxicity study, rats were exposed to respirable aerosols (particle size - less than 2 um in diameter) of paraquat dichloride which resulted in lung changes and extensive sores and swelling in the larynx.

A chronic toxicity study using dogs resulted in an increase in the severity and extent of chronic pneumonitis in the mid dose and high dose male and female dogs. Two chronic toxicity/carcinogenicity studies using rats were conducted with paraquat. In the first chronic toxicity study, paraquat did not appear to be carcinogenic in the lungs or the head region (middle ear, hard palate, head tissue and skin) of the rat. In the second study, paraquat resulted in non-tumor lesions in various organs and no evidence of carcinogenicity. Two chronic toxicity/carcinogenicity studies using mice were also conducted with paraquat. The first study resulted in

decreased body weight gain, kidney changes and no evidence of carcinogenicity. The second study using mice also resulted in no evidence of carcinogenicity. Based on these studies, paraquat was classified as a "Group E" chemical--one showing evidence of noncarcinogenicity for humans.

Four developmental/maternal toxicity studies were evaluated for paraquat. Treatment-related effects were seen (i.e., delayed hardening [ossification] in the forelimb and hindlimb digits, or retarded ossification of the posterior portion of the skull) in the fetuses only at the same or higher dose levels than effects in the mother. Therefore, the no-observed effect dose levels (NOEL) for maternal toxicity are at least as conservative (protective) as the NOEL based on developmental toxicity.

There is no evidence that paraquat is associated with reproductive effects. In a reproduction study using rats, paraquat had no effect on body weight gain, food consumption/utilization, fertility or length of gestation. Paraquat also shows no evidence of causing mutagenicity.

Dietary Exposure

People may be exposed to residues of paraquat through the diet. Tolerances or maximum residue limits have been established for well over 80 raw agricultural commodities, processed foods and feed (please see 40 CFR 180.205(a), (b); 185.4700; 186.4700). EPA has reassessed the paraquat tolerances and found that numerous revisions are necessary. Most of these revisions will be handled administratively.

The available data support the established tolerances on all but sorghum forage, ruminant kidney, oats, rye, soybeans and hops. The tolerance for sorghum forage was reassessed from 0.05 to .1 ppm, while kidney was reassessed from 0.3 ppm to 0.5 ppm, soybeans from 0.05 ppm to 0.25 ppm, and hops from 0.2 ppm to 0.5 ppm. As there are presently no registered uses of paraquat on rye, the tolerances for this commodity will be revoked. Also the tolerance on oats will be revoked, as the registrant has indicated that they do not wish to support this use. Additionally, the tolerances for poultry (except for eggs) will be revoked. Finally, a tolerance for popcorn (0.05 ppm) will be established (See Section IV, Tolerance Reassessment Summary and Table in the paraquat RED for further specifics).

Numerous international Codex maximum residue limits (MRLs) have been established for paraquat. Harmonization of Codex MRLs and U.S. tolerances for paraquat exists for many crops. However, at this time there remain some incompatibilities between U.S. tolerances and Codex MRLs on the following raw plant commodities because of differences in agricultural practices: cottonseed, dry hops, maize, olives, potatoes, rice, sorghum, and dry soya beans.

EPA has assessed the dietary risk posed by paraquat. The Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population

represents 10% of the Reference Dose (RfD), or amount believed not to cause adverse effects if consumed daily over a 70-year lifetime. The highest subgroup, non-nursing infants (<1 year old) occupies 31% of the RfD. This fraction of the allowable RfD is considered to be an acceptable dietary exposure risk.

Occupational and Residential Exposure

Exposure to homeowners is not expected since there are no residential uses. Based on current use patterns, handlers (mixers, loaders, and applicators) may be exposed to paraquat dichloride during and after normal agricultural use. Ground, aerial and backpack application methods were considered. All the dermal and inhalation Margins of Exposure (MOEs) were acceptable (greater than 100) except backpack applicators and resin-soaking uses. The registrant has agreed to reduce the concentration of paraquat dichloride allowed when using a backpack sprayer and make label changes for tree injection (resin soaking) use.

Human Risk Assessment

Paraquat generally is of moderate to high acute toxicity based on inhalation toxicity (Toxicity Category I), oral toxicity, and moderate to severe eye irritation (Toxicity Category II). It is a Group E chemical--one showing no evidence of carcinogenicity.

Although people may be exposed to residues of paraquat in many food commodities, the chronic dietary risk from all uses is considered minimal.

Of greater concern is the risk posed to paraquat handlers, particularly mixers/loaders/applicators. A dermal endpoint--based on maternal toxicity effects-- was used to assess risks to handlers. Margins of Exposure (MOEs) for dermal effects to paraquat are adequate (greater than 100) for all exposure scenarios considered except for backpack sprayer applicators (non-spot treatment) and low pressure sprayer (resin soaking) for mixer/loader/applicators. Even with gloves, the margin of exposure for handlers using a backpack sprayer was too low. Exposure and risk to workers will be mitigated by reducing the concentration of paraquat in backpack sprayers, and through the use of Personal Protective Equipment (PPE) required by the WPS, supplemented by gloves, a chemical-resistant apron and face shield for all occupational uses of paraquat end-use products, as required by this RED. PPE requirements for applicators and other handlers (other than mixers and loaders) include a long-sleeved shirt and long pants, chemical-resistant gloves and shoes plus socks. Based on a biological monitoring study, post-application reentry workers will be required to observe a 12-hour Restricted Entry Interval for the uses of paraquat for preemergent or early-season weed control and weed control for orchard and vegetable crops where the spray is directed solely at the weeds (not broadcast over the entire crop area). A 24-hour Restricted Entry Interval is required for desiccation and harvest aid applications of paraquat

since the Agency concludes such uses result in a greater degree of exposure to workers.

Food Quality Protection Act Considerations

In establishing or reassessing tolerances, FQPA requires the Agency to consider aggregate exposures to pesticide residues, including all anticipated dietary exposures and other exposures for which there is reliable information, as well as the potential for cumulative effects from a pesticide and other compounds with a common mechanism of toxicity. The Act further directs EPA to consider the potential for increased susceptibility of infants and children to the toxic effects of pesticide residue.

The Agency considered the appropriateness of an additional uncertainty factor to account for situations where available data indicate increased sensitivity of infants and children and concluded that it is not warranted based on an evaluation of the toxicology database. Regarding aggregate exposure, the Agency only considered dietary exposure because there are no residential or other non-occupational uses of paraquat, and exposure to paraquat in drinking water is not expected. The EPA estimates that paraquat residues in the diet of the general U.S. population account for 10% of the RfD, 24% of the RfD for children aged 1-6 years and 31% of the RfD for non-nursing infants (less than 1 year). Therefore, the Agency has determined that there is a reasonable certainty that no harm will result to infants and children or to the general population from aggregate exposure to paraquat dichloride residues. Further, based on the available data, the Agency does not believe that the effects produced by paraquat would be cumulative with those of other structurally related compounds. Therefore, based on these conclusions, the Agency considers the tolerances in the RED to be reassessed with regard to FQPA requirements.

Environmental Assessment

Environmental Fate

Paraquat dichloride was shown to be very immobile in soil. Paraquat does not hydrolyze, does not photodegrade in aqueous solutions, and is resistant to microbial degradation under aerobic and anaerobic conditions. The primary route of environmental dissipation of paraquat is adsorption to biological materials and soil clay particles. Due to the apparent adsorption strength of paraquat for soil clays, these bound residues do not appear to be environmentally available. Nevertheless, since paraquat is persistent, it could potentially be found in surface water systems associated with soil particles carried by erosion. However, detections would not be considered to be representative of normal paraquat use (since it binds so strongly to soil clay particles and becomes environmentally inactive). Therefore, paraquat is not expected or considered to be a groundwater concern from normal paraquat dichloride use patterns.

Ecological Effects

Paraquat is practically non-toxic to honey bees and slightly toxic to fish on an acute basis. Paraquat is moderately toxic to non-endangered and endangered terrestrial animals (birds and mammals), non-target terrestrial and semi-aquatic plants. Acute toxicity to terrestrial animals (birds) and mammals only exists immediately after application.

Ecological Effects Risk Assessment

Paraquat exposure to birds, mammals, non-target terrestrial and semi-aquatic plants including endangered species may result from paraquat spray drift during application.

The Agency levels of concern (LOCs) have been exceeded for acute effects for birds and small (herbivorous and insectivorous) mammals and for acute effects on semi-aquatic and terrestrial plants. However, the risk for birds and small mammals only exists shortly after application. Once the applied paraquat has dried (or becomes bound) its risk is greatly reduced. Therefore, the Agency concludes the registered uses of paraquat are not expected to pose significant risk to birds or mammals. The Agency LOCs have also been exceeded for non-endangered and endangered non-target terrestrial and semi-aquatic plants. Depending on the application method and application rate, the risk quotients ranged from acceptable to acute effects. To mitigate these risks, the registrant has agreed to lower the maximum use rate, amend all paraquat labels to include a warning about possible adverse effects to non-target and semi-aquatic plants due to drift and include spray drift language.

Risk Mitigation

To lessen the occupational and ecological risks posed by paraquat, EPA is requiring the following risk mitigation measures.

- For all risk concerns:

- Reduce the maximum rate of application from 1.6 lb cation/A to 1.0 lb cation/A and maintain the Restricted Use Classification.

- To protect workers:

- Additional PPE are being required for mixers and loaders: gloves, chemical-resistant apron and face shield. PPE requirements for applicators and other handlers (other than mixers and loaders) include: long-sleeved shirt and long pants, chemical-resistant gloves, and shoes plus socks.

- Further, the concentration of paraquat in backpack sprayers will be reduced and the resin soaking sections on the paraquat labels amended (i.e., delete plastic acid bottle use) to lessen the exposure and risk to applicators.

- To protect non-target terrestrial and semi-aquatic plants from drift:

- Aerial applications will include the most current spray drift language and all paraquat products must place a statement in the "Environmental Hazard" section of the label that warns the user about possible adverse effects to non-target and semi-aquatic plants due to drift.

Additional Data Required

EPA is requiring data to establish tolerances for paraquat dichloride on taro foliage, corn and soybean aspirated grain fractions, wheat and hay, cotton and gin byproducts and processed grapes. The Agency is also requiring data to confirm that the existing tolerances for field corn is adequate to cover the specialized use of paraquat as a harvest aid.

Additionally, the Agency is requiring product-specific data including product chemistry and acute toxicity studies, revised Confidential Statements of Formula (CSFs), and revised labeling for reregistration.

Product Labeling Changes Required

All paraquat dichloride end-use products must comply with EPA's current pesticide product labeling requirements and with the following. For a comprehensive list of labeling requirements, please see the paraquat dichloride RED document.

Application Rates and Label Deletions for End-Use Products

In cooperation with the Agency the registrant has agreed to the following application rates and label deletions:

- The maximum paraquat dichloride application rate for all products will be lowered from 1.6 lb cation/A to 1.0 lb cation/A.
 - For broadcast applications of paraquat with backpack sprayers, **non-spot**, the application rate should not exceed 0.625 lb cation/A and the application volume should be no less than 20 gallons per acre.
 - The maximum application rate for **spot spraying** on all paraquat labels will be no more than 0.0195 lbs cation/gallon.
- Delete the plastic acid bottle and the tree injection directions for use from the resin soaking sections of all paraquat dichloride labels.

Hazard Statement

The following hazard statement must be placed in the "Environmental Hazard" section of all paraquat labels to warn the user about possible adverse effects to non-target terrestrial and semi-aquatic plants due to drift:

"Paraquat dichloride is toxic to nontarget crops and plants if off-target movement occurs. Extreme care must be taken to ensure that off-target drift is minimized to the greatest extent possible."

PPE/Engineering Control Requirements for Pesticide Handlers

For **sole-active-ingredient** end-use products that contain paraquat, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this

section. Any conflicting PPE requirements on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain paraquat, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use (WPS and nonWPS)

Minimum (Baseline) PPE/Engineering Control Requirements

Although the MOE's were greater than 100 for all but two scenarios (backpack applicators and resin-soaking uses) without personal protective equipment requirements beyond long-sleeve shirt, long pants, shoes and socks, the Agency notes the relatively significant epidemiological evidence of poisonings from intentional/accidental swallowing and numerous non-systemic skin and eye effects in California (see OREB J. Blondell memo, 12/5/95). These considerations have led to the Agency establishing the following minimum (baseline) PPE is required for all occupational uses of paraquat end-use products:

"Mixers and loaders must wear:

- long-sleeved shirt and long pants,
- chemical-resistant gloves*,
- shoes plus socks,
- chemical-resistant apron,
- face shield"

Although there is no direct evidence that occupational handlers have ever ingested a lethal amount of paraquat from a splash or spill, the requirement for a face shield for all mixers and loaders reflects the Agency's particular concern about accidental swallowing in case of a spill or splash back.

"Applicators and other handlers (other than mixers and loaders) must wear:

- long-sleeved shirt and long pants,
- chemical-resistant gloves*,
- shoes plus socks"

* For the glove statement, use the statement established for paraquat through the instructions in Supplement Three of PR Notice 93-7.

Determining PPE Requirements for End-use Product Labels

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active-ingredient-based minimum (baseline) personal protective equipment specified above. The more protective PPE must be placed on the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7, and the format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Products Intended Primarily for Occupational Use

There are no registered homeowner-use products.

Entry Restrictions

For **sole-active-ingredient** end-use products that contain paraquat the product labeling must be revised to adopt the entry restrictions set forth in this section. Any conflicting entry restrictions on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain paraquat the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Products Intended Primarily for Occupational Use - Entry Restrictions and Labeling

WPS Uses

Restricted-entry interval:

"For preplant or preemergence (broadcast or banded) applications, post-emergence directed-spray applications, dormant-season applications, and "between cutting" alfalfa applications: Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 12 hours."

"For harvest-aid and desiccation applications: Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 24 hours."

Early-entry personal protective equipment (PPE):

The PPE required for early entry is:

- coveralls,
- chemical-resistant gloves*,
- shoes plus socks,
- protective eyewear.

* For the glove statement, use the statement established for paraquat through the instructions in Supplement Three of PR Notice 93-7.

WPS Notification Statement:

Not required on label.

NonWPS uses

Entry restrictions:

The Agency is establishing the following entry restrictions for nonWPS occupational uses of paraquat end-use products:

"Do not enter or allow others to enter the treated area until sprays have dried."

Placement in labeling:

If WPS uses are also on label -- Follow the instructions in PR Notice 93-7 for establishing a Non-Agricultural Use Requirements box, and place the appropriate nonWPS entry restrictions in that box.

If no WPS uses are on the label -- Place the appropriate nonWPS entry restrictions in the Directions for Use, under the heading "Entry Restrictions."

Products Intended Primarily for Homeowner Use

Entry restrictions:

There are no registered homeowner-use products.

Other Labeling Requirements

Products Intended Primarily for Occupational Use

The Agency is requiring the following labeling statements to be located on all end-use products containing paraquat that are intended primarily for occupational use.

Application Restrictions

"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."

Engineering Controls

"When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."

User Safety Requirements

"Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them."

"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washable, use detergent and hot water. Keep and wash PPE separately from other laundry."

"DO NOT USE AROUND HOMES, SCHOOLS, RECREATIONAL PARKS, GOLF COURSES, OR PLAYGROUNDS"

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."
- "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Spray Drift Labeling

Please see the paraquat dichloride RED document for the text of this Advisory, which must be contained on each paraquat product label that can be applied aurally.

Regulatory

The use of currently registered products containing paraquat

Conclusion

dichloride in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration.

Paraquat products will be reregistered once the required product-specific data, revised Confidential Statements of Formula, and revised labeling are received and accepted by EPA.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for paraquat dichloride during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet can be downloaded from the Pesticide Special Review and Reregistration Information System at 703-308-7224. They also are available on the Internet using ftp on *FTP.EPA.GOV*, or using WWW (World Wide Web) on *WWW.EPA.GOV*.

Printed copies of the RED and fact sheet can be obtained from EPA's National Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-2419, telephone 1-800-490-9198, fax 513-489-8695.

Following the comment period, the paraquat dichloride RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-487-4650.

For more information about EPA's pesticide reregistration program, the paraquat dichloride RED, or reregistration of individual products containing paraquat dichloride, please contact the Special Review and Reregistration Division (7508W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 9:30 am and 7:30 pm Eastern Standard Time, Monday through Friday.



AMERY



Reregistration Eligibility Decision (RED)

Paraquat Dichloride

Please NOTE that the
Entire RED has not been
provided in this section. The
information provided includes
an introduction, description and
use pattern information along
with the regulatory history through
the issuance of this RED in
1997.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

CERTIFIED MAIL

Dear Registrant:

I am pleased to announce that the Environmental Protection Agency has completed its reregistration eligibility review and decisions on the pesticide chemical case paraquat dichloride which includes the active ingredient 1,1'-dimethyl-4,4'-bipyridinium dichloride. The enclosed Reregistration Eligibility Decision (RED), which was signed on 9/30/96, contains the Agency's evaluation of the data base of these chemicals, its conclusions of the potential human health and environmental risks of the current product uses, and its decisions and conditions under which these uses and products will be eligible for reregistration. The RED includes the data and labeling requirements for products for reregistration. It may also include requirements for additional data (generic) on the active ingredients to confirm the risk assessments.

To assist you with a proper response, read the enclosed document entitled "Summary of Instructions for Responding to the RED." This summary also refers to other enclosed documents which include further instructions. You must follow all instructions and submit complete and timely responses. **The first set of required responses is due 90 days from the date of this letter. The second set of required responses is due 8 months from the date of this letter.** Complete and timely responses will avoid the Agency taking the enforcement action of suspension against your products.

Please note that the Food Quality Protection Act of 1996 ("FQPA") became effective on August 3, 1996, amending portions of both the pesticide law (FIFRA) and the food and drug law (FFDCA). This RED takes into account, to the extent currently possible, the new safety standard set by FQPA for establishing and reassessing tolerances. However, it should also be noted that in continuing to make reregistration determinations during the early stages of FQPA implementation, EPA recognizes that it will be necessary to make decisions relating to FQPA before the implementation process is complete. In making these early case-by-case decisions, EPA does not intend to set broad precedents for the application of FQPA. Rather, these early determinations will be made on a case-by-case basis and will not bind EPA as it proceeds with further policy development and any rulemaking that may be required.

If EPA determines, as a result of this later implementation process, that any of the determinations described in this RED are no longer appropriate, the Agency will pursue whatever action may be appropriate, including but not limited to reconsideration of any portion of this RED.

If you have questions on the product specific data requirements or wish to meet with the Agency, please contact the Special Review and Reregistration Division representative Venus Eagle at (703) 308-8045. Address any questions on required generic data to the Special Review and Reregistration Division representative, Ruby Whithers at (703) 308-8079.

Sincerely yours,

Lois Rossi, Division Director
Special Review and
Reregistration Division

Enclosures

**SUMMARY OF INSTRUCTIONS FOR RESPONDING TO
THE REREGISTRATION ELIGIBILITY DECISION (RED)**

1. **DATA CALL-IN (DCI) OR "90-DAY RESPONSE"**--If **generic data** are required for reregistration, a DCI letter will be enclosed describing such data. If **product specific data** are required, a DCI letter will be enclosed listing such requirements. If **both generic and product specific data** are required, a combined Generic and Product Specific DCI letter will be enclosed describing such data. However, if you are an end-use product registrant only and have been granted a generic data exemption (GDE) by EPA, you are being sent only the **product specific** response forms (2 forms) with the RED. Registrants responsible for generic data are being sent response forms for both generic and product specific data requirements (4 forms). **You must submit the appropriate response forms (following the instructions provided) within 90 days of the receipt of this RED/DCI letter; otherwise, your product may be suspended.**

2. **TIME EXTENSIONS AND DATA WAIVER REQUESTS**--No time extension requests will be granted for the 90-day response. Time extension requests may be submitted only with respect to actual data submissions. Requests for time extensions for product specific data should be submitted in the 90-day response. Requests for data waivers must be submitted as part of the 90-day response. All data waiver and time extension requests must be accompanied by a full justification. All waivers and time extensions must be granted by EPA in order to go into effect.

3. **APPLICATION FOR REREGISTRATION OR "8-MONTH RESPONSE"**--**You must submit the following items for each product within eight months of the date of this letter (RED issuance date).**

a. **Application for Reregistration** (EPA Form 8570-1). Use only an original application form. Mark it "Application for Reregistration." Send your Application for Reregistration (along with the other forms listed in b-e below) to the address listed in item 5.

b. **Five copies of draft labeling** which complies with the RED and current regulations and requirements. Only make labeling changes which are required by the RED and current regulations (40 CFR 156.10) and policies. Submit any other amendments (such as formulation changes, or labeling changes not related to reregistration) separately. You may, but are not required to, delete uses which the RED says are ineligible for reregistration. For further labeling guidance, refer to the labeling section of the EPA publication "General Information on Applying for Registration in the U.S., Second Edition, August 1992" (available from the National Technical Information Service, publication #PB92-221811; telephone number 703-487-4650).

c. **Generic or Product Specific Data**. Submit all data in a format which complies with PR Notice 86-5, and/or submit citations of data already submitted and give the EPA identifier (MRID) numbers. Before citing these studies, you must **make sure that they meet the Agency's acceptance criteria** (attached to the DCI).

d. **Two copies of the Confidential Statement of Formula (CSF)** for each basic and each alternate formulation. The labeling and CSF which you submit for each product must comply with P.R. Notice 91-2 by declaring the active ingredient as the **nominal concentration**. You have two options for submitting a CSF: (1) accept the standard certified limits (see 40 CFR §158.175) or (2) provide certified limits that are supported by the analysis of five batches. If

you choose the second option, you must submit or cite the data for the five batches along with a certification statement as described in 40 CFR §158.175(e). A copy of the CSF is enclosed; follow the instructions on its back.

e. **Certification With Respect to Data Compensation Requirements.** Complete and sign EPA form 8570-31 for each product.

4. **COMMENTS IN RESPONSE TO FEDERAL REGISTER NOTICE**--Comments pertaining to the content of the RED may be submitted to the address shown in the Federal Register Notice which announces the availability of this RED.

5. **WHERE TO SEND PRODUCT SPECIFIC DCI RESPONSES (90-DAY) AND APPLICATIONS FOR REREGISTRATION (8-MONTH RESPONSES)**

By U.S. Mail:

Document Processing Desk (RED-SRRD-PRB)
Office of Pesticide Programs (7504C)
EPA, 401 M St. S.W.
Washington, D.C. 20460-0001

By express:

Document Processing Desk (RED-SRRD-PRB)
Office of Pesticide Programs (7504C)
Room 266A, Crystal Mall 2
1921 Jefferson Davis Hwy.
Arlington, VA 22202

6. **EPA'S REVIEWS**--EPA will screen all submissions for completeness; those which are not complete will be returned with a request for corrections. EPA will try to respond to data waiver and time extension requests within 60 days. EPA will also try to respond to all 8-month submissions with a final reregistration determination within 14 months after the RED has been issued.

REREGISTRATION ELIGIBILITY DECISION

Paraquat Dichloride

LIST A

CASE 0262

**ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
SPECIAL REVIEW AND REREGISTRATION DIVISION**

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PARAQUAT DICHLORIDE REREGISTRATION ELIGIBILITY DECISION TEAM i

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GLOSSARY OF TERMS AND ABBREVIATIONS

ADI	Acceptable Daily Intake. A now defunct term for reference dose (RfD).
AE	Acid Equivalent
a.i.	Active Ingredient
ARC	Anticipated Residue Contribution
CAS	Chemical Abstracts Service
CI	Cation
CNS	Central Nervous System
CSF	Confidential Statement of Formula
DFR	Dislodgeable Foliar Residue
DRES	Dietary Risk Evaluation System
DWEL	Drinking Water Equivalent Level (DWEL) The DWEL represents a medium specific (i.e. drinking water) lifetime exposure at which adverse, non carcinogenic health effects are not anticipated to occur.
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End-Use Product
EPA	U.S. Environmental Protection Agency
FAO/WHO	Food and Agriculture Organization/World Health Organization
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FOB	Functional Observation Battery
FQPA	Food Quality Protection Act
GLC	Gas Liquid Chromatography
GM	Geometric Mean
GRAS	Generally Recognized as Safe as Designated by FDA
HA	Health Advisory (HA). The HA values are used as informal guidance to municipalities and other organizations when emergency spills or contamination situations occur.
HDT	Highest Dose Tested
LC ₅₀	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD ₅₀	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LD ₁₀	Lethal Dose-low. Lowest Dose at which lethality occurs.
LEL	Lowest Effect Level
LOC	Level of Concern
LOD	Limit of Detection
LOEL	Lowest Observed Effect Level
MATC	Maximum Acceptable Toxicant Concentration
MCLG	Maximum Contaminant Level Goal (MCLG) The MCLG is used by the Agency to regulate contaminants in drinking water under the Safe Drinking Water Act.
µg/g	Micrograms Per Gram
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MP	Manufacturing-Use Product
MPI	Maximum Permissible Intake
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
N/A	Not Applicable
NOEC	No effect concentration
NPDES	National Pollutant Discharge Elimination System
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
OP	Organophosphate
OPP	Office of Pesticide Programs

GLOSSARY OF TERMS AND ABBREVIATIONS

PADI	Provisional Acceptable Daily Intake
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRN	Pesticide Registration Notice
Q ₁	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RS	Registration Standard
RUP	Restricted Use Pesticide
SLN	Special Local Need (Registrations Under Section 24 (c) of FIFRA)
TC	Toxic Concentration. The concentration at which a substance produces a toxic effect.
TD	Toxic Dose. The dose at which a substance produces a toxic effect.
TEP	Typical End-Use Product
TGAI	Technical Grade Active Ingredient
TLC	Thin Layer Chromatography
TMRC	Theoretical Maximum Residue Contribution
torr	A unit of pressure needed to support a column of mercury 1 mm high under standard conditions.
ug/L	Micrograms per liter
WP	Wettable Powder
WPS	Worker Protection Standard

ABSTRACT

The U.S. Environmental Protection Agency has completed its reregistration eligibility decision of the pesticide paraquat dichloride. This decision includes a comprehensive reassessment of the required target data supporting the use patterns of currently registered products. This decision considered the requirements of the recently enacted "Food Quality Protection Act of 1996" which amended the Federal Food Drug and Cosmetic Act and the Federal Insecticide, Fungicide and Rodenticide Act, the two Federal statutes that provide the framework for pesticide regulation in the United States. FQPA became effective immediately upon signature and all reregistration eligibility decisions (REDs) signed subsequent to August 3, 1996 are accordingly being evaluated under the new standards imposed by FQPA.

In establishing or reassessing tolerances, FQPA requires the Agency to consider available information concerning aggregate exposures to pesticide residues, including all anticipated dietary exposures and other exposures for which there is reliable information, as well as the potential for cumulative effects from a pesticide and other compounds with a common mechanism of toxicity. The Act further directs EPA to consider the potential for increased susceptibility of infants and children to the toxic effects of pesticide residue.

Paraquat dichloride is currently registered for the control of weeds and grasses in agricultural and non-agricultural areas. It is used as a preplant or preemergence herbicide on vegetables, grains, cotton, grasses, sugarcane, peanuts, potatoes, and on areas for tree plantation establishment. Paraquat is applied as a directed spray postemergence herbicide around fruit crops, vegetables, trees, vines, grains, soybeans, and sugarcane. It is used for dormant season applications on clover and other legumes, and for chemical fallow. It is also used as a desiccant or harvest aid on cotton, dry beans, soybeans, potatoes, sunflowers, sugarcane and as a post harvest desiccant on tomatoes. Finally, it is applied to pine trees to induce resin soaking. Paraquat dichloride is also used on non-crop areas such as public airports, electric transformer stations and around commercial buildings to control weeds.

The Agency has reassessed paraquat dichloride food and feed tolerances under the standards of FQPA and determined that the existing tolerances with amendments and changes as specified in this document meet the safety standards of FQPA. Based on available information, there is a reasonable certainty that no harm will result to infants and children or to the general population from aggregate exposure to paraquat dichloride residues. The Agency only evaluated dietary exposure in the aggregate assessment since there are no residential or other non-occupational uses of paraquat. Further, based on paraquat's normal use patterns and unique environmental fate characteristics, exposures to paraquat in drinking water are not expected and not a concern. Based on the available data, the Agency does not believe that the effects produced by paraquat would be cumulative with those of other structurally related compounds, and therefore has considered only paraquat exposures in the aggregate assessment.

In reaching the determination of safety for infants and children, the Agency found that the toxicity database for paraquat is complete, based on current requirements, and that the effects observed in pre- and post-natal studies did not indicate any increased sensitivity of infants and children to paraquat. Therefore, no additional uncertainty factor was used in the risk assessment.

Under FIFRA, the Agency has concluded that all uses, as prescribed in this document, will not cause unreasonable risks to humans or the environment. Accordingly, the Agency has determined that all paraquat dichloride products are eligible for reregistration.

To mitigate risks of potential dermal exposure to handlers/workers the Agency is requiring, among other changes, modifications of the personal protective equipment and reentry intervals of 12 hours for preemergence and directed-spraying uses and 24 hours for desiccation and harvesting uses. Although a few use scenarios indicated LOC exceedances on an acute basis for birds, herbivorous and insectivorous mammals, the Agency has concluded (based on paraquat's unique environmental fate characteristics) that paraquat dichloride will not typically pose a threat to birds or mammals once it dries. Also, in agreement with the registrant, the maximum label rate for paraquat dichloride of 1 lb cation/Acre is being established to reduce environmental risks to non-target terrestrial and semi-aquatic plants from drift. Additional data for product chemistry, certain cropfield trials and spray drift studies are being required to confirm the Agency's risk assessment and conclusions.

Accordingly, before reregistering the products containing paraquat dichloride, the Agency is requiring that product specific data, revised Confidential Statements of Formula (CSF) and revised labeling be submitted within eight months of the issuance of this document. These data include product chemistry and acute toxicity testing for each registration. After reviewing these data and any revised labels and finding them acceptable in accordance with Section 3(c)(5) of FIFRA, the Agency will reregister a product. Those products which contain other active ingredients will be eligible for reregistration only when the other active ingredients are determined to be eligible for reregistration.

I. INTRODUCTION

In 1988, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act provides a schedule for the reregistration process to be completed in nine years. There are five phases to the reregistration process. The first four phases of the process focus on identification of data requirements to support the reregistration of an active ingredient and the generation and submission of data to fulfill the requirements. The fifth phase is a review by the U.S. Environmental Protection Agency (referred to as "the Agency") of all data submitted to support reregistration.

FIFRA Section 4(g)(2)(A) states that in Phase 5 "the Administrator shall determine whether pesticides containing such active ingredient are eligible for reregistration" before calling in data on products and either reregistering products or taking "other appropriate regulatory action." Thus, reregistration involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criterion of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) (Public Law 104-170) was signed into law. FQPA amends both the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 301 *et seq.*, and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136 *et seq.* The FQPA amendments went into effect immediately. Among other things, FQPA amended the FFDCA by establishing a new safety standard for the establishment of tolerances. The FQPA did not, however, amend any of the existing reregistration deadlines set forth in section 4 of FIFRA. Thus, the Agency is embarking on an intensive process, including consultation with registrants, States, and other interested stakeholders, to make decisions on the new policies and procedures that will be appropriate as a result of enactment of FQPA. This process will include a more in depth analysis of the new safety standard and how it should be applied to both food and non-food pesticide applications. However, in light of the unaffected statutory deadlines with respect to reregistration, the Agency will continue its ongoing reregistration program while it continues to determine how best to implement FQPA.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of paraquat dichloride (commonly referred to as "paraquat" in this document) including the risk to infants and children for any potential dietary, drinking water, accidental dermal or oral exposures, and cumulative effects as stipulated under the FQPA. The document consists of six sections. Section I is the introduction. Section II describes paraquat dichloride, its uses, data requirements and regulatory history. Section III discusses the human health and environmental assessment based on the data available to the Agency. Section IV presents the reregistration decision for paraquat dichloride. Section V discusses the reregistration requirements for paraquat dichloride. Finally, Section VI is the Appendices which support this Reregistration Eligibility Decision. Additional details concerning the Agency's review of applicable data are available on request.

II. CASE OVERVIEW

A. Chemical Overview

The following active ingredient(s) are covered by this Reregistration Eligibility Decision:

- **Common Name:** Paraquat dichloride
- **Chemical Name:** 1,1'-dimethyl-4,4'-bipyridinium dichloride
- **Chemical Family:** Bipyridylum, dipyridylum
- **CAS Registry Number:** 1910-42-5
- **OPP Chemical Code:** 061601
- **Empirical Formula:** $C_{12}H_{14}Cl_2N_2$
- **Trade and Other Names:** Cekuquat, Cyclone, Dextrone, Esgram, Gramoxone, Goldquat, Herboxone, Prelude, Pillarxone, Pillarquat, Surefire, Starfire, Total, Toxer
- **Basic Manufacturer:** Zeneca

B. Use Profile

The following is information on the currently registered uses with an overview of use sites and application methods. A detailed table of these use of paraquat is in Appendix A.

For Paraquat dichloride:

Type of Pesticide: Herbicide, Desiccant, Defoliant

Mode of Action: Contact herbicide, without residual soil activity. Destroys cell membranes and inhibits photosynthesis. Only contacted leaves are killed, so regrowth can occur from undamaged parts of perennials.

Use Groups and Sites:

TERRESTRIAL FOOD CROP

acerola (West Indies cherry); apricot; asparagus; avocado; banana; blackberry; blueberry; boysenberry; broccoli; cabbage; cabbage, Chinese; carrot (including tops); cauliflower; cherry; cocoa; coffee; collards; cucumber; eggplant; fig; filbert (hazelnut); garlic; groundcherry (strawberry tomato/tomatillo); guava; hops; kiwifruit; lettuce; loquat; macadamia nut (bushnut); manioc (cassava); melons; melons, cantaloupe; melons, musk; melons, water; mint; nectarine; olive; onion; papaya; passion fruit; peach; pear; pecan; pepino (melonpear); pepper; pepper (chili type); pineapple; pistachio; plum; potato, white/Irish; prune; pumpkin; raspberry (black, red); rhubarb; smallfruits; squash (all or unspecified); strawberry; sugarbeet; taro; walnut (English/black); yam; yautia

TERRESTRIAL FOOD+FEED CROP

almond; apple; barley; beans, asparagus; beans, dried-type; beans, mung; beans, succulent (lima); beans, succulent (snap); citrus fruits; corn (unspecified); corn, field; corn, pop; corn, sweet; cotton (unspecified); garbanzos (including chickpeas); grapes; guar; hops; legume vegetables; mint; oats; orchards (unspecified); peanuts; peanuts (unspecified); peas (unspecified); peas, field; peas, pigeon; peppermint; potato, white/Irish; safflower; safflower (unspecified); small fruits; small grains (unspecified); sorghum; sorghum (unspecified); soybeans (unspecified); soybeans, edible; spearmint; sugarbeet; sugar crops; sugarcane; sunflower; tomato; turnip; vegetables (unspecified); wheat

TERRESTRIAL FEED CROP

alfalfa; barley; beans; clover; crownvetch; legume vegetables; lespedeza; lupine; pastures; sainfoin; timothy; trefoil; tyfon; vetch; wheat

TERRESTRIAL NON-FOOD CROP

agricultural fallow/idleland; airports/landing fields; commercial/industrial lawns; commercial/institutional/industrial; premises/equipment (outdoor); fencerows/hedgerows; grasses grown for seed; industrial areas (outdoor); jojoba; nonagricultural outdoor buildings/structures; nonagricultural uncultivated areas/soils; ornamental and/or shade trees; peach (non-bearing, seed beds); recreation area lawns; tomato (post-harvest); wood protection treatment to forest products (seasoned)

FORESTRY

forest plantings (reforestation programs); pine (forest/shelterbelt); shelterbelt plantings

TERRESTRIAL NON-FOOD

ornamental and/or shade trees; ornamental herbaceous plants;
ornamental woody shrubs and vines; non-crop areas such as public
airports, electric transformer stations and around commercial buildings

Target Pests: Annual broadleaf and grassy weeds (top kill of
perennials).

Formulation Types Registered:

MANUFACTURING PRODUCT

Soluble concentrate/liquid 43.5000%

END USE PRODUCT

Soluble concentrate/liquid 23.2000 to 43.5000%
(23.2000%, 29.1000%, 29.4200%,
30.3000%, 37.000%, 43.5000%)

Multiple active ingredient products contain:
diuron (035505)

Method and Rates of Application:

TYPES OF TREATMENT

Band treatment; Bark treatment (cut); Basal spray treatment; Bore-hole
treatment; Broadcast; Directed spray; Ground spray; Soil band
treatment; Soil broadcast treatment; Spot soil treatment; Spot treatment;
Spray; Strip treatment.

EQUIPMENT

Aircraft; Backpack/Knapsack sprayer; Hand held spray wand; Sprayer;
Ground/Tractor-drawn ground boom.

TIMING

At cracking; At planting; August; Dormant; Early spring; Established
plantings; Fall; Fallow; Foliar; July; Postemergence; Postharvest;
Postplant; Posttransplant; Preemergence; Preharvest; Preplant; Preplant
(Spring); Ratoon; Seed bed; Seedling stage; Spring; Stubble; When
needed; Winter.

C. Estimated Usage of Pesticide

This section summarizes the best estimates available for the pesticide uses of
paraquat dichloride. These estimates are derived from a variety of published and
proprietary sources available to the Agency. The data, reported on an aggregate and
site (crop) basis, reflect annual fluctuations in use patterns as well as the variability in
using data from various information sources.

Estimates of paraquat usage vary widely from different sources. Rather than providing a range of estimates, the table below gives what the Agency believes to be the most likely estimate and also a likely maximum estimate. This maximum is not a strict upper bound limit, but an estimate. There is a very small probability that the actual amount of paraquat being used would exceed this estimated likely maximum.

Most of paraquat usage is for field crops because of the high acreage of these crops. The percent crop treated and average application rates for field crops is less than that for fruits and vegetables. The average percent crop treated on fruits is significantly higher than for vegetables and field crops. The highest usages in pounds a.i. are for corn, soybeans, cotton, and apples.

PARAQUAT QUANTITATIVE USAGE ANALYSIS

VEGETABLE/MELONS -----	Acres Planted	Acres Treated (000)		% of Crop Treated		Total AI (000 lbs)		Application
	(000)	Likely Estimate	Likely Max	Likely Estimate	Likely Max	Likely Estimate	Likely Max	lbs ai/year/ treated acres
Eggplant	4	1	2	25.0%	50.0%	2	2	2.0
Peppers	101	18	33	17.8%	32.7%	18	34	1.0
Lettuce	283	8	11	2.8%	3.9%	6	8	0.8
Sweet Corn	748	6	25	0.8%	3.3%	5	21	0.8
Potatoes	1,403	40	73	2.9%	5.2%	25	39	0.6
Tomatoes	480	73	93	15.2%	19.4%	75	111	1.0
Mint	147	39	.	26.5%	.	20	.	0.5
Cole Crops	263	2	4	0.8%	1.6%	1	2	0.5
Broccoli	107	.	1	.	1.0%	.	1	1.0
Cabbage	84	.	3	.	3.0%	.	1	0.2
Cauliflower	57	.	1	.	1.0%	.	1	1.0
Collards	15	.	0	.	1.0%	.	0	2.0
Cucurbits, not melons	250	15	24	6.0%	9.6%	12	19	0.8
Cucumbers	151	12	.	7.9%	.	10	.	0.8
Pumpkins	41	1	.	2.4%	.	1	.	1.0
Squash	58	2	.	3.4%	.	1	.	0.5
Melons	349	10	16	2.9%	4.6%	8	11	0.8
Cantaloupe	110	.	6	0.0%	5.5%	.	2	0.3
Watermelons	239	.	10	0.0%	4.2%	.	8	0.8
Vegetables, Other	330	20	30	6.1%	9.1%	13	23	0.8
Asparagus	55	9	12	16.4%	21.8%	6	8	0.7
Carrots	104	1	.	1.0%	.	1	.	0.5
Garlic	22	4	.	18.2%	.	3	.	0.8
Onions	149	6	.	4.0%	.	3	.	0.5
Subtotal	4,358	232	293			185	255	
Average				5.3%	6.7%			0.8

PARAQUAT QUANTITATIVE USAGE ANALYSIS (continued)

FRUITS/CITRUS/NUTS -----	Acres Planted	Acres Treated (000)		% of Crop Treated		Total AI (000 lbs)		Application
	(000)	Likely Estimate	Likely Max	Likely Estimate	Likely Max	Likely Estimate	Likely Max	lbs ai/year/ treated acres
Citrus	1,229	108	295	8.8%	24.0%	94	192	0.9
Grapefruit	201	15	35	7.5%	17.4%	14	24	0.9
Lemons	66	1	6	1.5%	9.1%	1	5	1.0
Oranges	911	80	240	8.8%	26.3%	70	150	0.9
Citrus, Other	51	12	14	23.5%	27.5%	9	13	0.8
Pome Fruits	768	251	315	32.7%	41.0%	248	305	1.0
Apples	656	230	280	35.1%	42.7%	220	264	1.0
Pears	84	19	26	22.6%	31.0%	25	35	1.3
Pome-Like, Other *	28	2	9	7.1%	32.1%	3	6	1.5
Stone Fruits	713	197	269	27.6%	37.7%	147	206	0.7
Cherries	132	48	54	36.4%	40.9%	46	56	1.0
Peaches	248	92	120	37.1%	48.4%	61	86	0.7
Plums & Prunes	138	27	42	19.6%	30.4%	20	30	0.7
Stone-Like, Other *	195	30	53	15.4%	27.2%	20	34	0.7
Grapes	874	162	200	18.6%	22.9%	101	125	0.6
Blueberries	59	9	.	15.3%	.	5	.	0.6
Raspberries	11	2	.	18.2%	.	1	.	0.5
Strawberries	30	6	9	20.0%	30.0%	6	9	1.0
Nut Trees	1,277	180	282	14.1%	22.1%	164	227	0.9
Almonds	455	75	130	16.5%	28.6%	80	96	1.1
Pecans	496	64	97	12.9%	19.6%	50	78	0.8
Walnuts	217	26	30	12.0%	13.8%	20	29	0.8
Nut Trees, Other	109	15	25	13.8%	22.9%	14	24	0.9
Subtotal	4,961	915	1,370			766	1,064	
Average				18.5%	27.6%			0.8

* Fruit trees, other

Pome-like, other includes kiwifruit, figs, and papayas.

Stone-like, other includes apricots, nectarines, avocados, and olives.

PARAQUAT QUANTITATIVE USAGE ANALYSIS (continued)

FIELD/CERERAL CROPS -----	Acres Planted	Acres Treated (000)		% of Crop Treated		Total AI (000 lbs)		Application
	(000)	Likely Estimate	Likely Max	Likely Estimate	Likely Max	Likely Estimate	Likely Max	lbs ai/year/ treated acres
Alfalfa	24,835	130	180	0.5%	0.7%	60	100	0.5
Hay, other	32,605	20	32	0.1%	0.1%	9	14	0.5
Pasture/Rangeland	0.1%	.	.	.
Corn	78,234	1,400	2,210	1.8%	2.8%	800	1,200	0.6
Cotton	13,944	900	2,330	6.5%	16.7%	280	740	0.3
Sorghum	10,307	150	450	1.5%	4.4%	56	120	0.4
Soybeans	61,564	1,020	1,940	1.7%	3.2%	540	960	0.5
Barley	6,838	28	55	0.4%	0.8%	11	22	0.4
Oats/Rye	5,085	4	7	0.1%	0.1%	2	3	0.5
Wheat	70,014	203	335	0.3%	0.5%	81	124	0.4
Wheat, Spring	20,861	3	7	0.0%	0.0%	1	2	0.3
Wheat, Winter	49,153	200	328	0.4%	0.7%	80	122	0.4
Hops	42	35	.	83.3%	.	23	.	0.7
Beans/Peas, Dry	2,223	20	70	0.9%	3.1%	7	18	0.4
Beans/Peas, Vegetable	719	10	21	1.4%	2.9%	5	9	0.5
Peanuts	1,691	464	930	27.4%	55.0%	72	140	0.2
Sunflower	2,044	15	.	0.7%	.	11	.	0.7
Safflower	323	31	.	9.6%	.	28	.	0.9
Sugar Beets	1,465	3	9	0.2%	0.6%	2	4	0.7
Sugarcane	879	40	110	4.6%	12.5%	18	55	0.5
Subtotal	312,812	4,473	8,679			2,005	3,509	
Average				1.4%	2.8%			0.4
ALL CROPS								
Total	322,131	5,620	10,342			2,955	4,828	
Average				1.7%	3.2%			0.5

NOTES:

Numbers may not agree due to rounding.

Likely estimates and maximums are not ranges and both may not be provided when data is insufficient.

Application (last column) is the likely estimate of total lb ai divided by acres treated.

SOURCES: EPA data, USDA, National Center for Food and Agricultural Policy

D. Data Requirements

Data required in the June 1987 Registration Standard for paraquat dichloride include studies on product chemistry, ecological effects, toxicology, environmental fate, and residue chemistry. A Data Call-In issued December 1991 required further testing for ecological effects, environmental fate and residue chemistry. These data were required to support the uses listed in the Registration Standard. Appendix B includes all data requirements identified by the Agency for currently registered uses needed to support reregistration.

E. Regulatory History

Paraquat was discovered in 1882 and has been used as an oxidation-reduction indicator under the name of methyl viologen since 1932. The first commercial paraquat formulation for agricultural use was produced by Imperial Chemical Industries, Ltd. in England and was registered there in 1962.

Paraquat dichloride was registered in the United States in 1964 for use as a contact herbicide to control or suppress a broad spectrum of emerged weeds. The Agency classified paraquat dichloride as a Restricted Use pesticide due to high acute toxicity to animals and people from intentional or inadvertent exposure. This action was taken by the Agency through regulations proposed in the September 1, 1977 (42 FR 44170) and finalized in the February 9, 1978 (43 FR 5782) issues of the FEDERAL REGISTER. Under the Restricted Use classification, only certified applicators are authorized to apply paraquat dichloride end-use products.

In 1978 paraquat dichloride was accepted as a candidate for the Special Review process based on the following areas where paraquat dichloride was believed to exceed the risk criteria under 40 CFR 162.11: teratogenicity, lack of emergency treatment, chronic effects, reproductive effects, oncogenicity (data gap), mutagenicity (data gap), and acute effects. Other areas of concern included mammalian toxicity and avian reproductive effects. Upon conclusion of the Special Review evaluation in October 1982 (43 FR 30613), the Agency issued a Final Position Document which concluded that the available data did not support paraquat dichloride being placed into the Special Review status since the risk criteria identified in 1978 had not been exceeded.

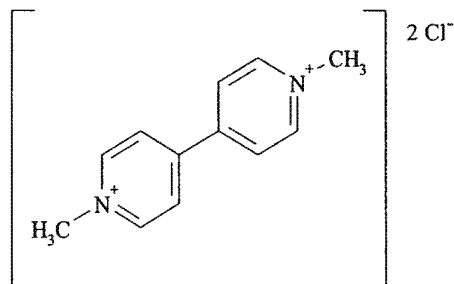
After the Special Review evaluation, the Agency believed that the acute effects level was very close to estimated applicator exposures. Therefore, a Data Call-In was issued for paraquat dichloride requiring additional dermal and inhalation data and more precise information to assess the potential of acute effects as a result of applicator exposure to this compound. A Registration Standard for paraquat dichloride was issued in June 1987 (NTIS #PB88-217005) in which the Agency

evaluated the studies submitted as a result of the previous DCI. This Reregistration Eligibility Decision reflects a reassessment of all data which were submitted in response to the Registration Standard and subsequent December 1991 DCI.

III. SCIENCE ASSESSMENT

A. Physical Chemistry Assessment

Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride) is a nonselective contact herbicide, desiccant, defoliant, and plant growth regulator primarily used on field crops and fruit and nut crops.



Empirical Formula: C₁₂H₁₄Cl₂N₂
Molecular Weight: 257.2
CAS Registry No.: 1910-42-5
OPP Chemical Code: 061601

Production of the paraquat dimethyl sulfate salt [1,1'-dimethyl-4,4'-bipyridinium bis(methyl sulfate); OPP Chemical Code 061602] has been discontinued; there are no active uses or products.

IDENTIFICATION OF ACTIVE INGREDIENT

Paraquat dichloride is an off-white, odorless hygroscopic (holding moisture) powder with a melting point of approximately 340 C. Paraquat dichloride is freely soluble in water, slightly soluble in alcohols, and insoluble in nonpolar organic solvents. The Technical Grade Active Ingredient (TGAI) is corrosive to metals, hydrolyzes under alkaline conditions, and decomposes photochemically.

MANUFACTURING-USE PRODUCTS

There are two paraquat dichloride manufacturing-use products (MPs) registered to Zeneca AG Products under OPP Chemical Code 061601; they are the 43.5% formulation intermediates (FIs) (EPA Reg. Nos. 10182-115 and 10182-362).

[Please contact Monty Dixon
At 336.632.7055 or
monty.dixon@syngenta.com if
for complete
RED if
desired.]



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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: 02/01/2006

MEMORANDUM

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

SUBJECT: REGISTRATION OF PARAQUAT DICHLORIDE GENERIC END-USE PRODUCTS

FROM: Hope Johnson, Biologist
Herbicide Branch, Registration Division

THROUGH: Dan Kenny, Chief
Herbicide Branch, Registration Division

TO: Lois Rossi, Director
Registration Division

SUMMARY:

After carefully reviewing all available data, the Agency has decided paraquat dichloride formulations that do not contain the Inteon™ Technology differ only in ways that will not significantly increase the risk of unreasonable adverse effects on the environment. However, the Agency intends to limit these registrations to two years (because it expects to receive additional data relevant to this determination in the upcoming years) but allow the registrants the opportunity to amend their registrations to eliminate the limitation.

BACKGROUND:

Chemical Information:

Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium ion) is a member of the bipyridylum family of herbicides. It is a non-selective contact herbicide, defoliant, desiccant, and plant growth regulator registered for use on a variety of terrestrial food and feed crops. Paraquat dichloride works by inhibiting photosynthesis. It was registered in the United States in 1964, and classified as a Restricted Use Pesticide (RUP) on February 9, 1978, so that only certified applicators are authorized to purchase and apply paraquat dichloride end-use products. It was

registered by the Agency in August of 1997.

Paraquat dichloride is currently registered for the control of weeds and grasses in agricultural and non-agricultural areas. It is used as a preplant, preemergence, or postemergence herbicide on vegetables, grains, soybeans, cotton, grasses, sugarcane, peanuts, potatoes, dry peas, field and pop corn, endive, persimmon, artichoke, and on areas for tree plantation establishment. It is also used as a desiccant or harvest aid on cotton, dry beans, soybeans, potatoes, sunflowers, sugarcane and as a post harvest desiccant on tomatoes. It is applied to pine trees to induce resin soaking. Paraquat dichloride is also used on non-crop areas such as public airports, electric transformer stations and around commercial buildings to control weeds. There are no residential or other non-occupational uses of paraquat dichloride.

There have been reported cases of paraquat dichloride poisoning due to accidental and intentional ingestion as well as heavy dermal exposure. Most of the fatal cases due to paraquat dichloride are related to suicidal or accidental ingestions. The inclusion of an emetic, dye, and a stenching agent in paraquat dichloride formulations has led to a reduction in paraquat poisonings. U.S. Poison Control Center data show a decline of almost 60 percent when comparing the proportion of all pesticide exposures due to paraquat ingestion for the four years pre- and post-1988. The Agency has reviewed all available incident information regarding accidental paraquat dichloride ingestions and has concluded as explained below that the range of deaths per year in the United States that can be attributed to accidental paraquat dichloride ingestions is 1.1 to 2.3.

In other parts of the world, deaths caused by paraquat dichloride far exceed the U.S. average. Mexico (mainly the state of Chiapas), Korea, and Sri Lanka have a problem with death from paraquat ingestion due to a large number of intentional ingestions for the purpose of self harm. A majority of the persons that intentionally ingest paraquat are small scale farmers that have a small container of paraquat in their house for use on the farm.

Paraquat dichloride Registrations/Applications:

On September 13, 2004, Syngenta Crop Protection Inc., the sole registrant of paraquat dichloride products at the time, submitted an application for registration of a new formulation of paraquat dichloride called Gramoxone Inteon[®]. The new formulation is a 30.1% active ingredient (2 lb epton per gallon) formulation, compared to the 43.8% formulation (3 lb epton per gallon) of EPA Registration Number 100-1074. The acute toxicity categories are identical. The new formulation contains a [REDACTED] that is designed to gel in the event it enters the human stomach as a result of accidental or intentional ingestion. The gelling agent and increased levels of emetic are intended to minimize entry of paraquat dichloride into the mesene where much of the absorption occurs. Syngenta Crop Protection Inc. submitted dog toxicokinetics studies in their application for registration to provide "proof of concept" and an indication of the level of improved safety. Based on tests with dogs, Syngenta Crop Protection Inc. originally claimed a 10X increase in the LD50 in dogs for the Inteon[®] formulation, and expects all deaths caused by unintentional ingestions of paraquat dichloride to be stopped. Syngenta Crop Protection Inc. also claims the efficacy of the product is unchanged by the addition of the gelling

Quoted from EPA Registration Number 100-1217 application letter. Dated September 13, 2004.

agent, Gramoxone Inteon™ was conditionally registered by the Agency on August 17, 2005, as EPA Registration Number 100-1217.

On September 14, 2005, Syngenta Crop Protection Inc. submitted a request for a conditional voluntary cancellation of Gramoxone Max™ (EPA Registration Number 100-1074). The conditions involved in the request were:

- 1) Syngenta requests cancellation of EPA Registration Number 100-1074 effective September 30, 2006, or such later date as EPA identifies in a formal cancellation order.
- 2) Syngenta will cease manufacture prior to the effective date of the cancellation.
- 3) Any minimal stocks that have been packaged, labeled, and released for shipment before the effective date of cancellation may be further legally distributed and sold until exhausted.
- 4) In the event that the state of California has not granted such a registration to Syngenta by July 31, 2006, Syngenta shall notify EPA of that fact by July 31, 2006, at which point the condition for Syngenta's request for voluntary cancellation shall be deemed not to have been met and therefore the request withdrawn.

All other registered paraquat dichloride end use formulations held by Syngenta Crop Protection Inc. were also requested to be cancelled; however, they did not contain any conditions in their respective cancellation requests.

On December 6, 2005, Syngenta Crop Protection Inc. submitted an amendment to their cancellation request for EPA Registration Number 100-1074. The amendment removed the conditional aspect of the cancellation request, and stated the cancellation shall be effective on such date after the April 26, 2006 close of the public comment period on Syngenta's request as EPA shall determine, and Syngenta will cease manufacture by the effective date of the cancellation as required by EPA.

On October 16, 2003, Simon Corporation submitted an application for registration for a "Me-Too" paraquat dichloride technical concentrate based upon Syngenta's registered product bearing EPA Registration Number 100-1067. On May 19, 2005, a conditional registration was granted as EPA Registration Number 70552-1.

On August 2, 2005, Simon USA Inc. submitted an application for registration for a "Me-Too" paraquat dichloride end use formulation based upon Syngenta's registered product bearing EPA Registration Number 100-1074. The pending end use product uses EPA Registration 70552-1 as the technical in its formulation. This application was granted an unconditional 3(c)(5) registration on January 25, 2006; however, the registration letter stipulated that:

"This registration will expire automatically, without opportunity for a hearing, upon the issuance of a cancellation order for EPA Reg. No. 100-1074. The registrant will be subject to the same conditions as contained in the cancellation order issued on that date for EPA Reg. No. 100-1074. The cancellation order for EPA Reg. No. 100-1074 will not be issued before April 26, 2006."

On August 27, 2004, Griffin Corporation submitted an application for registration for a

"Me-Too" paraquat dichloride technical concentrate based upon Syngenta's registered product bearing EPA Registration Number 100-1067. On August 2, 2006, this application was amended to a "Me-Too" application based upon Simon's registered product bearing EPA Registration Number 70552-1. This application is currently pending (EPA File Symbol Number 81876-R) with a renegotiated PRLA date of September 2, 2006. On August 27, 2004, Griffin Corporation also submitted an application for registration for a "Me-Too" paraquat dichloride end use formulation based upon Syngenta's registered product bearing EPA Registration Number [REDACTED]. The pending end use product uses the unregistered technical concentrate EPA File Symbol Number 81876-R in its formulation. This application is currently pending (EPA File Symbol Number 81876-E) with a renegotiated PRLA date of September 2, 2006.

On May 18, 2006, Makreshim Agran of North America, Inc. (MANA) submitted an application for registration for a "Me-Too" paraquat dichloride technical concentrate based upon Syngenta's registered product bearing EPA Registration Number 100-1067. Additionally, MANA submitted an application for registration for a "Me-Too" paraquat dichloride end use formulation based upon Syngenta's registered product bearing EPA Registration Number 100-1074. Both applications are currently pending (EPA File Symbol Numbers 66222-REG and 66222-RGN) with PRLA due dates of December 10, 2006, and December 11, 2006, respectively.

Syngenta Crop Protection Inc. has submitted Petitions to Deny for many of the above referenced paraquat dichloride applications. Syngenta Crop Protection claims a number of reasons for which to deny the applications, including health and safety concerns due to impurities, lack of stewardship, and the lack of Inteon™ technology. Syngenta Crop Protection Inc. also states many applications have data citation deficiencies.

RATIONALE:

In 2005, Syngenta Crop Protection Inc. met with Jim Jones, Director of the Office of Pesticide Programs to make a presentation on their newly registered Gramoxone Inteon™ product and to explain the increased safety the new product has over the old formulations of paraquat dichloride. After the meeting concluded, Jim Jones requested that a Risk-Benefit Assessment be conducted primarily to determine whether the non-Inteon™ formulations of paraquat dichloride differ only in ways that would not significantly increase the risk of unreasonable adverse effects on man or the environment when compared to the Inteon™ product.

HEALTH EFFECTS DIVISION (HED) REVIEW:

The Health Effects Division (HED) conducted a review of all the data available to the Agency regarding the different formulations of paraquat, including the Inteon™ and non-Inteon™ formulations. Below is a synopsis of HED's findings.

Background

After reviewing the allegations in Syngenta's petitions to deny, it appears that the applicants have submitted the necessary data and certified that they have made the necessary offers to pay the original data submitters.

The paraquat Inteon™ formulation, in addition to paraquat and other inert ingredients, includes a combination of increased emetic, addition of an emetic gel, and addition of a purgative. The gel is designed to slow dispersion (absorption) of paraquat and the purgative is designed to enhance rapid elimination of stomach contents via fecal elimination.

The HPD analysis focused on four issues: (1) analysis of submitted dog toxicokinetic studies; (2) estimates of paraquat dose based on volume of paraquat formulation ingested; (3) preliminary findings reported by Syngenta from an ongoing study in Sri Lanka; and (4) an estimate of the number of unintentional deaths from currently registered paraquat products in the United States.

Analysis of Dog Toxicokinetic Studies

Four separate studies with dogs submitted by Syngenta and reviewed by the Agency showed that two different Inteon formulations (combination of emetic, gelling agent, and purgative) appeared to be more protective in dogs than non-Inteon formulations that were tested (two separate formulations with lower emetic amounts and not currently registered in the U.S.). In response to Agency questions¹, subsequent submissions by Syngenta included clarifying data (MRID 46865500) and additional dog data (MRID 46865501 and Cockrill and Goburdham, 1988²).

Syngenta originally claimed that their Inteon™ formulation was ten times safer than the currently registered non-Inteon™ product (MRID 46865500). However, this was based on a comparison of lethality in the 12 mg paraquat ion/kg formulation (not the currently registered product; contained no emetic at all – the Cockrill and Goburdham, 1988 study) to the 128 mg paraquat ion/kg formulation (Inteon with emetic, gel, and purgative). Since the currently registered non-Inteon™ paraquat products (e.g., Gramoxone Max™, EPA Registration Number 100-1074) contain some amount of emetic, the Inteon™ formulation is likely less than 10 times more protective than the currently registered non-Inteon™ product because of the protection gained by use of the emetic alone. How much less than 10 depends on the acute lethality of the Inteon™ compared to the non-Inteon™ paraquat formulations.

Other data were provided on the effects of a paraquat formulation that contains an emetic at an increased level, more than what is contained in the currently registered non-Inteon™ product but approximating the emetic level in the Inteon formulation (MRID 46865500). HPD conducted an analysis³ to compare safety between the Inteon™ and non-Inteon™ formulations containing the extra emetic with the existing dog data by comparing estimated NOAELs (32 mg paraquat ion/kg [non-Inteon with extra emetic] vs. 64 mg paraquat ion/kg [Inteon] = 2X difference) or LOAELs (48 mg paraquat ion/kg [non-Inteon™ with extra emetic] vs. 128 mg paraquat ion/kg [Inteon] = 2.7X difference). The LOAEL of 128 mg paraquat ion/kg is based on lung lesions with the Inteon™ formulation and the LOAEL of 48 mg paraquat ion/kg is based on

¹ EAB #0052955 Memorandum from Alberto Pretzel to Hope Johnson dated July 29, 2005.

² Memorandum ("Discussion Piece on Paraquat Inteon Products") from Alberto Pretzel to Lois Rossi dated April 10, 2006.

³ Submitted via e-mail on July 27th, 2006.

⁴ Discussion piece prepared August 1, 2006 by Scarano and Pretzel.

symptoms (low appetite) with the non-InteonTM formulation with extra emetic.

Thus, the available dog data suggests a possible 2-3 fold difference between InteonTM and non-InteonTM formulations that contain extra emetic. However, the non-Inteon formulation tested in this experiment is not a currently registered product in the United States.

Estimate of Human Paraquat Dose Based on Paraquat Formulation Ingested

It is important to estimate the ingested dose of a paraquat formulation following unintentional or accidental exposures in humans. Unintentional ingestions can be estimated to amount to about 15 to 60 ml of concentrate (based on e-mail from J. Wells (Syngenta) to L. Scarano (EPA) dated 3/15/2005). These ingestion volumes result in the following exposures:

- Based on the composition of Paraquat Inteon A7813K (currently registered in the U.S.), ingestions on the range of 15 to 60 ml would correspond to ingestions of 3.8 to 15 g. of paraquat ion which would correspond to doses of 63 to 250 mg paraquat ion/kg bw, assuming a 60 kg person. A child weighing 10 kg would thus be exposed to doses of 480 to 1500 mg paraquat ion/kg bw.
- Based on the composition of Paraquat Inteon A387BU (currently registered in other parts of the world), ingestions on the range of 15 to 60 ml would correspond to ingestions of 3 to 12.2 g. of paraquat ion which would correspond to doses of 50 to 200 mg paraquat ion/kg bw, assuming a 60 kg person. A child weighing 10 kg would thus be exposed to doses of 300 to 1220 mg paraquat ion/kg bw.

The two paraquat Inteon formulations tested in the dog studies show that the highest dose at which no toxicity was observed was 64 mg paraquat ion/kg. The calculations above show that the Inteon formulation would not be protective against lethality at these levels of exposure based on estimated unintentional ingestions of paraquat.

Preliminary Findings from the Sri Lankan Study

The other information that Syngenta has submitted over the past month is the Sri Lanka data. Sri Lanka has conducted an observational monitoring survey to investigate the circumstances associated with ingestion and the impact of the new InteonTM formulation. The Agency does not have a complete report of the results of this study but has received preliminary data comparing intentional and non-intentional deaths in Sri Lanka comparing InteonTM and non-InteonTM formulations. According to the abstract that was submitted for presentation at the Asia Pacific Association of Medical Toxicologists Congress held August 6-8, 2006, data was collected from 586 patients over the course of 26 month period, of which 289 cases had confirmed or probable InteonTM ingestion. The new formulation improved overall survival from 25.6% to 30.3%, a difference of less than 10%. In other words, the preliminary analysis indicates that InteonTM paraquat may only prevent deaths in about 10% of the people who ingest paraquat. Additionally, survival was strongly associated with estimated ingestion volume.

This second point is entirely consistent with HED's findings as noted above, i.e. whether someone will die or not from ingesting paraquat is a function of how much they drank, not whether they drank InteonTM or non-InteonTM formulations. At higher doses, a person will die.

regardless of the formulation ingested.

Estimated Number of Unintentional Deaths Per Year from Paraquat Ingestion in the United States

HED evaluated several databases, including the American Association of Poison Control Center's Toxic Exposure Surveillance System (AAPCC's TESS), its (a)2 Incident Data System (IDS), Syngenta's PROSAR, NIOSH SENSOR, and the National Pesticide Information Center (NPIC) and concluded that between 1.1-2.3 deaths per year occurred between 1993 and 2003 in the United States due to the ingestion of paraquat (non-InteonTM) formulations.⁷ There is uncertainty as to whether these deaths could be categorized as unintentional or suicidal due to lack of information or insufficient detail in the various databases. In addition, HED cannot estimate with any certainty how much paraquat people consumed based on the incident data we have.

HED Conclusions

Based on the NOAEL and LOAEL numbers, it appears that the InteonTM technology may provide a small margin of safety over a paraquat formulation containing a higher level of emetic. However, because the amount of paraquat involved in accidental ingestions most likely will exceed 64 mg/kg (and even 128 mg/kg, the dose at which some effects were seen in dogs), the paraquat with InteonTM technology may not be sufficient to save any human lives. In addition, the preliminary data the Agency has received regarding the Sri Lanka study indicates that the InteonTM technology may only save lives in about 10% of the cases of paraquat ingestion, although as noted above, there is no information about how much paraquat was ingested by the patients involved in that study. Therefore, it does not appear that the InteonTM technology is significantly safer than a paraquat formulation with a higher level of emetic.

Finally, the reported range of possible paraquat (non-InteonTM) deaths due to ingestion in the United States is from 1.1 to 2.3 deaths per year. There is uncertainty around the estimated volume ingested in these data and, as noted earlier, the volume ingested is important for assessing the safety of InteonTM vs. non-InteonTM paraquat formulations. Given these uncertainties (the number of deaths, the volume ingested), it is difficult to estimate how the introduction of Inteon would be a safer alternative to the existing non-Inteon paraquat formulation.

BIOLOGICAL AND ECONOMIC ANALYSIS DIVISION (BEAD) REVIEW:

The Biological and Economic Analysis Division (BEAD) conducted an assessment to determine whether the potential benefit (i.e., the avoidance of unintentional death and illness due to accidental paraquat dichloride ingestion) of the new formulation of paraquat dichloride justifies the increased cost to growers. BEAD also determined the economic impacts of generic paraquat entry to the marketplace.

⁷ The lower bound of this estimate represents death identified as unintentional and the upper bound represents death identified as either unintentional or unclear.

The cost of Syngenta's new paraquat product, Gramoxone Inteon™, is approximately 5% higher than Gramoxone Max™.⁸ The new formulation [REDACTED] with the additional safety features would cost approximately [REDACTED] more per gallon of Gramoxone. The amount of Gramoxone Max™ sold each year in the United States is approximately 1 to 1.3 million gallons so the additional cost of the new formulation is about [REDACTED].

BEAD estimated the entry of a generic paraquat product into the herbicide market and concluded that the generic product will likely lower the market price of Gramoxone Max™, the currently registered paraquat end-use product, by 17%, and Gramoxone Inteon™ by 20%.¹⁰ This estimation was based on a paper entitled "The Effects of Generic Competition on Pesticide Markets" by Richard Just, which was submitted to the Agency in 2002. BEAD concurs with many fundamental elements within the Just study. His results show that price reductions from generic competition have been as high as 48% and are commonly over 20%. BEAD believes that the price reduction at best may reach the lower end of the range discussed by Just because the monopoly conditions analyzed in the Just study may not correspond to all market conditions. In the case of paraquat, this condition does not exist due to competing active ingredients and products within the same marketing niche.

For a standard market analysis of measuring the effects of a generic paraquat product entry on the market price, BEAD would need at the minimum 1) price elasticity of demand and supply for the pesticide from generic competitor, 2) anticipated market share for the generic producers, and 3) and other supporting market information related to product advantage or disadvantages to competing alternatives. Because such data is not available for this analysis, BEAD assumes when a new generic product enters the paraquat market, Syngenta will match its price to the competitor's price. BEAD also uses the average value of a generic manufacturer's price as a % of Gramoxone Max™ prices from 2001 to 2003 to approximate the potential decline in the price of Gramoxone Max™ if a generic product comes to the market. The expected price decline is estimated at 17% from the average price of Gramoxone Max™ from 2001 to 2003. The cost of Syngenta's new paraquat product, Gramoxone Inteon™, is approximately a 5% higher than Gramoxone Max™.¹¹ As a result, the expected price decline would be 20% from the price of Gramoxone Inteon™ if Gramoxone Max™ is replaced with this new formulation.

These estimates are consistent with the Just study, which shows that if a generic registration only obtains a small share of the market because of the other active ingredients competing within this weed and grass herbicide market, the price reduction is likely to be less than 20%.

A 17% price decline for Gramoxone Max™ would likely reduce the cost to growers by

⁸ This information was provided by Syngenta, Gramoxone manufacturer.

⁹ Approximately 3-4 million pounds of paraquat are applied each year (EPA proprietary data), while 3 pounds of paraquat cation are contained in a gallon of Gramoxone. This analysis was based on the assumption that all the paraquat used in the United States is sold as the product Gramoxone. However, there are other products available in the market, which make up an insignificant share of the market.

¹⁰ Memorandum, Economic Impacts of Generic Paraquat Entry, Dated April 27, 2006.

¹¹ This information was provided by Syngenta, Gramoxone manufacturer.

\$5.95 million to \$7.74 million per year. A 20% price decline for Gramoxone Inteon™ would likely reduce the cost of the new formulation by [REDACTED]. Because it is difficult to predict market responsiveness to a generic entry, there are uncertainties associated with the estimated figures and therefore are subject to a wide margin of variability.

The total benefit of the availability of generic paraquat to growers is estimated at \$7.75 to \$10.4 million, which is the sum of the price decrease of the currently registered paraquat end-use product [REDACTED] and the avoided cost increase of Syngenta's new paraquat product, Gramoxone Inteon™ [REDACTED].

In BEAD's original paraquat assessment in 2005², the total value of annual avoided death cases as a result of using new formulation with improved safety features was estimated at [REDACTED] with the avoided mortality cases of 0 to 2.4 per year. However, based on BEAD's revised calculation of the number of the possible reduced deaths that range from 1.1 to 2.3 and the unit value of [REDACTED] per death, the potential range of health benefits of the new formulation of paraquat dichloride was recalculated at [REDACTED].

Based on this information, the relative benefits of the paraquat with the Inteon™ technology and the paraquat without the Inteon™ technology are quite similar. Under the above analysis, the total economic value of annual avoided death cases as a result of excluding any generic paraquat registrations from the market and only registering the Gramoxone Inteon™ product is a range of [REDACTED]. In other words, at the lower estimated range of deaths per year (i.e., 1.1), registration of the Gramoxone Inteon™ product and exclusion of non-Inteon™ paraquat products from the market has a negative economic impact on farmers.

CONCLUSION

Based on the currently available information, it is not clear that Syngenta's Inteon™ technology will actually be demonstrably safer than a paraquat formulation that contains an increased amount of emetic. Under section 3(c)(7)(A), EPA is required to make a determination that when a product differs from a currently registered product, it is only in ways that will not significantly increase the risk of unreasonable adverse effects on the environment. In balancing the risks and benefits, a comparison of the higher cost of the Inteon™ product and the uncertainty of its actual benefits with the lower cost of the non-Inteon/increased emetic paraquat registrations weigh in favor of granting the non-Inteon/increased emetic paraquat registrations. Given the amount of paraquat that is estimated to be ingested accidentally, it is unlikely that Inteon™ will be much more effective at saving lives than a paraquat formulation with an increased emetic level; therefore, it would be unreasonable to pass the higher cost of this product onto the farmers. In light of the available information, it appears that the paraquat formulations with increased emetic levels differ from paraquat containing the Inteon™ technology only in ways that do not significantly increase the risk of unreasonable adverse effects on the environment.

However, the Agency anticipates receiving additional data in the near future (e.g., an additional dog study, the full report of the results of the Sri Lanka study, and any incident data

²Memorandum, Paraquat Assessment, D332323, Dated December 14, 2005.

that shows the actual effects of the InteonTM paraquat v. the non-InteonTM increased emetic paraquat products). Because there is a slight difference in the NOAEL and LOAEL levels of the Inteon paraquat formulation and the non-InteonTM increased emetic paraquat formulation, it is possible that future studies and/or incident data could demonstrate that the non-InteonTM increased emetic paraquat formulations do significantly increase the risk of unreasonable adverse effects on the environment when compared to the InteonTM products. Therefore, the Agency determines that non-InteonTM increased emetic paraquat formulations can be registered for a limited period of two years. Registrants of non-InteonTM increased emetic paraquat formulations could request an amendment to their registrations to remove that time limitation, at which point the Agency would review all data available at that time and re-evaluate whether the non-InteonTM increased emetic paraquat products continue to differ only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment.



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

DEC 19 2006

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Mr. John Abbott
Syngenta Crop Protection, Inc.
PO Box 18300
Greensboro, NC 27419-8300

Subject: Gramoxone Inteon
EPA Registration Number 100-1217
Protocol Response

Dear Mr. Abbott:

The U.S. EPA OPP Health Effects Division has reviewed the protocol for an acute toxicity study in dogs as provided in your PowerPoint presentation sent to us on September 1, 2006 (e-mail from John Abbott to Hope Johnson, EPA). Given this information and our review of the Inteon™/Non-Inteon™ issue over the past year, we have the following comments:

1. Again, as we stated at the August 30, 2006 meeting in which you first presented the protocol for this study, we are not asking for or requiring this study. In fact, it is not entirely clear how the study will add value to the current database. In a previous study, you have shown that the protection afforded by Inteon™ is being breached at 128 mg paraquat ion/kg (lung effects seen). Based on the relatively steep dose response curve [change from non-lethalities to lethalities with an increase of less than 10 mg paraquat ion/kg] the non lethal dose (or the minimum lethal dose as may be determined in the new study) will not be much greater than the 128 mg paraquat ion/kg observed in the initial study. Thus the protective non-lethal value is around 64 mg paraquat ion/kg. As pointed out in our calculations using a range of volumes ingested, this value does not guarantee survival in many cases of accidental ingestion (63 to 250 mg paraquat ion/kg bw, assuming a 60 kg person, from previous comments) and clearly not in cases of suicidal intention where the ingestion is much higher.
2. Our biggest concern is that the formulations proposed for the study (Slide 9) show that, in addition to the gel and purgative that are both present in Inteon™ compared to non-Inteon™, there is 3X more emetic in the Inteon™ formulations vs. the non-Inteon™ formulations. Thus, this may not answer the question as to what may be more protective: the presence of the gel, the purgative, or the additional emetic - or any combination of these three.
3. While we don't think this study is necessary, if you elect to do it, we note that you plan to use fresh animals as you increase the dose in the rising dose level process (Slide 10). This would be useful since earlier studies/protocols used the same dogs for multiple dose levels. In addition, it would be worthwhile to follow all dosed animals for a period of time to assess possible delayed/persistent effects following a acute exposure to paraquat.

DEC 27 2006

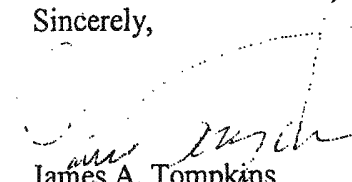
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Page 2

4. Again, if you still plan to do the study, it would be useful to get the details for determining "minimum lethal dose". You allude to them on Slide 12 ("endpoint thresholds for requiring termination"), but don't provide the necessary details.

We apologize for the delay in our response. If you have any questions, please contact Hope Johnson at 703-305-5410.

Sincerely,



James A. Tompkins

Product Manager 25

Herbicide Branch

Registration Division (7505P)

Paraquat Information Center > Paraquat Information Center > About this site > Overview

About this site



The Paraquat Information Center provides comprehensive information on Paraquat, its uses in agriculture, and its profile on human and environmental safety. This site is powered by [Syngenta](#) and sponsored by the [Global Paraquat Community](#).

Paraquat is an active ingredient used in crop protection products, commonly referred to as pesticides. Paraquat is used by farmers all over the world to help them produce a wide variety of crops. It controls a wide range of weeds (unwanted plants) that reduce both crop yield and quality by competing with the crop for water, nutrients, and light.

It is important to understand that the active ingredients found in all crop protection products need to be combined with water and additional materials to transform them into effective products. Therefore, the active ingredient paraquat is only available and can only be purchased by farmers as a fully formulated product concentrate ready for spraying once further diluted, up to 200 times, with water.

Paraquat has been used by farmers all over the world for over 40 years, resulting in a huge amount of information and data as well as extensive in-field experience.

Paraquat, like all other active ingredients used in crop protection, is constantly being reviewed by national and global authorities and other researchers. Due to the length of time paraquat has been on the market and its widespread use, many studies have been carried out on the product. These include studies examining:

- [Paraquat's short- and long-term effects on human health](#)
- [Ways in which paraquat can help farmers improve the profitability and sustainability of their farming systems](#)
- [Improvements in the efficacy and safety of paraquat.](#)

You are invited to explore this website, where you'll find key information about paraquat, including:

- [Why and where do farmers use paraquat?](#)
- [What are the advantages resulting from its use?](#)
- [How does paraquat fit into sustainable agriculture?](#)
- [How can paraquat be used safely?](#)
- [What is being done in order to ensure the safe use of paraquat, particularly in developing countries?](#)

In addition, you will find third-party [references](#) and useful [links](#) that provide a broader insight into paraquat and what has been experienced and examined over the years.

Views on paraquat vary widely around the world. As with many pesticides, there have

been concerns about paraquat's safety to users, the environment, and consumers. The Paraquat Information Center provides you with facts and figures to formulate your own, well-informed decision about this crop protection product.

We hope you will find the information you are looking for and that you consider the Paraquat Information Center a useful tool. Please contact us if you have any additional paraquat-related questions that are not answered by the information contained within this site.

Paraquat Information Center > Overview of benefits



Paraquat Benefits



Benefits to farmers

Benefits to the environment

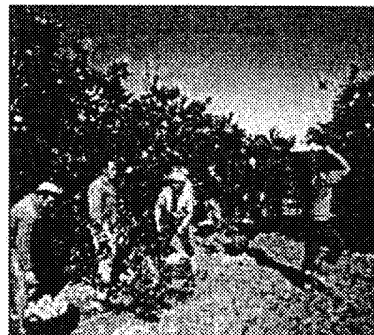
Benefits to society

Growing possibilities



Paraquat is a valuable herbicide tool in developed and developing countries benefiting farmers, society, and the environment.

When used in accordance with manufacturers' recommendations, paraquat can deliver safe, effective weed control and generate greater social and economic benefits, while protecting the land for future generations.



The key benefits of paraquat include:

- **Rapid action**

Paraquat's rapid speed of action is unique among non-selective herbicides. Signs of leaf damage become visible within hours of paraquat application and complete control of all green plant tissue is achieved within 1-7 days (compared with other products, which can take several weeks to reach maximum control). The speed of action quickly removes weed competition, allows rapid turn-around between crops, and can prevent the transmission of insect-borne diseases to newly planted crops.

- **Increased yields**

The timely removal of weeds by paraquat reduces competition for light, water, and nutrients giving improved crop growth, which often leads to better yields for farmers. Such yield improvements have been recorded in a wide range of crops including alfalfa, tea, corn, soybeans, and fruit and vegetables.

- **Ability to work in all weather conditions**

Paraquat is uniquely rain-fast within minutes, typically within 15 minutes to one hour, and its uptake is not dependent on temperature or soil moisture. Its rain-fast properties allow spraying in periods of unsettled weather, which is essential in many parts of the world, particularly those in tropical regions. Since activity is independent of active weed growth, paraquat can be sprayed during winter months or in very dry conditions. This ensures timely weed control and sowing or planting, which in turn promises maximum yield potential.

- **Excellent crop safety**

The precision contact action of paraquat is restricted to the part of the plant it touches and it is not translocated to other parts of the plant, making paraquat a 'chemical hoe' for smallholders and subsistence farmers around the world. This contact action makes paraquat ideal for use in orchards, vineyards, and plantations since it can be used safely around all trees and other vegetation. Any accidental spray reaching the foliage causes only localized scorch.

- **Reduced labor requirements**

Paraquat is an ideal tool for inter-row weeding. Its rapid, precision contact action makes paraquat the most effective and safe herbicide for use between vegetable rows. Throughout the world the use of Paraquat has released smallholder and subsistence farming families from much arduous and time-consuming hand weeding.

- **Reduces soil erosion**

Paraquat only affects the aerial (above-ground) parts of weeds and does not kill the root structure. Intact roots help to bind soil, thus reducing wind and water erosion of the soil. This property also makes paraquat ideal for use in conservation and no-till systems.

For more information about the benefits of soil conservation and no-till systems, visit the Web site for Soil and Water Protection, www.sowap.org, or the Web site for ProTerra, www.proterra.eu.com.

- **Rapid adsorption and deactivation upon soil contact**

Paraquat is rapidly adsorbed and biologically inactivated in contact with soil. Therefore, it may be sprayed at any time in the crop cycle from prior to planting to just before crop emergence. In addition, because there is no residual activity any crop may be planted almost immediately after spraying, including cover crops in orchards and plantations. Since it is immobile in soil paraquat also does not leach into groundwater.

- **Herbicide resistance management**

Paraquat is an increasingly important part of Integrated Weed Management (IWM) programs associated with glyphosate-tolerant crops and in other situations where glyphosate has been intensively used for long periods of time.

- **Compatibility with other herbicides**

Paraquat is compatible in tank mixtures with a wide range of herbicides, insecticides and liquid fertilizers. This property enables several products to be applied in one application, saving energy, labor, and time and reducing soil compaction.

Paraquat Information Center > Paraquat Information Center > Benefits of Paraquat > To farmers > Overview



Benefits to farmers



Paraquat has become one of the most widely used herbicides in the world thanks to one group of people - farmers. Though they span more than 120 countries and farm more than 100 different crops, farmers are united by their recognition of the benefits paraquat has to offer.

Rapid action

In Indonesia, paraquat's rapid action allows farmers, who would normally harvest two direct-seeded rice crops each year, to plant and harvest a third crop (Sembiring & Kartaatamadja, 2003).

Paraquat's speed of action quickly removes weed competition and allows rapid turn-around between crops. This is essential in many countries and regions such as China, Asia, and Latin America, where it enables small farmers to minimize the delay between crops and maximize income. The rapid action is also an important benefit for management of spray teams in plantation crops. Any missed area is visible within hours of spraying and can be quickly corrected.

Increased yield

The ability of paraquat to promote increased yield benefits farmers allows them to maximize income and/or food supplies.

Ability to work in all weather conditions

In Indonesia, tidal rice land is subject to two tidal inundations per day. Thanks to its broad weed spectrum and rapid rain-fastness, paraquat - the only herbicide that can be used in this environment - has made rice farming viable in that country.

The rain-fast properties of paraquat allow spraying in periods of unsettled weather, which is essential in many parts of the world, and provides farmers with maximum flexibility.

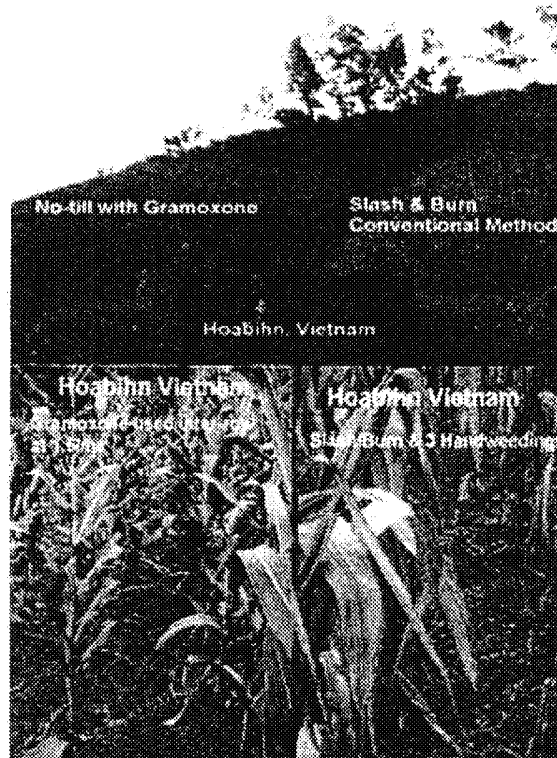
Reduced labor requirements

In Africa, Latin America, and Asia the use of paraquat on coffee plantations has reduced labor from 10-20 man days per one hectare of land (six times per season) for hand weeding to one day (three to four times per season) for spraying paraquat.

Paraquat is an ideal tool for inter-row weeding. Throughout the world it has released smallholder and subsistence farming families from much of the laborious and time-consuming hand weeding. The use of paraquat saves labor and allows farmers to take on more land or some form of paid labor. Perhaps most importantly this 'chemical hoe' has released children from these arduous tasks, enabling them to undertake an

education.

Two adjacent fields of corn demonstrate the benefits of paraquat. Field one (top and bottom left) shows the results of no-till, pre-plant and inter-row paraquat application. Field two (top and bottom right) showing the results of farmers' normal practice of "slash and burn" techniques and hand weeding.



Paraquat Information Center > To the environment - Facts and Information about the Benefits of Paraquat Use from the Paraquat Information Center



Benefits to the environment



"Paraquat- Farming for the future"

Over the past decade modern farming methods have attracted criticism, particularly for neglect of the environment and natural resources such as soil and water. Paraquat has not only been proven safe to the environment, but it has also demonstrated several key environmental benefits.

These benefits to the environment include:

Improved soil fertility

Paraquat's contact-only action allows farmers to control only weeds without killing the root structure, making it an ideal herbicide for use in conservation and no-till systems.

Field studies have shown that no-till systems using paraquat:

- increase organic matter
- reduce carbon dioxide emissions by allowing the soil to act as a better carbon sink
- have higher microbial populations and surface microarthropods
- have higher earthworm populations

Reduced soil erosion

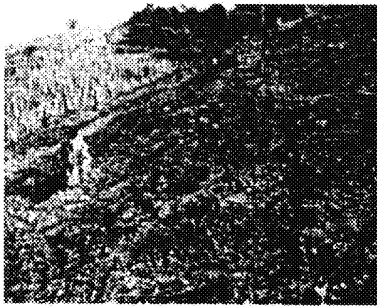
Because paraquat controls weeds without killing the root structure, it also contributes significantly to soil conservation. For more information about the benefits of soil conservation, visit the Web site for Soil and Water Protection, www.sowap.org, or the Web site for ProTerra, www.proterra.eu.com.

Preservation of soil moisture

By enabling no-tilling farming which preserves soil moisture, paraquat plays a vital role in helping growers to retain as much soil moisture as possible.

No residue

Since paraquat only exhibits contact action and there is no residual action, no detectable residues are found in most food crops.



A farmer's field after using slash and burn techniques and before corn planting. In addition to the heavy loss of organic matter from burning, the soil in this field is completely exposed to rain and at high risk for erosion risk. Paraquat, used in a non-till system, has been shown to increase organic matter in the soil and reduce soil erosion.

Paraquat Information Center > Benefits of Paraquat to society - Facts and Information about the Benefits of Paraquat Use to Society from the Paraquat Information Center



Benefits to society

XLAL

"Paraquat – A harvest of hope"

In many parts of the world, climate and labor conditions have not been conducive to the farming of certain staple crops and to improvements in sustainable agriculture practices such as conservation tillage. Paraquat's unique properties have made possible the cultivation of many of these crops - to the benefit of farmers and of society.

Benefits to society include:

- **Reduction in labor needs** related to hand-weeding crops and de-suckering vines, freeing up farmers and their families to pursue paid labor and/or educational opportunities.
- **Increase in viable crop options** resulting in improved food supplies, increased revenue, and additional employment opportunities.
- **Stimulated economies.** The fast action of paraquat quickly eliminates weed competition and since it is also non-residual it is an ideal tool for multi-cropping, allowing farmers to maximize income from their land.

For an overall assessment of paraquat's contribution to sustainable agriculture, read "Paraquat and Sustainable Agriculture" by Richard Bromilow.

"Paraquat has the unusual property of being active only by direct spray...such properties allow paraquat to be used in many crops such as those grown by low tillage methods." - Pest Management Science 2003 (60:340-349)

Paraquat Information Center > Paraquat Information Center > What Regulators Say > Overview



Overview



Paraquat, like other active ingredients, is constantly being studied by national and global authorities and other researchers. These experts support that when used properly, paraquat can deliver safe, effective weed control, generating greater social and economic benefits, while protecting the land for future generations.

A summary of recent regulatory decisions related to paraquat as well as a list of countries in which paraquat is currently registered is available [here](#).

Recent Regulatory Decisions

In the last decade paraquat has been approved for re-registration following rigorous evaluation by regulatory authorities all over the world. Paraquat has also received periodic re-evaluations of both toxicology and dietary residues by the [WHO](#) and [FAO](#), respectively. A new FAO specification for paraquat was also established under the revised process for FAO and WHO specifications for pesticides.

The most recent regulatory decisions are from New Zealand where paraquat received a full re-registration in November 2007. Read about this [here](#).

A judgment by the Court of First Instance (CFI) on 11th July 2007 was that the Commission Directive (2003/112/EC of 1st December 2003) that included paraquat in Annex I to Council Directive 91/414/EEC was annulled.

The CFI decision to annul the Annex I inclusion of paraquat criticised the way in which the re-registration procedure was handled and the manner in which the Commission interpreted the relevant laws and applied them to its analysis of the data. The CFI decision does not mean that paraquat cannot be included in Annex I but it does mean that the previous inclusion of paraquat in Annex I is no longer valid.

The CFI decision is not in itself a ban on paraquat, but as a result of both the decision and the expiry of measures permitting Member State authorisations to remain in force during the previous review of paraquat for inclusion in Annex I, some Member States have withdrawn their national authorisations.

The major manufacturer of paraquat, Syngenta, has said that it intends to prepare for a re-submission for annex 1 registration. Read about Syngenta's viewpoint [here](#).

This decision does not affect the ability of farmers outside of the EU to use paraquat on products that they export to the EU. The Maximum residue levels required for this to happen remain in place and can be found on official EU documents [here](#).

In August 1997, the US Environmental Protection Agency concluded "The use of currently registered products containing paraquat dichloride in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for re-registration"

A fact sheet and re-registration eligibility document are available [here](#)

- In December 2003, the EU concluded "*It has appeared from the various examinations made that there are uses of plant protection products containing paraquat which may be expected to satisfy, in general, the requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC, provided appropriate risk-mitigation measures and restrictions are applied.*"

This statement, and the references therein, means that the EU has concluded that there are uses of paraquat, following good agricultural practice, which will not have any harmful effects on human or animal health or on groundwater, or have any unacceptable influence on the environment. This decision allows for continued registration of paraquat products in EU countries. The decision was subject to compliance with various requirements, including a stewardship program for operator safety and a monitoring program for operator health problems and wildlife incidents.

The full technical review report and regulatory decision are available [here](#)

- In 2003, paraquat was reviewed under a periodic re-evaluation of toxicology under the Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Its toxicological properties were evaluated and the acceptable daily intake (ADI) of paraquat was established. This allows an assessment of consumer safety to be made.
The 2003 JMPR report is available online [here](#)
- In 2004, paraquat was reviewed under a periodic re-evaluation of dietary residues under the Joint FAO/WHO Meeting on Pesticide Residues (JMPR), "*The Meeting concluded that the intake of residues of paraquat resulting from uses considered by the current JMPR was unlikely to present a public health concern.*"
The 2004 JMPR report is available [here](#)
- In 2003, the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS) decided to establish a revised specification under the new FAO/WHO procedure. These specifications promote the manufacture, distribution and use of pesticides that meet basic quality requirements. The specifications provide an international point of reference against which products can be judged, either for regulatory purposes or in commercial dealings, and thus help prevent the trading of inferior products.

The March 2006 revision of the FAO Manual on development and use of FAO and WHO specifications for pesticides confirms that:

- The old FAO specifications that were first established for paraquat in 1994 were superseded and cancelled
- Syngenta are the only paraquat manufacturer who can claim that their paraquat material complies with the specification as they are the only manufacturer who has submitted a data package and specification (which have then been evaluated as acceptable) in accordance with current JMPS procedures.
- Paraquat materials from other manufacturers no longer comply.
- In line with their obligations under Article 6.2.4 of the FAO International Code of Conduct on the Distribution and Use of Pesticides (2002), any other paraquat manufacturer should, at the earliest opportunity, provided data packages and specifications to the JMPS under the new procedure, for assessment of equivalence

- The revised paraquat specification is available [here](#)

Paraquat Registrations

Paraquat is registered and used in over 100 developed and developing countries around the world including key major agricultural markets with some of the most demanding regulatory systems such as Canada, Australia, USA, Japan, and New Zealand . A list of the countries in which Paraquat is registered and sold as of Nov 2007 appears below:

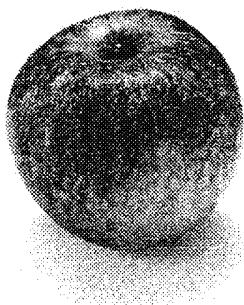
Albania	Guinea	Peru
Algeria	Guyana	Philippines
Angola	Haiti	Rwanda
Antigua & Barbuda	Honduras	Samoa
Argentina	India	Sao Tome & Principe
Australia	Indonesia	Serbia Montenegro
Bahamas	Iran	Sierra Leone
Bahrain	Iraq	Singapore
Bangladesh	Israel	Solomon Isl.
Barbados	Jamaica	Somalia
Belize	Japan	South Africa
Bolivia	Jordan	South Korea
Bosnia-Herzegovina	Kenya	Sri Lanka
Botswana	Kiribati	St Kitts & Nevis
Brazil	Lebanon	St Lucia
Burundi	Liberia	St Vincent & Grenadines
Cameroon	Macedonia	Sudan
Canada	Madagascar	Suriname
Chile	Malawi	Swaziland
China	Malaysia	Tahiti
Colombia	Marshall Isl.	Taiwan
Cook Isl.	Mauritius	Tanzania
Costa Rica	Mexico	Thailand
Croatia	Morocco	Tonga
Cuba	Mozambique	Trinidad & Tobago
Dominica	Myanmar	Turkey
Dominican Republic	Namibia	Tuvalu
Ecuador	Nauru	Uganda
El Salvador	New Zealand	Uruguay
Ethiopia	Nicaragua	US
Fiji	Niue	Vanuatu
Gabon	Pakistan	Venezuela
Ghana	Panama	Vietnam
Grenada	Papua New Guinea	Zambia

Guatemala	Paraguay	Zimbabwe
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Paraquat Information Center > Regulators Dismiss Public Health Concerns

About Paraquat

Regulators Dismiss Public Health Concerns Related to Paraquat



Paraquat, one of the most widely used herbicide active ingredients in the world for the control of annual and perennial weeds, was reviewed as part of a periodic re-evaluation of dietary residues under the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 2004.

The results of this review were published in the 2004 JMPR report, which stated that: *"The Meeting concluded that the intake of residues of paraquat resulting from uses considered by the current JMPR was unlikely to present a public health concern."*

A complete copy of the 2004 JMPR report is available [here](#).

This conclusion supports findings of other regulatory bodies throughout the years, including the US EPA, which in 1997 concluded that:

"there is a reasonable certainty that no harm will result in infants and children or to the general population from aggregate exposure to paraquat dichloride residues. Further, based on the available data, the Agency does not believe that the effects produced by Paraquat would be cumulative with those of other structurally related compounds" (US EPA, 1997)

For more information on recent regulatory decisions related to paraquat, visit the ["What Regulators Say"](#) section of this website.

Paraquat Information Center > EU Dismisses NGO Case Against Paraquat

EU Dismisses NGO Case Against Paraquat



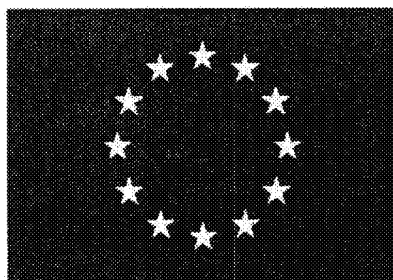
The Court of First Instance of the European Communities has dismissed the case brought by various NGOs against the European Commission's decision to re-register paraquat. On 28 November 2005, the court rejected the claim on the basis that the NGOs are not individually concerned by the contested decision and do not, therefore, meet the requirements in order to bring this case to court.

In the case T-94/04, The NGOs sought a ruling that Directive 2003/112/EC - the Directive that confirmed the re-registration of paraquat by inclusion on Annex I to Directive 91/414 - was null and void. This directive allows for continued registration of paraquat products in EU countries.

The decision to include paraquat in this directive followed a review in which the EU concluded that there are uses of paraquat, following good agricultural practice, which will not have any harmful effects on human or animal health or on groundwater, or have any unacceptable influence on the environment. To that end, the report states:

"It has appeared from the various examinations made that there are uses of plant protection products containing paraquat which may be expected to satisfy, in general, the requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC, provided appropriate risk-mitigation measures and restrictions are applied."

For more information and a link to the EU's 2003 report approving the inclusion of paraquat in the Directive, [click here](#).



For a copy of the November 2005 Court of First Instance of the European Communities's written document dismissing the case against paraquat click on the following [link](#).

Paraquat Information Center > Experts Endorse Paraquat Information Center

Experts Endorse Paraquat Information Center



Members of the Global Paraquat Community represent leading agricultural and environmental organizations around the world. The Paraquat Information Center is pleased to welcome additional industry experts as members of the Global Paraquat Community sponsoring this site.

"I was stationed in one of the largest rain-fed areas in Java (Central Java), where most farmers adopted dry-direct seeded rice. Herbicides are essential in rain-fed rice in order to prevent weed problems during fertilizer application. As a member of the Global Paraquat Community, I can share information about my team's experience using paraquat in rice farming systems."

- **Dr. Ir. Prihasto Setyanto, MSi**, Head of Head of Research Station for Agricultural Environment Preservation, in Central Java, Indonesia

The Global Paraquat Community

Members of the Global Paraquat Community include:

David Browne, of Venture Exports, New Zealand

Dr. Ir. Hamdan Pane, MS, Weed Science Expert from the Indonesia Rice Research Institute
Dr. Ir. Syamsudin Koloj, MSi, Head of the Weed Science Society of Indonesia (WSSI)

Dr. Drs. Orbanus Naharia, MSi, from UNIMA Manado University in North Sulawesi

Dr. Ir. Prihasto Setyanto, MSi, Head of the Research Station for Agricultural Environment Preservation, in Central Java, Indonesia

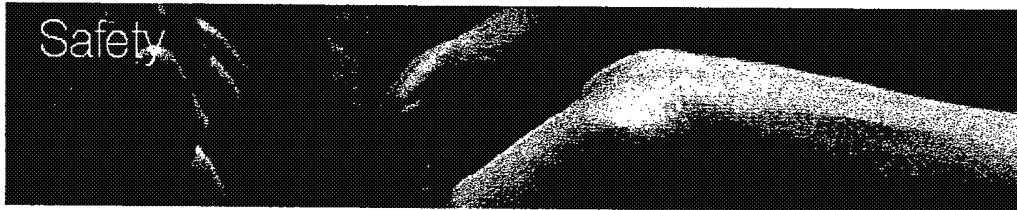
Dr. Klewphun, Weed Science Expert and President of the Weed Science Society, Thailand

Dr. Apichai Daorai, from the Kasetsart University and member of the Registration Subcommittee / Label Committee
Dr. Pornchai, Weed Scientist at the Chiangmai University, Thailand.

Paraquat Investigation Team, Pharmacology and Toxicology Department, Universidad de Antioquia, Colombia

The Paraquat Information Center provides comprehensive information on paraquat, its uses in agriculture, and its profile on human and environmental safety. This site is powered by Syngenta and sponsored by the Global Paraquat Community. For more information see [About this Site](#).

Paraquat Information Center > Overview of Paraquat Safety - Facts and Information about Paraquat Safety from the Paraquat Information Center



Safety



The Safety of Paraquat

As with many crop protection products, there have been concerns about paraquat's safety to users, the environment, consumers, and others. Like all active ingredients, paraquat is constantly being studied by national and global authorities and other researchers. These experts support that when used properly, paraquat can deliver safe, effective weed control, generating greater social and economic benefits, while protecting the land for future generations.

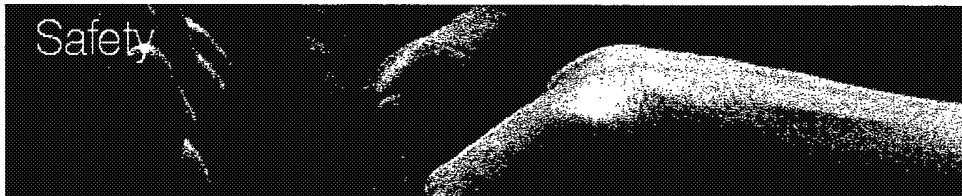
More information on the safety of paraquat is available using the links below.

Paraquat safety:

- [Safety to the environment](#)
- [Safety in humans](#)
- [Safety to operators and bystanders](#)
- [Safety to the public](#)
- [Safety concerns](#)

You can also find additional details by visiting the "[What Regulators Say About Paraquat](#)" and "[Answers to Your Questions About Paraquat](#)" sections of this website.

Paraquat Information Center > Paraquat Safety to the Environment



Safety to the Environment



Extensive long-term field studies confirm—and governments and regulatory authorities, worldwide, agree—that normal uses of paraquat in accordance with the simple label instructions do not cause an unacceptable environmental impact.

These studies have shown that:

Paraquat is inactive in soil - When paraquat residues come into contact with the soil the paraquat active ingredient rapidly becomes adsorbed and strongly bound to clay and organic matter in the soil. It becomes biologically inert and as a result it cannot be taken up by plant roots or other organisms. Paraquat does not sterilize the soil and it cannot be released or re-activated by the application of water or other agrochemicals.

All soils, not only those with high clay content, have a high capacity to absorb paraquat. In most agricultural areas, applications could take place annually for more than 100 years without exceeding the adsorption capacity of just the top two inches of soil.

- In their review report for paraquat the European Commission (EC) noted that there was "*very strong adsorption in all the soils tested*" (EC, 2003)
- In their Reregistration Eligibility Decision (RED) document, the US Environmental Protection Agency (EPA) concluded that "*due to the apparent adsorption strength of paraquat for soil clays, these bound residues do not appear to be environmentally available.*" (US EPA, 1997)

Paraquat cannot travel through soil - Paraquat binds to soils and cannot be 'leached' or travel to contaminate groundwater. This has been confirmed under laboratory conditions and in field studies involving vastly exaggerated rates of paraquat and other paraquat containing herbicides over 40 years.

- In their review report for paraquat the EC concluded that "*all studies indicate that paraquat is immobile*" (EC, 2003)
- In their RED document, the US EPA declared that "*paraquat dichloride was shown to be very immobile in soil*" (US EPA, 1997)

Paraquat does not accumulate in soil – Bioavailable paraquat is rapidly degraded by soil microorganisms in a matter of days into natural products such as CO₂ and water.

Since this is an equilibrium process, the net result is that the build-up of paraquat in soil is prevented. This has been demonstrated by long-term field trials.

- In their review report for paraquat, the EC concluded that accumulation studies conducted in the UK and US demonstrated soil residues that were 17% and 26% of the theoretical maximum, respectively after 20 years (EC, 2003)

Paraquat does not contaminate ground water - Paraquat binds so strongly with clay particles that it cannot be released to contaminate ground water. In fact, it binds so strongly that to release the paraquat from soil samples for analysis in laboratory conditions, the clay particles have to be broken down and destroyed through a boiling process in concentrated acid for several hours.

- In their RED facts document, the US EPA concluded that *"paraquat is not expected or considered to be a groundwater concern from normal paraquat dichloride use patterns"* (US EPA, 1997)
- In their review report for paraquat the EC observed that *"paraquat will not be used under conditions where contamination of the saturated zone occurs"* (EC, 2003)

Paraquat poses no risk to earthworms or soil microorganisms Since paraquat is deactivated by soil, the residues of paraquat application also have no harmful effects on earthworms. Likewise it has no significant effect on the micro-biological activity and fertility of the soil. Normal biological processes such as nitrogen and carbon mineralization are not affected.

- In their review report for paraquat, the EC concluded that *"No adverse effects were observed on earthworm populations in a field study following application of up to 720 kg as/ha in one year"* (EC, 2003)

Paraquat is not hazardous to fish in normal use - As with any pesticide it is possible that small amounts of paraquat could enter water through spray drift or when using paraquat to control weeds on the banks of irrigation channels or ditches. Although there is a variation in the toxicity of paraquat to different species of fish there is a big margin of safety between the levels which might accidentally contaminate water during normal use and those which are toxic in prolonged tests over 96 hours, to even the most sensitive species. Similar studies showed there was no evidence of any toxic effect on invertebrates found in the water.

- In their RED document, the US EPA concluded that *"the registered uses of paraquat dichloride are not expected to pose an acute risk to any aquatic organisms"* (US EPA, 1997)
- In their review report for paraquat the EC instructed Member States to *"pay particular attention to the protection of aquatic organisms. Conditions of authorization should include risk mitigation measures, where appropriate"* (EC, 2003)

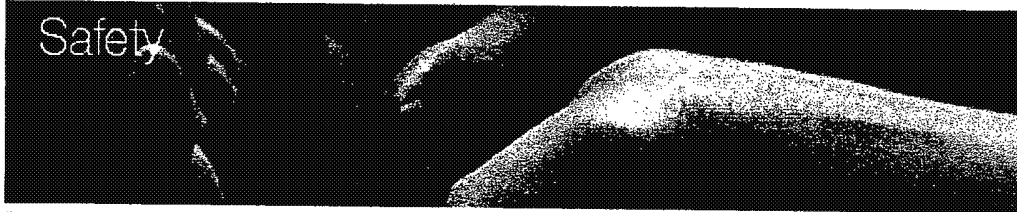
Paraquat poses no risk to domestic or farm animals - There is no health risk to domestic animals, which enter fields that have been sprayed with paraquat at normal recommended dilutions or to cattle and sheep if they graze on sprayed vegetation, provided the spray deposit has dried. Studies have shown there is no harmful effect or build-up of paraquat in farm animals that drink water accidentally contaminated by spraying operations.

Paraquat poses no significant hazard to wildlife - Forty years of experience and field trials have established that there is no significant hazard to wildlife from normal use of paraquat. Residues, even on freshly sprayed vegetation, would not be expected to present a hazard to birds. Wild bird populations were monitored over a five-year period on a farm where paraquat use was much higher than usual, including use

beneath hedgerows and along fence lines. Even this very intensive use during the five years did not adversely affect the birds in population density or variety of species.

- In their RED document, the US EPA concluded that "*acute toxicity to terrestrial animals (birds) and mammals only exists immediately after application*" (US EPA, 1997)
 - In their review report for paraquat, the EC note that the Standing Committee on the Food Chain and Animal Health concluded that the risk to ground-nesting birds and hares "*Would be acceptable if appropriate risk mitigation measures are applied*" Member States were instructed to pay particular attention to the protection of ground-nesting birds and hares. (EC, 2003)
-

Paraquat Information Center > Paraquat Safety in Humans - Facts and Information about Paraquat Safety from the Paraquat Information Center



Safety in Humans



"Paraquat concentrate can be fatal if swallowed in sufficient quantities"

As with all chemicals, including pesticides such as paraquat, care must be taken to minimize human exposure. Provided this care is applied and the product is used as directed, there is no risk to human safety with the use of paraquat. This is the conclusion reached on the basis of exhaustive laboratory toxicology studies with paraquat and over 40 years of experience in use. A consensus on the interpretation of these studies exists among the leading regulatory authorities globally.

The following comments relate to the acute toxicity of paraquat dichloride. Formulations of paraquat may have different acute toxicity.

- In their Recommended Classification of Pesticides by Hazard, the World Health Organization (WHO) classified paraquat as "*Moderately hazardous, class II*" (WHO, 2002)
- In their RED facts document the US Environmental Protection Agency (EPA) concluded that "*paraquat is moderately toxic (Category II) by the oral route*" (US EPA, 1997)
- The European Chemicals Bureau classified paraquat as "*R25, toxic if swallowed*" (ECB, 2004)

Paraquat is slightly toxic by the dermal (skin) route - The following comments relate to the acute toxicity of paraquat dichloride. Formulations of paraquat may have different acute toxicity.

- In their RED facts document, the US EPA concluded that paraquat is "*slightly toxic (Category III) by the dermal route*" (US EPA, 1997)
- The European Chemicals Bureau classified paraquat as "*R24, toxic in contact with skin*" (ECB, 2004)

Paraquat is an irritant to skin and eyes - The following comments relate to the acute toxicity of paraquat dichloride. Formulations of paraquat may have different acute toxicity.

- In their report of a periodic re-evaluation of toxicity for the Joint FAO/WHO

<http://www.paraquat.com/paraquat/Safety/SafetyinHumans/tabid/243/Default.aspx>

1/18/2008

Meeting on Pesticide Residues (JMPR), the WHO considered paraquat "to be a mild skin irritant and a moderate eye irritant" (JMPR, 2003)

- In their RED facts document, the US EPA concluded that "paraquat will cause moderate to severe eye irritation and minimal dermal irritation, and has been placed in Toxicity Categories II and IV for these effects" (US EPA, 1997)
- The European Chemicals Bureau classified paraquat as "R36/37/38, irritating to eyes, respiratory system and skin" (ECB, 2004)

Paraquat is not a skin sensitizer - The following comments relate to the acute toxicity of paraquat dichloride. Formulations of paraquat may have different acute toxicity.

- In their report of a periodic re-evaluation of toxicity for JMPR, the WHO considered paraquat "was not a skin sensitizer in the Magnusson and Kligman test" (JMPR, 2003)
- In their RED facts document, the US EPA concluded that paraquat was "not a skin sensitizer under the conditions of the maximization test of B Magnusson and AM Kligman" (US EPA, 1997)
- In their review report for paraquat, the European Commission (EC) concluded that paraquat was "negative in Magnusson & Kligman protocol" (EC, 2003)

Paraquat is highly toxic by the inhalation (lungs) route - The following comments relate to the acute toxicity of paraquat dichloride. Formulations of paraquat may have different acute toxicity.

- In their RED facts document, the US EPA concluded that "paraquat has been shown to be highly toxic by the inhalation route and has been placed in Toxicity Category I (the highest of four levels) for acute inhalation effects. However, the Agency has determined that particles used in agricultural practices (400 to 800um) are well beyond the respirable range and therefore inhalation toxicity is not a toxicological endpoint of concern" (US EPA, 1997)
- The European Chemicals Bureau classified paraquat as "R26, very toxic by inhalation" (ECB, 2004)

See below for information about the **ability** to inhale paraquat into the lungs.

Paraquat is not inhaled in to the lungs - Paraquat dichloride is non-volatile and formulations containing paraquat are not applied through spray equipment, which would generate a significant proportion of respirable spray droplets. Paraquat is applied with conventional hydraulic spray equipment for which the droplets produced are generally too large to be inhaled, being typically ~ 200-400um. Only a small fraction of the total particle distribution is of respirable size with <0.2% less than 10um. The inhalable fraction <30um that is taken into the nose and the mouth during breathing is also too large to reach the alveolar region of the lung. This fraction could, however, be swallowed and is therefore a source of secondary oral ingestion. Mist blowers, which produce large numbers of very fine droplets (50 microns and less), are not recommended for spraying paraquat.

- In their RED facts document, the US EPA concluded that for paraquat "particles used in agricultural practices (400 to 800um) are well beyond the respirable range and therefore inhalation toxicity is not a toxicological endpoint of concern" (US EPA, 1997)

Paraquat is poorly absorbed after oral administration

- In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO considered paraquat to be "*not well-absorbed*" (JMPR, 2003)
- In their RED facts document, the US EPA concluded that "*paraquat was poorly absorbed after oral administration to rats, dogs and mice*" (US EPA, 1997)
- In their review report for paraquat, the EC concluded that paraquat was poorly absorbed "*approximately 10% absorption*" (EC, 2003)

Paraquat can not readily be absorbed through the skin - Undamaged skin is an effective barrier to paraquat in concentrated or diluted spray strength solution. It is water soluble and easily washed off. Prolonged and repeated contact of spray-strength paraquat with skin, through leaking spray equipment or poor personal hygiene can cause skin irritation and even damage in severe cases. These are visible warnings to the user that he or she is doing something wrong and they come in good time to avoid any further health risk.

- In their RED facts document, the US EPA concluded that "*0.3% of the applied 14C-paraquat dichloride was absorbed through intact skin*" (US EPA, 1997)
- In their review report for paraquat the EC concluded that the dermal absorption of paraquat was "*0.5% based on overall weight of evidence*" (EC, 2003)

Paraquat is not significantly metabolized - Any absorbed paraquat is generally excreted unchanged with little or no metabolism.

- In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO considered "*paraquat is largely eliminated unchanged*" but some studies "*have shown a small degree of metabolism probably occurring in the gut as a result of microbial metabolism*" (JMPR, 2003)
- In their RED facts document, the US EPA concluded that "*paraquat was not metabolized by rats*" (US EPA, 1997)
- In their review report for paraquat the EC concluded that paraquat was subject to "*minimal metabolism, representing <1% of recovery*" (EC, 2003)

Paraquat is rapidly excreted - Paraquat is not stored or accumulated in the body. In the unlikely event of minute amounts of the spray-strength product being absorbed, it would be rapidly and effectively eliminated via the urine. In laboratory studies it has been shown that any absorbed paraquat is generally rapidly excreted.

- In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO noted that for paraquat "*excretion of the radiolabel was rapid; about 90% was excreted within 72h.*" (JMPR, 2003)
- In their RED facts document, the US EPA concluded that for paraquat "*most of the radioactivity was detected in feces with 2-3 days after dosing and in urine, within 1 day after dosing*" (US EPA, 1997)
- In their review report for paraquat, the EC concluded that the rate of excretion of paraquat was "*>90% in 72h,*" (EC, 2003)

Paraquat is not genotoxic in vivo - Paraquat has been evaluated for genotoxic potential in a range of *in vitro* and *in vivo* test systems. These studies provide a substantial body of data to indicate that paraquat does not have significant genotoxic potential. Paraquat has produced positive responses in some *in vitro* assays. These are

considered not to be due to paraquat itself but to the action of paraquat within cellular systems. Paraquat is not genotoxic in higher tier *in vivo* assays.

- In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO concluded that *"paraquat is unlikely to pose a genotoxic risk to humans"* (JMPR, 2003)
- In their RED facts document, the US EPA concluded that *"paraquat shows no evidence of causing mutagenicity "* (US EPA, 1997)
- In their review report for paraquat the EC concluded that genotoxicity studies with paraquat were *"negative in vivo. Some in vitro positives"* (EC, 2003)

Paraquat is not carcinogenic - The chronic toxicity and potential carcinogenicity of paraquat have been examined in two-year studies in rats and mice. Effects on the lung were the principal effects noted in the chronic feeding studies, which is consistent with the findings from sub-chronic toxicity studies.

- In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO concluded that *"the weight of evidence suggested that paraquat was not carcinogenic in the rat. Paraquat was not considered to be tumorigenic in two studies in mice."* (JMPR, 2003)
- In their RED facts document, the US EPA *"classified paraquat as a Group E carcinogen (evidence of non-carcinogenicity for humans), based on a lack of evidence of carcinogenicity in acceptable studies with two animal species "* (US EPA, 1997)
- In their review report for paraquat the EC concluded that paraquat was *"not carcinogenic"* (EC, 2003)

Paraquat is not a developmental toxin - No teratogenic potential has been demonstrated in developmental toxicity studies in rats and mice.

- In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO concluded that *"teratogenicity was not seen at any dose in any study in either rats or mice."* (JMPR, 2003)
- In their RED facts document, the US EPA noted that *"the no-observed effect dose levels (NOEL) for maternal toxicity are at least or more conservative (protective) than the NOEL based on developmental toxicity"* (US EPA, 1997)
- In their review report for paraquat, the EC concluded that paraquat was only *"embryotoxic at maternally toxic doses"* (EC, 2003)

Paraquat is not a reproductive toxin - Paraquat has been demonstrated not to interfere with reproduction in a three-generation reproduction study.

- In their report of a periodic re-evaluation of toxicity for JMPR, the WHO concluded that *"impaired fertility was not seen in these studies"* (JMPR, 2003)
- In their RED facts document, the US EPA noted that *"there is no evidence that paraquat is associated with reproductive effects"* (US EPA, 1997)
- In their review report for paraquat, the EC concluded that reproductive toxicity studies with paraquat demonstrated *"no specific effects on reproduction"* (EC, 2003)

Paraquat is not an endocrine disruptor - The available data for paraquat have been

reviewed and are considered not to show evidence of endocrine disruption.

- mammalian studies: including rat reproduction (multigeneration), rat and mouse developmental (teratology), one-year dog, lifetime rat and mouse;
- and environmental species: including a life-cycle study in daphnia and reproduction studies in the bobwhite quail and mallard; and.

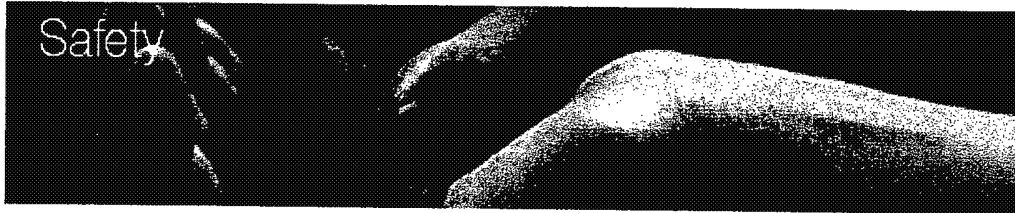
In its report, "Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption" for the European Commission DG ENV, BKH Consulting Engineers lists paraquat as a group III substance, which means there is no scientific basis for inclusion on the endocrine disruptor list.

Paraquat is not a neurotoxicity hazard – The neurotoxic potential of paraquat has been extensively studied in laboratory animals. No clinical signs of neurotoxicity or consistent neuropathological changes have been reported following long-term exposures of dietary administration of paraquat to rodents or dogs in regulatory-compliant studies.

- In their RED facts document, the US EPA observed that paraquat "*does not affect morphology of the central and peripheral nervous systems*" (US EPA, 1997)
- In their review report for paraquat, the EC concluded paraquat provided "*no indication of neurotoxicity*" (EC, 2003)

In their report of a periodic re-evaluation of toxicity for the JMPR, the WHO concluded that "*studies on the effects of paraquat on the central nervous system have used a variety of routes, including subcutaneous or intraperitoneal injection and direct injection into the central nervous system, and end points observed have been behavioral, morphological and neurochemical. Behavioral effects and loss of neurons in the substantia nigra were observed and, neurochemically, depletion of dopamine was reported in many, but not all, of these studies. However, the design of these studies renders the relevance of these data questionable for the risk assessment of dietary exposure to paraquat residues.*" It was then concluded that "*the available mechanistic and other animal studies did not support the hypothesis that paraquat residues in food are a risk factor for Parkinson's disease in humans*" (JMPR, 2003)

Paraquat Information Center > Paraquat safety in operators and bystanders - Facts and Information on Paraquat Safety from the Paraquat Information Center



Safety in operators and bystanders



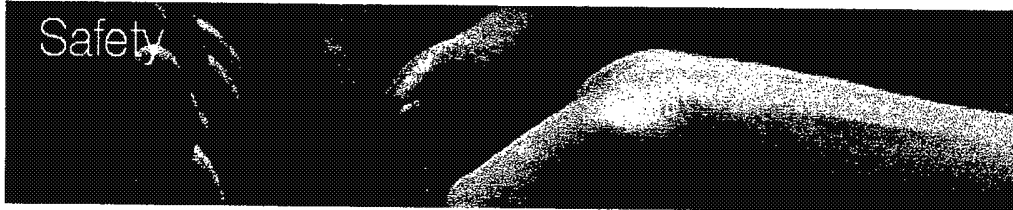
There is a consensus among the leading regulatory authorities globally that paraquat must be used with care because formulations of paraquat are irritant to eyes and skin. However, provided that basic good agricultural practices are observed, paraquat can be used without significant health risk to operators and bystanders.

- In their Health and Safety Guide No. 51, the International Program on Chemical Safety (a collaborative program of the United Nations Environment program, the International Labor Organization, and the World Health Organization (WHO)) concluded that *"with reasonable work practices, including safety precautions, hygiene measures, and proper supervision, occupational exposure during the manufacture, formulation and use of paraquat will not cause a hazard. However, the undiluted concentrate must be handled with great care, because improper work practices may result in the contamination of the eyes and skin"*
- In the European Union (EU), the opinion of the independent expert Scientific Committee for Plants (SCP) was that *"the results of the field studies conducted in various countries indicate that the exposure models markedly overestimate the actual exposure to paraquat in real working situations. Thus modelled exposures cannot be used as the only basis for operator risk assessment. Based on the field exposure studies, corroborated by information on health surveys on operators, the SCP is of the opinion that when paraquat is used as a plant protection product as recommended under prescribed good working practices, its use does not pose any significant health risk for the operators."* (SCP, 2002).
- In their review report for paraquat, the European Commission (EC) required that Member States pay particular attention to the protection of operators, in particular for knapsack and handheld users. *"The availability of the product should be limited to bona fide agriculturalists, horticulturalists and professional users"* and *"the maximum spray concentration must not exceed 2g bipyridyl/litre for knapsack and hand held applications"* (EC, 2003)
- In their RED facts document, the US Environmental Protection Agency (EPA) required that post-application, re-entry workers observe *"a 12-hour Restricted Entry Interval for the uses of paraquat for pre-emergent or early-season weed control and weed control for orchards and vegetable crops"* and *"a 24-hour Restricted Entry Interval is required for dessication and harvest aid applications of paraquat"*. The US EPA concluded that margins of exposure were generally acceptable but required a reduction in the spray concentration of paraquat to mitigate risk to backpack sprayers and required that mixers and loaders of paraquat products wear additional personal protective equipment (PPE) compared

<http://www.paraquat.com/SafetyofParaquat/Safetyinoperatorsandbystanders/tabid/245/Def...> 1/18/2008

to that required for applicators: *"Additional PPE are being required for mixers and loaders: gloves, chemical resistant apron and face shield" (EPA, 1997)*

Paraquat Information Center > Paraquat Safety to the Public - Facts and Information about the Safety of Paraquat from the Paraquat Information Center



Safety to the Public



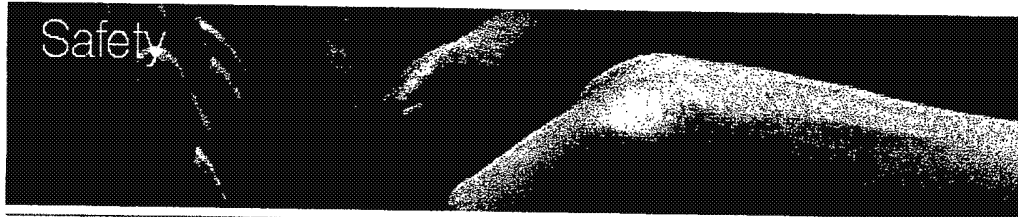
There is very little exposure to paraquat for the consumer of treated crops as the vast majority of paraquat uses do not result in detectable residues ($>0.05\text{mg/kg}$) in foodstuffs.

No Risks from Residues in the Food Most of the uses for paraquat involve spraying weeds and not the crop. Because the paraquat active ingredient becomes inactive on contact with the soil, it cannot be taken up by the roots of the plants. Consequently for the vast majority of uses no residues are expected in harvested crops. This has been confirmed over many years by analysis of crops harvested after the use of paraquat as an herbicide. There are a few situations where crops are treated directly when paraquat is used as a pre-harvest desiccant. These uses are approved by regulatory authorities who have confirmed such treatments do not leave residues at levels, which represent a risk to humans.

No Risks from Residues in Livestock Paraquat binds to plant tissues once it is in contact with foliage and so is not easily absorbed by animals and it is readily eliminated via urine. There is no significant transfer to milk, meat or eggs. Similarly there is no practical health risk to livestock if they are accidentally fed on treated herbage.

- In their report of a periodic re-evaluation of residues for the Joint FAO/WHO Meeting on Pesticide Residues (JMPR), the World Health Organization (WHO) concluded that, *"the intake of residues of paraquat resulting from uses considered by the current JMPR was unlikely to present a public health concern"* (JMPR, 2004)
 - In their RED facts document, the US Environmental Protection Agency (EPA) concluded that *"the Agency has determined that there is reasonable certainty that no harm will result to infants and children or to the general population from aggregate exposure to paraquat dichloride residues"* (US EPA, 1997)
 - In their review report for paraquat the European Commission (EC) concluded *"the review has established that the residues arising from the proposed uses, consequent on application consistent with good agricultural practice, have no harmful effects on human or animal health"* (EC, 2003)
-

Paraquat Information Center > Safety concerns - Facts and Information about Paraquat Safety from the Paraquat Information Center



Safety concerns

Paraquat is toxic if swallowed and the concentrated formulations are irritants to eyes and skin. There have been highly publicized reports of fatalities related to the ingestion of paraquat.

Accidental ingestion

When paraquat was first introduced in the 1960s, a common malpractice was to decant pesticides into smaller containers such as drink bottles, without appropriate labeling. The original paraquat formulations were odorless reddish-brown liquids, which led them to be mistaken for drinks such as cola, tea, or red wine. Regrettably a series of fatal poisonings due to mistaken ingestion occurred.

Steps were introduced more than 20 years ago to address this problem:

- Pack sizes were changed to discourage the practice of decanting
- A new global labelling standard was introduced
- Stewardship and training efforts were enhanced to ensure that people handling paraquat were aware that it contains chemicals and should be used exclusively for the control of weeds. These were directed in particular towards smallholder farmers in developing countries, where the majority of incidents occurred
- Paraquat formulations were given three 'safening' agents to avoid accidental ingestion and to deter misuse:
 - a blue dye,
 - an alerting agent (a strong and deterring odor), and
 - an emetic (to induce vomiting).

The combination of these measures has proven effective in addressing the problem of accidental ingestion and fatalities from such incidents are now extremely rare.

Deliberate ingestion

Unfortunately, there have been incidences reported of deliberate exposure to paraquat by people intent on committing suicide. While crop protection products are one of the methods used to commit suicide, they are not one of the most frequent and paraquat is not the most frequently used product (WHO, 2001, FDA, 2003, Ministry of Agriculture,

India, 2000). Following a peak in the 1980s, suicide fatalities involving paraquat have decreased (Sabapathy, 1995).

Irritation effects

Paraquat is irritating and harmful to eyes and skin, especially in its concentrated form, so gloves and eye protection should be worn (as with all pesticides when mixing concentrates). Prolonged and repeated contact of spray-strength paraquat with skin, through leaking spray equipment or poor personal hygiene, can cause skin irritation and even damage in severe cases. Similar poor practices have been reported to be associated with nail damage and nose bleeds. These are visible warnings to the user that he or she is doing something wrong and these warnings come in good time to avoid any further health risk. If the basic label precautions are followed, these symptoms will clear quickly with no lasting effect. The skin irritation and related symptoms heal when exposure to paraquat ceases and the affected areas are washed or treated as needed. To put this into context, one would not leave skin in prolonged contact with oven cleaner, degreaser, oil, petrol, solvents, dishwasher fluid or many other common substances without experiencing skin damage and effects on health.

Enhancing human safety through product stewardship and education

Some companies, such as Syngenta, which manufacture paraquat have initiated stewardship and education programs for customers around the world in order to train farmers on the safe and appropriate use of paraquat. The results of these educational efforts offer compelling evidence that basic education can significantly increase safe practices among farmers. For more information visit the "[Paraquat Stewardship & Education](#)" section of this website.

Please visit the [FAQ](#) section of this website for additional information about the safety of paraquat.

Paraquat Information Center > Paraquat FAQs: Answers to Your Frequently Asked Questions About the Human Safety of Paraquat from the Paraquat Information Center

Human Safety



Q. Is paraquat safe to farmers and their families?

A.

Under normal use conditions (i.e., as recommended on the label) paraquat is safe to the user and to the bystander. Using eye protection and gloves when handling concentrated product and wearing normal work wear like long-sleeved shirts, long trousers, and waterproof shoes are advised for spraying pesticides generally. Following this recommendation already provides a high and sufficient level of safety for the agricultural use of paraquat.

In 2004, paraquat was again reviewed by leading international organizations, including the FAO (Food and Agricultural Organization) and the UN Joint Meeting on Pesticide Residues (JMPPR), which is comprised of experts from the WHO (World Health Organization) and the FAO. These experts support that, when used as directed, there is no safety hazard associated with the use of paraquat. Its physical properties make it safe to handle, when used according to label directions.

Europe's Scientific Committee on Plants (SCP) stated:

"Based on the field exposure studies, corroborated by information on health surveys on operators, the SCP is of the opinion that when Paraquat is used as a plant protection product as recommended under prescribed good working practices, its use does not pose any significant health risk to the operators."(SCP, 2002)

The conclusion derived from more than four decades of its use and various reviews by international regulatory bodies, is that paraquat is safe to users, the environment, consumers and wildlife when used for its intended purpose as herbicide. Its safety has been confirmed by its registration for use in over 120 countries all around the globe including those with the most stringent regulatory requirements such as the US and the EU.

Q. What is the safety of paraquat to farmers when used long-term?

Q. Has paraquat been found to cause cancer, birth defects or to be neurotoxic?

Q. Is paraquat an endocrine disruptor?

Q. Does paraquat cause Parkinson's Disease?

Q. Does paraquat cause harm to humans when entering the respiratory tracts?

Q. Is paraquat poisonous to people? With which substances can paraquat be compared?

Paraquat Information Center > Paraquat FAQs: Answers to Your Frequently Asked Questions About the Human Safety of Paraquat from the Paraquat Information Center

Human Safety



Q. Is paraquat safe to farmers and their families?

Q. What is the safety of paraquat to farmers when used long-term?

A. The potential long-term hazard associated with the use of paraquat has also been studied. The World Health Organization concluded (Environmental Health Criteria, 1984) that there were no significant differences in all health parameters measured between paraquat users and non-paraquat users, which led the authors to suggest that the long-term use of paraquat was not associated with harmful effects on health. This has been confirmed in detailed surveys comparing the health of long-term users of paraquat with unexposed people.

Q. Has paraquat been found to cause cancer, birth defects or to be neurotoxic?

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Human Safety

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Q. Is paraquat safe to farmers and their families?

Q. What is the safety of paraquat to farmers when used long-term?

Q. Has paraquat been found to cause cancer, birth defects or to be neurotoxic?
A.

No. The current EPA registration documentation for paraquat (EPA 'RED', August 1997) clearly indicates that the EPA does not consider neurotoxicity to be an issue with the compound. The EPA also stated that a developmental neurotoxicity study was not required.

According to the World Health Organization (Environmental Health Criteria 39, 1984) paraquat has not been found to be teratogenic (to cause birth defects) or carcinogenic (to cause cancer) in long-term studies on rats and mice.

More recently the European Union came to a similar conclusion in its exhaustive review of the product, which concluded in December 2003 with its continued registration of paraquat for an additional 10 years.

Q. Is paraquat an endocrine disruptor?

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Paraquat Information Center > Paraquat FAQs: Answers to Your Frequently Asked Questions About the Human Safety of Paraquat from the Paraquat Information Center

Human Safety



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Q. Has paraquat been found to cause cancer, birth defects or to be neurotoxic?

Q. Is paraquat an endocrine disruptor?

A.

An endocrine disruptor is a synthetic chemical that when absorbed into the body either mimics or blocks hormones and disrupts the body's normal functions. Like all crop protection products, paraquat has been subjected to a full regulatory toxicological evaluation, including the required mammalian studies. Such studies allow for the examination of toxicological affects following repeated exposure of a range of species to paraquat. Studies such as these evaluate the ability of materials to cause significant adverse effects through endocrine disruption and no evidence linking endocrine disruption to paraquat has been found.

In its report, "Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption" for the European Commission DG ENV,

BKH Consulting Engineers lists paraquat as a group III substance, which means there is no scientific basis for inclusion on the endocrine disruptor list. In reaching this conclusion, BKH cites two mammal *in vivo* studies, which are negative for endocrine disruption.

Paraquat appears on the World Wildlife Fund's (WWF) list of substances of 'reproductive and /or endocrine effects'. However the criteria used to determine this placement are unclear. WWF's data were considered by BKH in developing its recommendation. A copy of the BKH list is available [here](#).

Q. Does paraquat cause Parkinson's Disease?

Q. Does paraquat cause harm to humans when entering the respiratory tracts?

Q. Is paraquat poisonous to people? With which substances can paraquat be compared?

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Human Safety



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Q. Has paraquat been found to cause cancer, birth defects or to be neurotoxic?

Q. Is paraquat an endocrine disruptor?

Q. Does paraquat cause Parkinson's Disease?

A.

There is no scientific or reliable epidemiological evidence so far to link paraquat with Parkinson's Disease. Previous studies have demonstrated that paraquat does not cross the blood-brain barrier easily, meaning that it does not reach the specific location in the brain necessary to produce Parkinson's symptoms. Epidemiology studies in areas of high and long-term paraquat usage have shown no increase of neurotoxic incidents.

Nevertheless, the apparent structural similarity between paraquat and MPTP, an agent known to cause Parkinson's-like symptoms, has led some researchers to test paraquat. The WHO's recent review of the evidence stated that: "*the available mechanistic and other animal studies did not support the hypothesis that Paraquat residues in food are a risk factor for Parkinson's Disease in humans.*" (JMPR, 2004).

Q. Does paraquat cause harm to humans when entering the respiratory tracts?

Q. Is paraquat poisonous to people? With which substances can paraquat be compared?

Paraquat Information Center > Paraquat FAQs: Answers to Your Frequently Asked Questions About the Human Safety of Paraquat from the Paraquat Information Center

Human Safety



Q. Is paraquat safe to farmers and their families?

Q. What is the safety of paraquat to farmers when used long-term?

Q. Has paraquat been found to cause cancer, birth defects or to be neurotoxic?

Q. Is paraquat an endocrine disruptor?

Q. Does paraquat cause Parkinson's Disease?

Q. Does paraquat cause harm to humans when entering the respiratory tracts?

A.

No. Paraquat is not volatile and vapor from the product cannot enter into the respiratory system.

Additionally, the spray droplets produced by knapsack or tractor sprayers used to apply products containing paraquat, or any other CPP, are too large to be respired. Most droplets emitted from spray equipment are between 100 and 200 microns in diameter, but a particle must be 10 microns or less to enter the air spaces in the lungs. The large spray droplets cannot be inhaled into the respiratory system. The US EPA concluded that, "*particles used in agricultural practices are well beyond the respirable range and therefore inhalation toxicity is not a toxicological endpoint of concern*" (US EPA, 1997).

Q. Is paraquat poisonous to people? With which substances can paraquat be compared?

Paraquat Information Center > Paraquat FAQs: Answers to Your Frequently Asked Questions About the Human Safety of Paraquat from the Paraquat Information Center

Human Safety



- Q. Is paraquat safe to farmers and their families?
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- Q. Does paraquat cause Parkinson's Disease?
- Q. Does paraquat cause harm to humans when entering the respiratory tracts?
- Q. Is paraquat poisonous to people? With which substances can paraquat be compared?

A.

Like many readily available chemicals, paraquat is harmful and fatalities have occurred when the concentrated product has been swallowed in sufficient quantity, usually in an attempt to commit suicide. The label for products containing paraquat states that the product should always be kept in its original container and never stored in food, drink, or other containers. Products containing paraquat should also be locked away when not in use.

In order to ensure that people handling paraquat are aware that it contains chemicals that should be used exclusively for the control of weeds, paraquat formulations manufactured by Syngenta (the leading manufacturer of paraquat) have been given three 'safening' agents to avoid accidental ingestion and to deter misuse: a blue dye, an alerting agent (a strong and deterring odor), and an emetic (to induce vomiting). It is widely believed that these developments have contributed to a reduction in accidents.

The WHO International Program for Chemical Safety classification system of pesticides classifies over 500 chemicals.

Class	Number of AIs
"Extremely hazardous, class Ia"	29
"Highly hazardous, class Ib"	61
"Moderately hazardous, class II"	123

"Slightly hazardous, class III"	122
"Unlikely to present acute hazard"	246

Paraquat is classified as "moderately hazardous" (WHO class II) along with more than 100 other AIs. Information about the full classification system is available here:

<http://www.inchem.org/documents/pds/pdsother/class.pdf>

General Regulatory Timeline for Paraquat Registration Actions from EPA (note: not exhaustive review)

Date	Action
13-Sep-93	EPA grants registration approval to Zeneca for Cyclone Concentrate (EPA Reg. No. 10182-372)
18-Apr-01	Syngenta submits Notification for registration number/name change for Cyclone Concentrate (EPA Reg #10182-372) to reflect new company name: Syngenta
27-Apr-01	Notification of name change approved. Registration number changed to 100-1074
13-Sep-04	Syngenta submits for approval of Gramoxone Inteon
19-May-05	EPA grants Sinon registration of Paraquat Tech. Concentrate (EPA Reg No. 70552-1)
17-Aug-05	EPA grants registration for Gramoxone Inteon (EPA Reg. No. 100-1217)
14-Sep-05	Syngenta submits voluntary cancellation request for Cyclone Concentrate (100-1074)
28-Oct-05	EPA publishes Notice to voluntary cancel Paraquat Products Vol 70, No. 208, pg 62112
25-Jan-06	EPA grants unconditional registration to Sinon for Paraquat concentrate (EPA Reg No. 82557-1)
22-Feb-06	EPA prints notice of cancellation order in federal register Vol 71, No. 35
22-Aug-06	EPA grants cancellation of Cyclone Concentrate
4-Oct-06	EPA changes Shinon's unconditional registration (EPA Reg No. 82557-1) to conditional registration
4-Oct-06	EPA reverses Cyclone Concentrate (EPA Reg. No. 100-1074) cancellation order issued Aug 22, 2006.
27-Nov-06	EPA reinstates the Cyclone Concentrate (EPA Reg No. 100-74) cancellation.
5-Dec-06	EPA grants Makhteshim (MANA) conditional registration of Parazone 3SL (EPA Reg No. 66222-130) expires 9/2008
5-Dec-06	EPA grants conditional registration to Celcius Property CV (c/o MANA) Paraquat Dichloride Technical (EPA Reg. No. 83558-5)
11-Oct-07	EPA grants Source Dynamics conditional registration of Paraquat Concentrate (EPA Reg No. 82542-3) expires 9/2008

PH 25-10182-372

10455

US ENVIRONMENTAL PROTECTION AGENCY OFFICE OF PESTICIDES PROGRAMS REGISTRATION DIVISION (75-767) WASHINGTON, DC 20460	EPA REGISTRATION NO. 10182-372	DATE OF ISSUANCE SEP 13 1993
	TERM OF ISSUANCE	
	NAME OF PESTICIDE PRODUCT Cyclone Concentrate Herbicide	

NOTICE OF PESTICIDE: ☒ REGISTRATION
☐ REREGISTRATION
(Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended)

NAME AND ADDRESS OF REGISTRANT (Include ZIP code)
Mr. Wayne R. Hillebrecht
Zeneca Inc.
Zeneca Ag Products
P. O. Box 751
Wilmington, DE 19897

NOTE: Changes in labeling formula differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above U.S. EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby Registered/Reregistered under the Federal Insecticide, Fungicide, and Rodenticide Act.

A copy of the labeling accepted in connection with this Registration/Reregistration is returned herewith.

Registration is in no way to be construed as an indorsement or approval of this product by this Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA sec. 3(c)(7)(A) provided that you:

1. Submit and/or cite all data required for registration/re-registration of your product under FIFRA sec. 3(c)(5) and sec. 4 when the Agency requires all registrants of similar products to submit such data.
2. Add the phrase, "EPA Registration No. 10182-372" to your label before you release the product for shipment.
3. Submit five (5) copies of your final printed labeling before you release the product for shipment. Refer to the A-79 Enclosure for a further description of final printed labeling.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA sec. 6(e). Your release for shipment of the product constitutes acceptance of these conditions.

A stamped copy of the label is enclosed for your records.

☐ ATTACHMENT IS APPLICABLE

SIGNATURE OF APPROVING OFFICIAL	DATE
--	-------------

201 55

-2-

This acceptance of your label does not relieve you of any obligation to comply with the Worker Protection Standard (WPS). Under the WPS labeling regulations at 40 CFR part 156, subpart k, sec. 156.200(c)(3), you are prohibited from distributing or selling any product within the scope of the WPS requirements after April 21, 1994, without amended labeling accepted by the Agency.

uku

RESTRICTED USE PESTICIDE
Due to Acute Toxicity

For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

CYCLONE® Concentrate

A Weed, Grass, and Harvest Aid Herbicide

COMPLETE DIRECTIONS FOR USE

ACCEPTED
with COMMENTS
In EPA Letter Dated:

Inside of Front Cover

DIRECTIONS FOR USE AND
CONDITIONS OF SALE AND WARRANTY

SEP 13 1993
Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.
10162-372

IMPORTANT: Read the entire Directions for Use and the Conditions of Sale and Warranty before using this product.

CONDITIONS OF SALE AND LIMITED WARRANTY:

The Directions for Use of this product are believed to be reliable and should be followed carefully. However, it is impossible to eliminate all risks inherently associated with the use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as timing and method of application, weather and crop conditions, mixture with other chemicals not specifically recommended or other influencing factors in the use of the product, all of which are beyond the control of the seller. All such risks shall be assumed by Buyer and User, and Buyer and User agree to hold Seller harmless for any claims relating to such factors.

Seller warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated on the label, subject to the inherent risks referred to above, when used in accordance with directions under normal conditions of use. This warranty does not extend to the use of this product contrary to label instructions, or under abnormal conditions or under conditions not reasonably foreseeable to or beyond the control of Seller and Buyer and User assume the risk of any such use. SELLER DISCLAIMS ALL OTHER WARRANTIES EXPRESSED OR IMPLIED INCLUDING ANY WARRANTY OF FITNESS OR MERCHANTABILITY.

100-1074

4/27/2001

Page 1 of 65

Please read instructions on reverse before completing form.

United States Environmental Protection Agency Washington, DC 20460		<input type="checkbox"/> Registration <input type="checkbox"/> Amendment <input checked="" type="checkbox"/> Other	OPP Identifier Number NOTIFICATION
Application for Pesticide - Section I			
1. Company/Product Number 100-1074		2. EPA Product Manager (acting) Dan Rosenblatt	
4. Company/Product (Name) CYCLONE® CONCENTRATE (GRAMOXONE® MAX, STARFIRE® CONCENTRATE)		3. Proposed Classification <input type="checkbox"/> None <input type="checkbox"/> Restricted	
5. Name and Address of Applicant (Include ZIP Code) Syngenta Crop Protection, Inc. Registrations & Regulatory Affairs 410 Swing Road PO Box 18300 Greensboro NC 27409-8300 <input checked="" type="checkbox"/> Check if this is a new address		6. Expedited Review. In accordance with FIFRA Section 3(c)(3) (b)(i), my product is similar or identical in composition and labeling to: EPA Reg. No. _____ Product Name _____	
Section - II			
<input type="checkbox"/> Amendment - Explain below. <input type="checkbox"/> Resubmission in response to Agency letter dated _____ <input checked="" type="checkbox"/> Notification - Explain below.		<input type="checkbox"/> Final printed labels in response to Agency letter dated _____ <input type="checkbox"/> "Me Too" Application. <input type="checkbox"/> Other - Explain below.	
NOTIFICATION			
APR 27 2001			
Explanation: Use additional page(s) if necessary. (For Section I and Section II.) This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula of this product. I understand that it is a violation of 18 U.S.C. Sec. 1001 to willfully make any false statement to EPA. I further understand that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be subject to enforcement action and penalties under sections 12 and 14 of FIFRA. The following changes are being made via this notification: 1) Company name and address have been updated to reflect Syngenta Crop Protection, Inc., 2) EPA Reg. No. changed to new Company number, 3) The copyright date reflects Syngenta, 4) Trademark statements have been updated to reflect Syngenta for those products for which Syngenta holds the trademark. 5) The Internet address has been changed to reflect Syngenta. 6) Other places in the label which refer to the company name have been updated.			
Section - III			
1. Material This Product Will Be Packaged In:			
Child-Resistant Packaging <input type="checkbox"/> Yes* <input type="checkbox"/> No *Certification must be submitted	Unit Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No If "Yes" Unit Packaging wgt. No. per Container	Water Soluble Packaging <input type="checkbox"/> Yes <input type="checkbox"/> No If "Yes" Unit Packaging wgt. No. per container	2. Type of Container <input type="checkbox"/> Metal <input type="checkbox"/> Plastic <input type="checkbox"/> Glass <input type="checkbox"/> Paper <input type="checkbox"/> Other (Specify) _____
3. Location of Net Contents Information <input type="checkbox"/> Label <input type="checkbox"/> Container		4. Size(s) Retail Container	
		5. Location of Label Directions <input type="checkbox"/> On Label <input type="checkbox"/> On Labeling accompanying product	
6. Manner in Which Label is Affixed to Product		<input type="checkbox"/> Lithograph <input type="checkbox"/> Paper glued <input type="checkbox"/> Stenciled <input type="checkbox"/> Other _____	
Section - IV			
1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)			
Name Martina A. Haw		Title Regulatory Assistant II Telephone No. (Include Area Code) 302 / 476-2373	
Certification I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.			6. Date Application Received (Stamped)
2. Signature <i>Martina A. Haw</i>		3. Title Regulatory Assistant II	
4. Typed Name Martina A. Haw		5. Date April 18, 2001	

2 9 6 5

PAPERWORK REDUCTION ACT NOTICE and INSTRUCTIONS

PAPERWORK REDUCTION ACT NOTICE: Public reporting burden for this collection of information is estimated to average 0.85 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, (2136), U.S. Environmental Protection Agency, 401 M Street, SW, Washington, DC 20460.

INSTRUCTIONS: This form is to be used for all applications for new registration, end use reregistration, amendment, resubmission, to applications for notifications, final printed labeling, reregistration, etc. In order to process an application for a new registration submitted on this form, the following material must accompany the application:

1. Certification with Respect to Citation of Data (EPA Form 8570-29). [If not exempted by 40 CFR 152.81 (b) (4)];
2. Confidential Statement of Formula (EPA Form 8570-4);
3. Formulator's Exemption Statement (EPA Form 8570-27);
4. Five copies of draft labeling;
5. Three copies of any data submitted;
6. Authorization letter where applicable;
7. Matrices where applicable.

Submission of Labeling - Labeling should first be submitted in the form of draft labels with all applications for new registration. Such draft labels may be in the form of typed label text on 8.5 x 11 inch paper for submission or a mockup of the proposed label. If prepared for mockup, it should be constructed in a way as to facilitate storage in an 8.5 x 11 inch file. Mockup labels significantly smaller than 8.5 x 11 inches should be mounted on 8.5 x 11 inch paper for submission.

Submission of Data - Data submitted in support of this application must be submitted in accordance with PR Notice 86-5.

SPECIFIC INSTRUCTIONS: Please read the instructions listed below before completing this application. First determine the type of registration action, listed in Block A, for which you are submitting this application. For applications submitted in connection with New Registration actions, Sections I, III, and IV must be completed by the applicant. For applications submitted in connection with amended reregistration actions, resubmissions, notifications, reregistrations, etc., Sections I, II, and IV must be completed by the applicant.

Block A - Check the appropriate action for which you are submitting this form.

SECTION I - This section must be completed, as applicable, for all registration actions.

1. Company/Product Number - Insert your Company Number, if one has been assigned by EPA. This number may have been assigned to you as a basic registrant, a distributor, or as an establishment. If your product is registered, insert the Product Number.
2. EPA Product Manager - If known, fill in the name and PM number of the EPA Product Manager.
3. Proposed Classification - Specify the proposed classification of this product.
4. Product Name - Enter the complete product name of this pesticide as it will appear on the label. The name must be specific to this product only. Duplication of names is not permitted among products of the same company. Do not include any brand name or company line designations.
5. Name and Address of Applicant - The name of the firm or person and address shown in your application is the person or firm to whom the registration will be issued. If you are acting in behalf of another party, you must submit authorization from that party to act for them in registration matters. An applicant not residing in the United States must have an authorized agent residing in the United States to act for them in all registration matters. The name and complete mailing address of such an agent must accompany this application.
6. Expedited Review - FIFRA section 3 (c) 3 (B) provides for expedited review of applications for registration, or amendments to existing registrations, that are similar or identical to other pesticide products that are currently registered with the EPA. In order for your application to be eligible for expedited review, you must provide us with the EPA Registration Number and product name of the product you believe is similar to or identical to your product. The product must be similar or identical in both formulation and labeled uses.

SECTION II - This section must be completed for all applications submitted to amend the registration only of a currently registered product (Amendment), for a resubmission in response to an Agency letter, for notifications to the Agency, for the submission of final printed labeling, for reregistration and for any other action that pertains to a specific EPA-registered product. This section is not to be used for a new application for registration.

1. Subject of submission - Check the applicable block and provide the Agency letter date if appropriate. Provide a brief explanation of the purpose(s) for the submission, such as "the addition of a site, pest or crop (specify)"; "amend the Confidential Statement of Formula by..."; "reregistration submission"; "general label revision of use directions." Attach a separate page if additional space is needed.

SECTION III - (Packaging and Container Information) - This Section must be completed for all applications submitted in connection with new registration or applicable amendments.

1. Type of Packaging - Check the appropriate block if your product will be packaged in the indicated packaging types. Indicate the size of the individual packets and number per retail container.
2. Type of Retail Container - Indicate type of container in which product will be marketed.
3. Location of Net Contents - Indicate the location of the net contents information for your product.
4. Size(s) of Retail Container - Specify the net contents of all retail containers for your product.
5. Location of Use Directions - Indicate the location of the use directions for your product.
6. Manner in which label is affixed to product - Indicate the method product label is attached to retail container.

SECTION IV (Contact Point) - This Section must be completed for all applications for Registration actions, i.e., new products registration, resubmission, "me-too," reregistration, etc.

- 1-5. Self-explanatory.
6. EPA Use Only

RESTRICTED USE PESTICIDE

Due to Acute Toxicity

For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

CYCLONE® Concentrate

W Weed, Grass, and Harvest Aid Desiccant/Defoliant Herbicide

ACTIVE INGREDIENT:

Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride) 43.8%

INERT INGREDIENTS 56.2%

Total 100.0%

Contains 3.0 pounds paraquat cation per gallon as 4.143 pounds salt per gallon.
Contains stench (odor) and emetic.

KEEP OUT OF REACH OF CHILDREN

O
DANGER POISON
X
PELIGRO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

- NEVER PUT INTO FOOD, DRINK OR OTHER CONTAINERS.
- IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID. **NOTIFICATION**
- SYMPTOMS ARE PROLONGED AND PAINFUL.
- DO NOT USE OR STORE IN OR AROUND THE HOME.
- DO NOT REMOVE CONTENTS EXCEPT FOR IMMEDIATE USE.

APR 27 2001


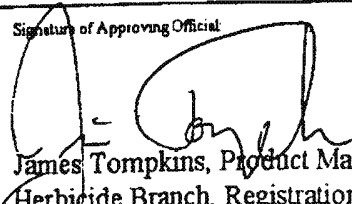
See additional precautionary statements and directions
for use (inside booklet; on back panel; on side panel)

EPA Reg. No. 100-1074
EPA Est. No.

Syngenta Crop Protection, Inc.
Greensboro, North Carolina 27409
www.syngenta-us.com

SCP 100-xxxx

Net Weight/U.S. Standard Measure

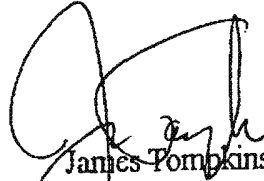
	U.S. ENVIRONMENTAL PROTECTION AGENCY Office of Pesticide Programs Registration Division (7505C) 1200 Pennsylvania Ave., N.W. Washington, D.C. 20460	EPA Reg. Number:	Date of Issuance:
		70552-1	5/19/2005
		Term of Issuance: Conditional	
(under FIFRA, as amended)		Name of Pesticide Product: Paraquat Technical Concentrate	
Name and Address of Registrant (include ZIP Code): Sinon Corporation 111, Chung-Shan Road Ta-Tu Hsiang, Taichung Hsien 432 Taiwan, ROC			
<small>Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.</small>			
<p>On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.</p> <p>Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.</p> <p>This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A) provided you agree in writing to:</p> <ol style="list-style-type: none">1. Submit the following: guideline 830.6317 (One Year Storage Stability Study) and guideline 830.6320 (Corrosion Characteristics Study) within one (1) year from the date of this registration letter.2. Change EPA Reg. No. on label from 70552-R to 70552-1.3. Remove "Refer to the booklet 'Paraquat Poisoning. A Practical Guide to Diagnosis, First Aid and Hospital Treatment'. (http://syngenta.com/poisonguide)." from the NOTE TO PHYSICIAN statement.4. Remove "Open dumping is prohibited" from directly under the STORAGE AND DISPOSAL header, and move to under the subsection PESTICIDE DISPOSAL.			
Signature of Approving Official:  James Tompkins, Product Manager (25) Herbicide Branch, Registration Division (7505C)		Date: 5/19/2005	

EPA Form 8770-6

Please note that Agency approval of the label should not be construed as a decision by the Agency that the language on the Warranty Statement is not misleading.

You will submit one (1) copy of your final printed labeling before you release the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). A stamped copy of labeling is enclosed for your records.

If you have any questions, please contact Hope Johnson at 703-305-5410.



James Tompkins
Product Manager (25)
Herbicide Branch
Registration Division (7505C)

3/7

Paraquat Technical Concentrate

For Formulation of Paraquat Herbicide Products Only

ACTIVE INGREDIENT

Paraquat dichloride (1,1'-dimethyl, 4,4'-bipyridinium dichloride) 46.2%

INERT INGREDIENTS 53.8%

TOTAL 100.0%

Contains 3.16 pounds paraquat cation per gallon
Contains emetic.

EPA Reg. No. 70552-R

EPA Establishment No. 70552-TWN-001

KEEP OUT OF REACH OF CHILDREN

DANGER - PELIGRO



POISON

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail).

- NEVER PUT INTO FOOD, DRINK OR OTHER CONTAINERS
- IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID STATEMENT. SYMPTOMS ARE PROLONGED AND PAINFUL.

ACCEPTED
with COMMENTS
in EPA Letter Dated

MAY 19 2005

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No

70552-1

100-1217

08/17/2005

1/79



U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505C)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

EPA Reg.
Number:

Date of Issuance:

8/17/2005

100-1217

Term of Issuance:

Conditional

Name of Pesticide Product:

Gramoxone Inteon

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419-8300

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A) provided you agree in writing to:

1. As a condition of registration, submit the outstanding guideline studies 830.6317 (storage stability) and 830.6320 (corrosion characteristics) within 1 year from the date of registration.
2. Add the appropriate establishment number to the label.
3. Change the registration number on the label from 100 to 100-1217.
3. Place the FIRST AID STATEMENTS in the following order: If Swallowed, If Inhaled, If In Eyes, If on Skin Or Clothing.
4. On page 3, in the PPE section (Mixers and Loaders must wear), remove "Protective eyewear plus" from the statement "Protective eyewear plus a dust mist respirator with any N, R, P or HE filter."

Signature of Approving Official:

Date:

8/17/2005

James Tompkins, Product Manager (25)
Herbicide Branch, Registration Division (7505C)

EPA Form 8570-6

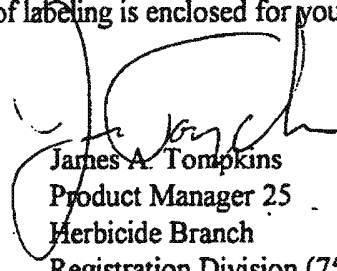
2/7/77

5. On page 3, remove "Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove contaminated clothing and wash clothing before reuse." from the PRECAUTIONARY STATEMENTS, as these are recommended in the User Safety Recommendations section.

6. On page 41, in the section Lentils, under the column Precautions, change the second bullet statement to: "May also be applied as a split application. If applied as a split application, do not exceed a total of 2 pints/A per season. Split application may improve coverage." Add a bullet BEFORE this statement that states "Do not exceed a total of 2 pints/A per season."

The basic formulation [dated 7-26-04] and the alternate formulation [dated 1-10-05] of the product referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act as amended is acceptable. The basic CSF and alternate formulation will be added to your file.

You will submit one (1) copy of your final printed labeling before you release the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). A stamped copy of labeling is enclosed for your records.


James A. Tompkins
Product Manager 25
Herbicide Branch
Registration Division (7505C)

3/29

(Booklet – 2.5, 30, 120 Gallons and Bulk)

RESTRICTED USE PESTICIDE
Due to Acute Toxicity

For retail sale to and use only by Certified Applicators or persons under their direct supervision and only for those uses covered by the Certified Applicator's certification.

Gramoxone Inteon™

Herbicide

A Weed, Grass, and Harvest Aid Desiccant/Defoliant Herbicide

Active Ingredient:

Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride) 30.1%

Other Ingredients: 69.9%

Total: 100.0%

Contains 2.0 pounds paraquat cation per gallon as 2.762 pounds salt per gallon.
Contains alerting agent (odor), emetic, dye and Inteon Technology

EPA Reg. No.100

EPA Est.

KEEP OUT OF REACH OF CHILDREN.



DANGER / POISON
PELIGRO

ACCEPTED
with COMMENTS
in EPA Letter Dated

AUG 17 2005

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

100-1217

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

- **NEVER PUT INTO FOOD, DRINK OR OTHER CONTAINERS.**
- **IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID STATEMENT. SYMPTOMS ARE PROLONGED AND PAINFUL.**
- **DO NOT USE OR STORE IN OR AROUND THE HOME.**
- **DO NOT REMOVE CONTENTS EXCEPT FOR IMMEDIATE USE.**
- **THE ODOR OF THIS PRODUCT IS FROM THE ALERTING AGENT WHICH HAS BEEN ADDED, NOT FROM PARAQUAT.**

risks associated with the proposed use of 4-(p-acetoxypheyl)-2-butanone (Cuelure), and information on social, economic, and environmental benefits to be derived from use. Specifically, the Agency has considered the nature of the chemical and its pattern of use, application methods and rates, and level and extent of potential exposure. Based on these reviews, the Agency was able to make basic health and safety determinations which show that use of 4-(p-acetoxypheyl)-2-butanone (Cuelure) in accordance with widespread and commonly recognized practice, will not generally cause unreasonable adverse effects to the environment.

III. Approved Application

EPA issued a notice, published in the **Federal Register** of September 24, 2004 (69 FR 57284) (FRL-7674-5), which announced that Farma Tech International Corporation, P.O. Box 27227, Fresno, CA 93729-7227, had submitted an application to register the pesticide product, Cuelure (File Symbol 81325-R), a semiochemical attractant for manufacturing end-use products for the control of certain Tephritidae flies of the order Diptera, containing the active ingredient 4-(p-acetoxypheyl)-2-butanone at 98.00%, an active ingredient not included in any previously registered product.

The application was approved on September 29, 2005 as Cuelure for manufacturing end-use products to control certain Tephritidae flies of the order Diptera (EPA Registration Number 81325-1).

List of Subjects

Environmental protection, Chemicals, Pesticides and pests.

Dated: October 19, 20005.

Janet L. Andersen,

Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

[FR Doc. 05-21462 Filed 10-27-05; 8:45 am]

BILLING CODE 6560-50-S

ENVIRONMENTAL PROTECTION AGENCY

[OPP-2005-0285; FRL-7743-6]

Notice of Receipt of Requests to Voluntarily Cancel Certain Pesticide Registrations

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: In accordance with section 6(f)(1) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, EPA is issuing a notice of receipt of request by registrants to voluntarily cancel certain pesticide registrations.

DATES: Unless a request is withdrawn by April 26, 2006, orders will be issued canceling these registrations. The Agency will consider withdrawal requests postmarked no later than April 26, 2006.

FOR FURTHER INFORMATION CONTACT: John Jamula, Information Technology and Resource Management Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 305-6426; e-mail address: jamula.john@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general. Although this action may be of particular interest to persons who produce or use pesticides, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the information in this notice, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket.* EPA has established an official public docket for this action

under docket identification (ID) number OPP-2005-0285. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305-5805.

2. *Electronic access.* You may access this **Federal Register** document electronically through the EPA Internet under the "Federal Register" listings at <http://www.epa.gov/fedrgstr/>.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at <http://www.epa.gov/edocket/> to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select "search," then key in the appropriate docket ID number.

II. What Action is the Agency Taking?

This notice announces receipt by the Agency of applications from registrants to cancel 91 pesticide products registered under section 3 or 24(c) of FIFRA. These registrations are listed in sequence by registration number (or company number and 24(c) number) in Table 1 of this unit:

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION

Registration no.	Product Name	Chemical Name
000100-01002	Gramoxone Super Herbicide	Paraquat dichloride
000100-01009	Cyclone Herbicide	Paraquat dichloride
000100-01010	Surefire Herbicide	Diuron
		Paraquat dichloride
000100-01043	Gramoxone Extra Herbicide	Paraquat dichloride

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
000100-01074	Cyclone Concentrate Herbicide	Paraquat dichloride
000192-00217	Marman Temephos 1% Granule	Temephos
000192-00218	Marman Temephos 4 EC	Temephos
000228-00209	Riverdale Team 1.50 Lawn Weed and Feed	Trifluralin
		Benfluralin
000228-00254	Riverdale Team Tm .88 Lawn Weed and Feed	Trifluralin
		Benfluralin
000228-00255	Riverdale Team 1.11% Lawn Weed and Feed	Trifluralin
		Benfluralin
000228-00257	Riverdale Team .67% Lawn Weed and Feed	Trifluralin
		Benfluralin
000241-00325	Passport Herbicide	Trifluralin
		Ammonium salt of (+/-)-2-(4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl)-5-e
000264-00628	Betanex 70 WP	Desmedipham
000264-00629	Betamix 70WP	Phenmedipham
		Desmedipham
000264-00945	Gustafson Flo-Pro IMZ Flowable	Imazalil
000264 CA-80-0146	Guthion 50% Wettable Powder In Water Soluble Packets	Azinphos-Methyl
000264 CO-02-0009	Gustafson Flo-Pro Imz Flowable	Imazalil
000264 ID-98-0014	Gustafson Flo-Pro IMZ Flowable	Imazalil
000270-00344	Adams Flea and Tick Dust II	Carbaryl
		Piperonyl butoxide
		Pyrethrins
		Silica gel
000270-00361	Mycodex Pet Shampoo with Carbaryl	Carbaryl
000303-00079	Tor Germicidal Cleaner	Alkyl* dimethyl benzyl ammonium chloride *(60%C14, 30%C16, 5%C18,5%C12)
		Alkyl* dimethyl ethylbenzyl ammonium chloride *(50%C12, 30%C14, 17%C16,3%C18)
000303-00209	Ascend	Alkyl* dimethyl benzyl ammonium chloride *(50%C14, 40%C12,10%C16)
		1-Decanaminium, N-decyl-N,N-dimethyl-, chloride
000303-00210	Q-Cide	Alkyl* dimethyl benzyl ammonium chloride *(50%C14, 40%C12,10%C16)
		1-Decanaminium, N-decyl-N,N-dimethyl-, chloride
000303-00226	Tor II	Alkyl* dimethyl benzyl ammonium chloride *(50%C14, 40%C12,10%C16)

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
		1-Decanaminium, N-decyl-N,N-dimethyl-, chloride
000432-00773	Bioresmethrin ULV	Bioresmethrin
000464-00713	Ucarcide P200 Antimicrobial	1,2-Benzenedicarboxaldehyde
000769-00579	R & M Flea & Tick Spray #1	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
000769-00580	R & M Flea & Tick Shampoo #1	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
000769-00581	R & M Flea & Tick Spray #2	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
000769-00582	R & M Flea & Tick Shampoo #2	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
000769-00606	Sureco Insect Repellent Spray	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Diethyl toluamide
000769-00615	R & M Flea and Tick Shampoo #7	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
000769-00905	Gibberellic Acid Wonder-Brel	Gibberellic acid, monopotassium salt
000829-00131	SA-50 Brand Sevin 1.75% Dust	Carbaryl
000829-00182	SA-50 Brand Bait Pellets Kill Land Snails & Slugs	Metaldehyde
		Carbaryl
002212-00002	Elimstaph No. 2 Germicidal Cleaner	Alkyl* dimethyl benzyl ammonium chloride *(50%C14, 40%C12,10%C16)
002724-00501	Elite Flea & Tick Shampoo #8	2,5-Pyridinedicarboxylic acid, dipropyl ester

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
002935-00537	Clean Crop Captan 5% Potato Seed Treater	Captan
002935-00538	Potato Seed Treater with Bark	Captan
005481-00256	Royal Brand Ferbam Dust	Ferbam
005481-00268	76W Ferbam Fungicide	Ferbam
007401-00072	Ferti-Lome Improved Bug Bait	Metaaldehyde
		Carbaryl
007401-00081	Ferti-Lome Carbaryl-Sulfur 10-40 Dust	Carbaryl
		Sulfur
007401-00083	Ferti-Lome Carbaryl Garden Spray	Carbaryl
007401-00148	Sevin & Molasses Insect Bait	Carbaryl
007401-00154	10% Sevin Dust	Carbaryl
007401-00210	Hi-Yield Sevin Emulsifiable Concentrate	Carbaryl
007401-00291	Hi-Yield Mater-Tater and Other Vegetable Dust	Carbaryl
007401-00310	Hi-Yield Sevin Plus Dipel Dust	Bacillus thuringiensis (Berliner)
		Carbaryl
007401-00334	Hi-Yield Sos Garden Dust	Carbaryl
		Sulfur
007401-00386	Ferti-Lome Gypsy Moth, Japanese Beetle and Pine Moth	Carbaryl
008660-00068	Ferbam Fungicide	Ferbam
008660-00139	Vertagreen Fertilizer for Professional Use with Balan	Benfluralin
		Oryzalin
008660-00146	Vertagreen Pre-Emergence Weed & Feed	Benfluralin
		Oryzalin
009444-00028	Fly Foam Insect Repellent for Horses	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
009444-00098	Purge Wasp & Hornet Jet Freeze	Carbaryl
		Piperonyl butoxide
		Pyrethrins
009444-00190	Wasp & Hornet Jet Freeze I	Carbaryl
		Piperonyl butoxide

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
		Pyrethrins
010159-00002	VPG 5% Sevin Dust	Carbaryl
010163-00032	Prokil Carbaryl Bait	Carbaryl
010163-00060	Gowan Carbaryl 4	Carbaryl
010163-00124	Gowan Carbaryl 10 Dust	Carbaryl
010163-00133	Gowan Carbaryl 80 WP	Carbaryl
010163-00134	Gowan Carbaryl 80 WSB	Carbaryl
010163 UT-01-0005	Prokil Carbaryl Bait	Carbaryl
012455 PA-82-0016	Ditrac Rat and Mouse Bait	Diphacinone
019713-00068	Drexel Ziram 76	Ziram
019713-00279	IDA, Inc. Ziram 76 A Wettable Fungicide	Ziram
034911-00006	Hi-Yield 5% Sevin Dust	Carbaryl
034911-00008	Hi-Yield Bug Bait	Metaldehyde
		Carbaryl
040849-00057	Enforcer Flea & Tick Spray X	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
040849-00058	Enforcer Flea & Tick Shampoo X	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
040849-00073	Fleapro Ear Mite Treatment	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
042964-00002	A-3	Alkyl* dimethyl benzyl ammonium chloride *(60%C14, 30%C16, 5%C18,5%C12)
042964-00029	Asepticare Spray Cleaner/Disinfectant	Alkyl* dimethyl benzyl ammonium chloride *(60%C14, 30%C16, 5%C18,5%C12)
		Alkyl* dimethyl benzyl ammonium chloride *(50%C14, 40%C12,10%C16)
		Alkyl* dimethyl ethylbenzyl ammonium chloride *(68%C12, 32%C14)
045735-00024	Carbaryl 99% Technical Grade Insecticide	Carbaryl
045735-00025	Carbaryl 4L Flowable	Carbaryl
047000-00134	Clean Crop Equinol Horse Spray	2,5-Pyridinedicarboxylic acid, dipropyl ester

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
		4,7-Methano-1H-isindole-1,3(2H)-dione,2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
047000-00142	Horse Fly Spray R	2,5-Pyridinedicarboxylic acid, dipropyl ester
		Piperonyl butoxide
		Pyrethrins
048273-00003	Ametryne 80W	Ametryn
051036 PA-03-0001	Diazinon AG 500	Diazinon
051036 TX-01-0014	Diazinon AG 500	Diazinon
051036 WA-03-0011	Diazinon AG 500	Diazinon
053883-00041	Martin's 10% Sevin Dust	Carbaryl
053883-00042	Martin's 5% Sevin Dust	Carbaryl
053883-00043	M Martin's Lice Killer contains Sevin	Carbaryl
056938-00003	Fresh & Clean	EDTA, tetrasodium salt
		1-Decanaminium, N-decyl-N,N-dimethyl-, chloride
		Sodium metasilicate
		Sodium carbonate
067760 WA-00-0004	Cheminova Methyl Parathion 4 EC	Methyl parathion

Unless a request is withdrawn by the registrant within 180 days of publication of this notice, orders will be issued canceling all of these registrations. Users of these pesticides or anyone else desiring the retention of a registration should contact the applicable registrant directly during this 180-day period.

In addition to the registrations listed in Table 1, the Agency received requests to cancel four additional registrations. Under terms of a memorandum of agreement the effective date of cancellation for these four registrations will be December 31, 2005, and the existing stocks date will be December 31, 2006. The four registrations in question are: 001812-00451 Finitron Brand Sulfuramid AB MUP; 001812-00348 Volcano Ant Bait; 000279-03154 Fluoguard Ant Control Baits; and 000499-00459 Micro-Gen Ant Reactor.

Table 2 of this unit includes the names and addresses of record for all registrants of the products in Table 1 of

this unit, in sequence by EPA company number:

TABLE 2.—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION

EPA Company no.	Company Name and Address
000100	Syngenta Crop Protection, Inc., Attn: Regulatory Affairs, PO Box 18300, Greensboro, NC 27419-8300
000192	Value Gardens Supply, LLC, d/b/a Value Gardens Supply, PO Box 585, Saint Joseph, MO 64502
000228	Nufarm Americas Inc., 1333 Burr Ridge Parkway, Suite 125a, Burr Ridge, IL 60527-0866
000241	BASF Corp., PO Box 13528, Research Triangle Park, NC 27709-3528

TABLE 2.—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION—Continued

EPA Company no.	Company Name and Address
000264	Bayer Cropscience LP, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709
000270	Farnam Companies Inc., PO Box 34820, Phoenix, AZ 85067
000279	FMC Corp. Agricultural Products Group, 1735 Market St, Philadelphia, PA 19103
000303	Huntington Professional Products, A Service of Ecolab, Inc., 370 N. Wabasha Street, St. Paul, MN 55102

TABLE 2—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION—Continued

EPA Company no.	Company Name and Address
000432	Bayer Environmental Science, A Business Group of Bayer Cropscience LP, PO Box 12014, Research Triangle Park, NC 27709
000464	Dow Chemical Co., The, Attn: Rhonda Vance-Moeser, 1803 Building, Midland, MI 48674
000499	Whitmire Micro-Gen Research Laboratories Inc., 3568 Tree Ct. Industrial Blvd., St Louis, MO 63122-6682
000769	Value Gardens Supply, LLC, d/b/a Value Garden Supply, PO Box 585, Saint Joseph, MO 64502
000829	Southern Agricultural Insecticides, Inc., PO Box 218, Palmetto, FL 34220
001812	Dupont Crop Protection/stine-Haskell Research Center, Agent For: Griffin L.L.C., PO Box 30, Newark, DE 19714-0030
002212	Walter G. Legge Co., Inc., PO Box 591, Peekski, NY 10566
002724	Wellmark International, 1501 E. Woodfield Rd., Suite 200 W, Schaumburg, IL 60173
002935	Wilbur Ellis Co., PO Box 1286, Fresno, CA 93715
005481	Amvac Chemical Corp., Attn: Jon C. Wood, 4695 Macarthur Ct., Suite 1250, Newport Beach, CA 92660-1706
007401	Brazos Associates, Inc., Agent For: Voluntary Purchasing Group Inc., 1806 Auburn Drive, Carrollton, TX 75007-1451
008660	Sylor Plant Corp., PO Box 142642, St. Lou, MO 63114-0642
009444	Waterbury Companies Inc., PO Box 640, Independence, LA 70443
010159	Brazos Associates, Inc., Agent For: Voluntary Purchasing Group Inc., 1806 Auburn Drive, Carrollton, TX 75007-1451
010163	Gowan Co, PO Box 5569, Yu, AZ 85366-5569

TABLE 2—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION—Continued

EPA Company no.	Company Name and Address
012455	Bell Laboratories Inc., 3699 Kinsman Blvd., Madison, WI 53704
019713	Drexel Chemical Co, PO Box 13327, Memphis, TN 38113-0327
034911	Brazos Associates, Inc., Agent For: Hi-Yield Chemical Co., 1806 Auburn Drive, Carrollton, TX 75007-1451
040849	Acuity Specialty Products Group, Inc., Agent For: Enforcer Products, 1420 Seaboard Industrial Blvd. NW, Atlanta, GA 30318
042964	Airkem Professional Products, Division of Ecolab, Inc., Ecolab Center, St. Paul, MN 55102
045735	Burlington Scientific Corp., 71 Carolyn Blvd., Farmingdale, NY 11735
047000	Steven E. Rogosheske, Agent For: Chem-Tech Ltd., 1479 W. Pond Rd, Eagan, MN 55122
048273	Nufarm Co., Agent For: Marman USA Inc., 1333 Burr Ridge Parkway #125A, Burr Ridge, IL 60527
051036	Micro-Flo Co. LLC, 530 Oak Ct. Drive, Memphis, TN 38117
053883	Control Solutions, Inc., 5903 Genoa-Red Bluff, Pasadena, TX 77507-1041
056938	ABC Corp., 94-085 Leonui Street, Waipahu, HI 96797
067760	Cheminova Inc., 1700 Route 23 - Ste 300, Wayne, NJ 07470

III. What is the Agency's Authority for Taking this Action?

Section 6(f)(1) of FIFRA provides that a registrant of a pesticide product may at any time request that any of its pesticide registrations be canceled. FIFRA further provides that, before acting on the request, EPA must publish a notice of receipt of any such request in the **Federal Register**. Thereafter, the Administrator may approve such a request.

IV. Procedures for Withdrawal of Request

Registrants who choose to withdraw a request for cancellation must submit such withdrawal in writing to the person listed under **FOR FURTHER INFORMATION CONTACT**, postmarked before April 26, 2006. This written withdrawal of the request for cancellation will apply only to the applicable FIFRA section 6(f)(1) request listed in this notice. If the product(s) have been subject to a previous cancellation action, the effective date of cancellation and all other provisions of any earlier cancellation action are controlling. The withdrawal request must also include a commitment to pay any reregistration fees due, and to fulfill any applicable unsatisfied data requirements.

V. Provisions for Disposition of Existing Stocks

The effective date of cancellation will be the date of the cancellation order. The orders effecting these requested cancellations will generally permit a registrant to sell or distribute existing stocks for 1 year after the date the cancellation request was received. This policy is in accordance with the Agency's statement of policy as prescribed in the **Federal Register** of June 26, 1991 (56 FR 29362) (FRL-3846-4). Exceptions to this general rule will be made if a product poses a risk concern, or is in noncompliance with reregistration requirements, or is subject to a data call-in. In all cases, product-specific disposition dates will be given in the cancellation orders.

Existing stocks are those stocks of registered pesticide products which are currently in the United States and which have been packaged, labeled, and released for shipment prior to the effective date of the cancellation action. Unless the provisions of an earlier order apply, existing stocks already in the hands of dealers or users can be distributed, sold, or used legally until they are exhausted, provided that such further sale and use comply with the EPA-approved label and labeling of the affected product. Exception to these general rules will be made in specific cases when more stringent restrictions on sale, distribution, or use of the products or their ingredients have already been imposed, as in a Special Review action, or where the Agency has identified significant potential risk concerns associated with a particular chemical.

List of Subjects

Environmental protection, Pesticides and pests.

Dated: October 20, 2005.

Robert A. Forrest,

Acting Director, Information Technology and Resource Management Division, Office of Pesticide Programs.

[FR Doc. 05-21532 Filed 10-27-05; 8:45 am]

BILLING CODE 6560-50-S

FEDERAL RESERVE SYSTEM**Change in Bank Control Notices; Acquisition of Shares of Bank or Bank Holding Companies**

The notificants listed below have applied under the Change in Bank Control Act (12 U.S.C. 1817(j)) and § 225.41 of the Board's Regulation Y (12 CFR 225.41) to acquire a bank or bank holding company. The factors that are considered in acting on the notices are set forth in paragraph 7 of the Act (12 U.S.C. 1817(j)(7)).

The notices are available for immediate inspection at the Federal Reserve Bank indicated. The notices also will be available for inspection at the office of the Board of Governors. Interested persons may express their views in writing to the Reserve Bank indicated for that notice or to the offices of the Board of Governors. Comments must be received not later than November 14, 2005.

A. Federal Reserve Bank of St. Louis (Glenda Wilson, Community Affairs Officer) 411 Locust Street, St. Louis, Missouri 63166-2034:

1. **Clarence Ray Brewer, Jr.**, Central City, Kentucky; to acquire voting shares of Community Bancorp of McLean County, Kentucky, Inc., Island, Kentucky, and thereby indirectly acquire voting shares of First Security Bank and Trust, Island, Kentucky.

Board of Governors of the Federal Reserve System, October 25, 2005.

Robert deV. Frierson,

Deputy Secretary of the Board.

[FR Doc. E5-5979 Filed 10-27-05; 8:45 am]

BILLING CODE 6210-01-S

FEDERAL RESERVE SYSTEM**Sunshine Act Meeting**

AGENCY HOLDING THE MEETING: Board of Governors of the Federal Reserve System.

TIME AND DATE: 1:45 p.m., Wednesday, November 2, 2005.

PLACE: Marriner S. Eccles Federal Reserve Board Building, 20th Street

entrance between Constitution Avenue and C Streets, N.W., Washington, D.C. 20551.

STATUS: Open.

We ask that you notify us in advance if you plan to attend the open meeting and provide your name, date of birth, and social security number (SSN) or passport number. You may provide this information by calling (202) 452-2474 or you may **register on-line**. You may pre-register until close of business November 1, 2005. You also will be asked to provide identifying information, including a photo ID, before being admitted to the Board meeting. The Public Affairs Office must approve the use of cameras; please call (202) 452-2955 for further information. If you need an accommodation for a disability, please contact Penelope Beattie on (202) 452-3982. For the hearing impaired only, please use the Telecommunication Device for the Deaf (TDD) on (202) 263-4869.

Privacy Act Notice: Providing the information requested is voluntary; however, failure to provide your name, date of birth, and social security number or passport number may result in denial of entry to the Federal Reserve Board. This information is solicited pursuant to Sections 10 and 11 of the Federal Reserve Act and will be used to facilitate a search of law enforcement databases to confirm that no threat is posed to Board employees or property. It may be disclosed to other persons to evaluate a potential threat. The information also may be provided to law enforcement agencies, courts, and others, but only to the extent necessary to investigate or prosecute a violation of law.

MATTERS TO BE CONSIDERED:**Summary Agenda:**

1. Proposed 2006 Private Sector Adjustment Factor.

Discussion Agenda:

1. Proposed 2006 fee schedules for priced services and electronic access.

NOTE: This meeting will be recorded for the benefit of those unable to attend. Cassettes will be available for listening in the Board's Freedom of Information Office and copies may be ordered for \$6 per cassette by calling (202) 452-3684 or by writing to: Freedom of Information Office, Board of Governors of the Federal Reserve System, Washington, D.C. 20551.

FOR FURTHER INFORMATION CONTACT: Michelle A. Smith, Director, Office of Board Members; 202-452-2955.

SUPPLEMENTARY INFORMATION: You may call (202) 452-3206 for a **recorded announcement** of this meeting; or you may contact the Board's Web site at

<http://www.federalreserve.gov> for an **electronic announcement**. (The Web site also includes procedural and other information about the open meeting.)

Board of Governors of the Federal Reserve System, October 26, 2005.

Robert deV. Frierson,

Deputy Secretary of the Board.

[FR Doc. 05-21648 Filed 10-26-05; 3:23 pm]

BILLING CODE 6210-01-S

DEPARTMENT OF HEALTH AND HUMAN SERVICES**Office of the Secretary**

[Document Identifier: OS-0990-0208]

Agency Information Collection Activities: Proposed Collection; Comment Request

Agency: Office of the Secretary, HHS.

In compliance with the requirement of section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, the Office of the Secretary (OS), Department of Health and Human Services, is publishing the following summary of a proposed collection for public comment. Interested persons are invited to send comments regarding this burden estimate or any other aspect of this collection of information, including any of the following subjects: (1) The necessity and utility of the proposed information collection for the proper performance of the agency's functions; (2) the accuracy of the estimated burden; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) the use of automated collection techniques or other forms of information technology to minimize the information collection burden.

Type of Information Collection

Request: Regular Clearance, Extension of a currently approved collection;

Title of Information Collection:

Applicant Background Survey;

Form/OMB No.: OS-0990-0208;

Use: This form will be used to ask applicants for employment, how they learned about a vacancy to ensure that recruitment sources yield qualified women and minority applicants, as well as applicants with disabilities, in compliance with EEOC management directives;

Frequency: Reporting;

Affected Public: Individuals or households;

Annual Number of Respondents:

30,000.00;

Total Annual Responses: 30,000.00;

Average Burden Per Response: 1/2 hour;



U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505C)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

EPA Reg.
Number:

82557-1

Date of Issuance:

January 25,
2006

Term of Issuance:

Unconditional

Name of Pesticide Product:

Parquat SL Herbicide

Name and Address of Registrant (include ZIP Code):

Sinon USA Inc.
1080 Carol Lane, Suite 264
Lafayette, CA 94549

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is registered in accordance with FIFRA section 3(c)(5).

This registration will expire automatically, without opportunity for a hearing, upon the issuance of a cancellation order for EPA Reg. No. 100-1074. The registrant will be subject to the same conditions as contained in the cancellation order issued on that date for EPA Reg. No. 100-1074. The cancellation order for EPA Reg. No. 100-1074 will not be issued before April 26, 2006."

Submit the outstanding product chemistry data requirements 830.6317 (Storage Stability) and 830.6320 (Corrosion Characteristics) within 1 year from the date on this registration letter.

Signature of Approving Official:


James Tompkins, Product Manager (25)
Herbicide Branch, Registration Division (7505C)

Date:


January 25, 2006

Make the following label changes before you release the product for shipment

1. Change EPA Reg. No. on label from 82557-R to 82557-1.
2. Add an appropriate EPA Establishment number to the label.
3. On page 3, in the PRECAUTIONARY STATEMENTS, add "Harmful if absorbed through skin." before "Avoid contact with skin."
4. On page 19, in the General Information for Chemical Fallow section, add the following statement "The minimum total spray per acre allowed is 5 gallons for ground and 5 gallons for air application."
5. On page 40, in the section SUNFLOWER- Preplant or Preemergence Broadcast or Banded Over Row, in the Rate Column change "1.7- 2.7 pts" to "1.7- 2.7 pts."

You will submit one (1) copy of your final printed labeling before you release the product for shipment. A stamped copy of labeling is enclosed for your records.

If you have any questions, please contact Hope Johnson at 703-305-5410.


James Tompkins
Product Manager (25)
Herbicide Branch
Registration Division (7505C)

RESTRICTED USE PESTICIDE
DUE TO ACUTE TOXICITY
FOR RETAIL SALE TO AND USE ONLY BY CERTIFIED APPLICATORS OR PERSONS
UNDER THEIR DIRECT SUPERVISION AND ONLY FOR THOSE USES COVERED
BY THE CERTIFIED APPLICATOR'S CERTIFICATION.

PARAQUAT SL HERBICIDE™

Defoliant and desiccant herbicide
for the control of weeds and grasses and as a harvest aid.

- NEVER PUT INTO FOOD, DRINK OR OTHER CONTAINERS.
- IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID.
- SYMPTOMS ARE PROLONGED AND PAINFUL.
- DO NOT USE OR STORE IN OR AROUND THE HOME.
- DO NOT REMOVE CONTENTS EXCEPT FOR IMMEDIATE USE.
- THE ODOR OF THIS PRODUCT IS FROM THE STENCHING AGENT WHICH HAS BEEN ADDED, NOT FROM PARAQUAT.

Active Ingredient:

Paraquat dichloride (1,1'-dimethyl-4,4'-Bipyridinium dichloride) 43.8%

Other Ingredients: 56.2%

Total: 100.0%

Contains 3.0 pounds paraquat cation per gallon as 4.143 pounds salt per gallon. Contains stench (odor) and emetic.

KEEP OUT OF REACH OF CHILDREN

DANGER/PELIGRO



POISON

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

EPA Reg. No. 82557-R

EPA Est.:

Net Contents:

ACCEPTED
with COMMENTS
in EPA Letter Dated

JAN 25 2006

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

82557-1



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
ARIEL RIOS BUILDING - 1200 PENNSYLVANIA AVENUE, N.W.
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

August 22, 2006

Dear Sir or Madam:

This letter is a final cancellation order, advising you that under Section 6(f)(1) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, EPA hereby cancels the registrations listed on the enclosure per your request for voluntary cancellation as listed in the Federal Register Notice dated February 22, 2006. The effective date of this cancellation order is the date of this letter.

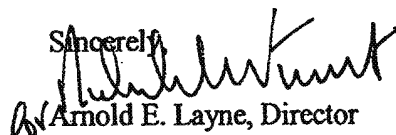
As the basic registrant of the listed product(s) you may legally distribute or sell existing stocks of the canceled products until the disposition date listed on the enclosure. Existing stocks are defined as those stocks of a registered pesticide product which are currently in the United States and which have been packaged, labeled, and released for shipment prior to the effective date of the cancellation order.

It would be a violation of FIFRA for your or any supplementally registered distributor of your product(s) to distribute or sell any stocks currently in the United States which have been produced, packaged, labeled or released for shipment after the effective date of cancellation, or any existing stocks after the indicated disposition date. The Agency also expressly reserves the right to amend the existing stocks provisions of this Order if events should so warrant.

It is your responsibility as the basic registrant to notify any and all supplementally registered distributors of your product(s) that this cancellation order also applies to their supplementally registered products. You may be held liable for violations committed by your distributors.

Unless the provisions of an earlier order apply, existing stocks already in the hands of dealers or users can be distributed, sold or used legally until they are exhausted, provided that such sale and use comply with the EPA-approved label and labeling of the affected product(s).

Sincerely,


Arnold E. Layne, Director
Information Technology and Resource Management Division

AUG 29 2006
K

VOLUNTARY CANCELLATION ORDER (ENCLOSURE)

SYNGENTA CROP PROTECTION, INC.

EPA CO NR: 000100

PO BOX 18300

GREENSBORO

NC 27419

EPA PRODUCT REGISTRATION =====	DISP DATE =====	PRODUCT NAME =====
ID010007	02/22/2007	CYCLONE CONCENTRATE/GRAMOXONE MAX
000100-01074	02/22/2007	CYCLONE CONCENTRATE HERBICIDE

iv. Describe any assumptions and provide any technical information and/or data that you used.

v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.

vi. Provide specific examples to illustrate your concerns, and suggest alternatives.

vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.

viii. Make sure to submit your comments by the comment period deadline identified.

II. Registration Applications

EPA received applications as follows to register pesticide products containing active ingredients not included in any previously registered products pursuant to the provision of section 3(c)(4) of FIFRA. Notice of receipt of these applications does not imply a decision by the Agency on the applications.

1. *File Symbol:* 66330-AN. *Applicant:* Arysta LifeSciences, North America, 100 First St., Suite 1700, San Francisco, CA 94105. *Product name:* Midas EC Gold. *Active ingredients:* Iodomethane at 33% and Chloropicrin at 62%. *Proposed classification/Use:* For pre-plant fumigation onto fields intended for commercial production of strawberries, tomatoes, peppers and ornamental flowers, plants and bushes, and for the control of soil-borne pests, including nematodes, insects, weed and grass seeds, and diseases.

2. *File Symbol:* 66330-LI. *Applicant:* Arysta LifeSciences, North America, 100 First St., Suite 1700, San Francisco, CA 94105. *Product name:* Midas EC Bronze. *Active ingredients:* Iodomethane at 50% and Chloropicrin at 45%. *Proposed classification/Use:* For pre-plant fumigation onto fields intended for commercial production of strawberries, tomatoes, peppers and ornamental flowers, plants and bushes, for the control of soil-borne pests, including nematodes, insects, weed and grass seeds, and diseases.

3. *File Symbol:* 66330-LO. *Applicant:* Arysta LifeSciences, North America, 100 First St., Suite 1700, San Francisco, CA 94105. *Product name:* Midas 33:67. *Active ingredients:* Iodomethane at 33% and Chloropicrin at 67%. *Proposed classification/Use:* For pre-plant fumigation onto fields intended for commercial production of strawberries, tomatoes, peppers and ornamental flowers, plants and bushes, and for the control of soil-borne pests, including nematodes, insects, weed and grass seeds, and diseases.

4. *File Symbol:* 66330-LT. *Applicant:* Arysta LifeSciences, North America, 100 First St., Suite 1700, San Francisco, CA 94105. *Product name:* Midas 50:50. *Active ingredients:* Iodomethane at 50% and Chloropicrin at 50%. *Proposed classification/Use:* For pre-plant fumigation onto fields intended for commercial production of strawberries, tomatoes, peppers and ornamental flowers, plants and bushes, and for the control of soil-borne pests, including nematodes, insects, weed and grass seeds, and diseases.

List of Subjects

Environmental protection, Pesticides and pest.

Dated: February 7, 2006.

Lois Rossi,

Director, Registration Division, Office of Pesticide Programs.

[FR Doc. 06-1458 Filed 2-21-06; 8:45 am]

BILLING CODE 6560-50-S

ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-OPP-2006-0084; FRL-7762-4]

Notice of Receipt of Requests to Voluntarily Cancel Certain Pesticide Registrations

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: In accordance with section 6(f)(1) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, EPA is issuing a notice of receipt of request by registrants to voluntarily cancel certain pesticide registrations.

DATES: Unless a request is withdrawn by August 21, 2006, orders will be issued canceling these registrations. The Agency will consider withdrawal requests postmarked no later than August 21, 2006.

FOR FURTHER INFORMATION CONTACT: John Jamula, Information Technology and Resource Management Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 305-6426; e-mail address: jamula.john@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general. Although this action may be

of particular interest to persons who produce or use pesticides, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the information in this notice, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket.* EPA has established an official public docket for this action under docket identification (ID) number EPA-HQ-OPP-2006-0084. The official public docket consists of the documents specifically referenced in this action, any public comments received, and other information related to this action. Although a part of the official docket, the public docket does not include Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. The official public docket is the collection of materials that is available for public viewing at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305-5805.

2. *Electronic access.* You may access this **Federal Register** document electronically through the EPA Internet under the "**Federal Register**" listings at <http://www.epa.gov/fedrgstr/>.

EDOCKET, EPA's electronic public docket and comment system was replaced on November 25, 2005, by an enhanced Federal-wide electronic docket management and comment system located at <http://www.regulations.gov/>. Follow the on-line instructions.

An electronic version of the public docket is available through EPA's electronic public docket and comment system, EPA Dockets. You may use EPA Dockets at <http://www.epa.gov/edocket/> to submit or view public comments, access the index listing of the contents of the official public docket, and to access those documents in the public docket that are available electronically. Although not all docket materials may be available electronically, you may still access any of the publicly available docket materials through the docket facility identified in Unit I.B.1. Once in the system, select "search," then key in the appropriate docket ID number.

II. What Action is the Agency Taking?

This notice announces receipt by the Agency of applications from registrants

to cancel 90 pesticide products
registered under section 3 or 24(c) of

FIFRA. These registrations are listed in
sequence by registration number (or

company number and 24(c) number) in
Table 1 of this unit:

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION

Registration no.	Product Name	Chemical Name
000100-01074	Cyclone Concentrate Herbicide	Paraquat dichloride
000100 CA 91-0022	Gramoxone Extra Herbicide	Paraquat dichloride
000100 CA 92-0006	Gramoxone Extra Herbicide	Paraquat dichloride
000100 ID 01-0007	Cyclone Concentrate/Gramoxone Max	Gas cartridge (as a device for burrowing animal control)
		Paraquat dichloride
000228-00202	Riverdale Dibro Granular Weed Killer	Bromacil
		Diuron
000228-00233	Dibro 1 Granular Weed Killer	Bromacil
		Diuron
000228-00234	Riverdale Dibro 2+4	Bromacil
		Diuron
000228-00235	Riverdale Dibro 4+4 Granular Weed Killer	Bromacil
		Diuron
000228-00236	Riverdale Dibro 5+4	Bromacil
		Diuron
000228-00273	Riverdale Diuron 80 WP Weed Killer	Diuron
000228-00308	Topsite 2.5G Herbicide	Diuron
		Imazapyr
000241-00268	Prowl DG Herbicide	Pendimethalin
000241-00321	Scepter O.T. Herbicide	Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-, sodium salt
		3-Quinolinecarboxylic acid, 2-(4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl)
000241-00338	Pentagon 60 DG Herbicide	Pendimethalin
000264 OR 80-0063	Nemacur 3 Emulsifiable Nematicide	Fenamiphos
000264 OR 81-0039	Sencor 4 Flowable Herbicide	Metribuzin
000264 OR 81-0040	Sencor 75 Wettable Granular Herbicide	Metribuzin
000264 OR 84-0032	Di-Syston 8	Disulfoton
000264 OR 85-0019	Sencor 4 Flowable Herbicide	Metribuzin
000264 OR 91-0027	Di - Syston 8	Disulfoton
000264 OR 93-0012	Bayleton 50% Wettable Powder	Triadimefon

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
000264 OR 99-0049	Guthion Solupak 50% Wettable Powder Insecticide	Azinphos-Methyl
000270-00260	Farnam Turbo	Diazinon
		Piperonyl butoxide
000352 CA 00-0007	Dupont Oust Herbicide	Sulfometuron
000352 ID 00-0019	Dupont Oust Herbicide	Sulfometuron
000352 MN 95-0006	Dupont Oust Herbicide	Sulfometuron
000352 NV 99-0009	Dupont Oust Herbicide	Sulfometuron
000352 SC 95-0001	Dupont Oust Herbicide	Sulfometuron
000352 WA 00-0008	Dupont Oust Herbicide	Sulfometuron
000352 WA 93-0002	Dupont Krovar I DF Herbicide	Bromacil
		Diuron
000352 WA 95-0021	Dupont Oust Herbicide	Sulfometuron
000352 WI 96-0001	Dupont Oust Herbicide	Sulfometuron
000829-00142	SA-50 Brand Sevin 50W Insecticide	Carbaryl
002749-00059	Diuron 80 WP Weed Killer	Diuron
004787-00037	Cyren MUC	Chlorpyrifos
004787-00039	Cyren 150 Concentrate	Chlorpyrifos
004787-00047	Griffin Methyl Parathion MUP	Methyl parathion
007501 OK 93-0001	Tops 90	Thiophanate-methyl
007501 TX 93-0006	Tops 90 Peanut Seed Treatment	Thiophanate-methyl
007969-00077	Galaxy Herbicide	3-Isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide, sodium salt
		Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-, sodium salt
007969-00080	Blazer 2S Herbicide	Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-, sodium salt
007969-00168	Conclude Ultra Herbicide	3-Isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide, sodium salt
		Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-, sodium salt
		Sethoxydim
007969-00179	Conclude Xact	3-Isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide, sodium salt
		Benzoic acid, 5-(2-chloro-4-(trifluoromethyl)phenoxy)-2-nitro-, sodium salt
		Sethoxydim
008999-00004	Aquarium Algae Clear Liquid	Copper sulfate pentahydrate
		Diuron

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
008999-00005	Algae Clear	Copper sulfate pentahydrate
		Diuron
009198-00106	The Andersons Tee Time Fertilizer with Sevin (r)	Carbaryl
010163 WA 98-0015	Gowan Endosulfan 3EC	Endosulfan
010163 WA 99-0025	Gowan Endosulfan 3EC	Endosulfan
010163 WA 99-0032	Gowan Endosulfan 3EC	Endosulfan
011715-00006	Speer Insect Killer (with .35% SBP-1382)	Resmethrin
011715-00023	Speer Equine Spray	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
011715-00047	Speer Aircraft Insecticide Aerosol	Piperonyl butoxide
		Pyrethrins
011715-00091	Magic Guard Automatic Sequential Insecticide	Piperonyl butoxide
		Pyrethrins
011715-00119	Better World Dairy Spray	Piperonyl butoxide
		Pyrethrins
011715-00148	Magic Guard Automatic Room Fogger Formula II	2-Methyl-4-oxo-3-(2-propenyl)-2-cyclopenten-1-yl d-trans-2,2-dimethyl-3-(2-methyl-1-propenyl)
		Piperonyl butoxide
		Resmethrin
011715-00158	Magic Guard with Rotenone/pyrethrins	Pyrethrins
		Rotenone
		Cube Resins other than rotenone
011715-00159	Speer E-Z Way Residual Crack & Crevice Injection Sy	Tetramethrin
		Fenvalerate
011715-00165	Better World Residual Roach and Flea Spray	2-Methyl-4-oxo-3-(2-propenyl)-2-cyclopenten-1-yl d-trans-2,2-dimethyl-3-(2-methyl-1-propenyl)
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Fenvalerate
011715-00169	Better World Insecticide	Resmethrin
011715-00173	Speer Stable Spray	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
		Piperonyl butoxide
		Pyrethrins
011715-00177	Magic Guard Non-Flammable Wasp Spray	4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
011715-00180	Speer E-Z II Residual Spray	4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Pyrethrins
		Fenvalerate
011715-00230	Farnam Super-Sheen Wipe-Plus	Bioallethrin
		Butoxypolypropylene glycol
		2,5-Pyridinedicarboxylic acid, dipropyl ester
		Piperonyl butoxide
011715-00234	Farnam Wipe II Fly Protectant	Butoxypolypropylene glycol
		2,5-Pyridinedicarboxylic acid, dipropyl ester
		Tetramethrin
		Phenothrin
011715-00235	Farnam Wipe-P Fly Protectant	2,5-Pyridinedicarboxylic acid, dipropyl ester
		Piperonyl butoxide
		Pyrethrins
019713-00052	Drexel Carbaryl 50-W	Carbaryl
019713-00334	Aldex Sevin-10G 10% Sevin Granular Insecticide	Carbaryl
019713-00369	Drexel Carbaryl 50% Manufacturing Concentrate	Carbaryl
033955-00462	Acme Sevin 5% Dust	Carbaryl
033955-00533	Acme Liquid Sevin Spray	Carbaryl
034704-00694	Clean Crop Acephate 80 DF Seed Protectant	Acephate
045735-00024	Carbaryl 99% Technical Grade Insecticide	Carbaryl
045735-00025	Carbaryl 4L Flowable	Carbaryl
051036-00310	Thiophanate-Methyl Technical	Thiophanate-methyl
051036 MS 02-0021	Acephate 90SP	Acephate
054705-00012	Hose'em Yard Insect Spray	Permethrin
055431-00001	Termiticide T/C	Chlorpyrifos
059623 CA 77- 0078	Geigy Diazinon 50W (50% Wettable Powder) Insecticide	Diazinon
061282 OR 05-0021	Prozap Zinc Phosphide Pellets	Zinc phosphide (Zn3P2)

TABLE 1.—REGISTRATIONS WITH PENDING REQUESTS FOR CANCELLATION—Continued

Registration no.	Product Name	Chemical Name
062719-00312	Drexel Atrazine 4F	Atrazine
062719-00313	Atrazine 90	Atrazine
066222-00081	Pendimethalin Technical	Pendimethalin
066222-00082	Repose	Pendimethalin
066222-00088	Prodiamine Technical	1,3-Benzenediamine, 2,6-dinitro-N1,N1-dipropyl-4-(trifluoromethyl)-
068688-00022	Elite Residual Mist Plus	Butoxypolypropylene glycol
		2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
		Permethrin
068688-00026	Elite Residual Mist Plus Concentrate	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
		Permethrin
068688-00030	Elite Flea and Tick Spray #8	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
068688-00031	Elite Aloe Repellent Lotion #8	2,5-Pyridinedicarboxylic acid, dipropyl ester
		4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-
		Piperonyl butoxide
		Pyrethrins
068688-00050	Heartland Freeze Brand Wasp and Hornet Killer	Resmethrin
080697-00002	Krop-Max	Cyanamide

Unless a request is withdrawn by the registrant within 180 days of publication of this notice, orders will be issued canceling all of these registrations. Users of these pesticides or anyone else desiring the retention of a registration should contact the applicable registrant directly during this 180-day period.

Table 2 of this unit includes the names and addresses of record for all registrants of the products in Table 1 of

this unit, in sequence by EPA company number:

TABLE 2.—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION

EPA Company no.	Company Name and Address
000100	Syngenta Crop Protection, Inc., Attn: Regulatory Affairs, PO Box 18300, Greensboro, NC 274198300.

TABLE 2.—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION—Continued

EPA Company no.	Company Name and Address
000228	Nufarm Americas Inc., 1333 Burr Ridge Parkway, Suite 125A, Burr Ridge, IL 605270866.
000241	BASF Corp., PO Box 13528, Research Triangle Park, NC 277093528.
000264	Bayer Cropscience LP, 2 T.W. Alexander Drive, Research Tri- angle Park, NC 27709.
000270	Farnam Companies Inc., PO Box 34820, Phoenix, AZ 85067.
000352	E.I. Du Pont De Ne- mours, Inc., Dupont Crop Protection (S300/427), PO Box 30, Newark, DE 197140030.
000829	Southern Agricultural Insecticides, Inc., PO Box 218, Pal- metto, FL 34220.
002749	Aceto Agriculture Chemicals Corp., One Hollow Lane, Lake Success, NY 110421215.
004787	Cheminova Inc., Agent For: Cheminova A/ S, 1620 Eye Street Nw, Suite 615, Washington, DC 20006.
007501	Gustafson LIC, PO Box 660065, Dallas, TX 75266.
007969	BASF Corp., Agricul- tural Products, PO Box 13528, Re- search Triangle Park, NC 277093528.
008999	Interpet LIC, d/b/a Aquarium Products, 180 L Penrod Ct., Glen Burnie, MD 21061.

TABLE 2.—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION—Continued

EPA Company no.	Company Name and Address
009198	The Andersons Lawn Fertilizer Division, Inc., dba/ Free Flow Fertilizer, PO Box 119, Maumee, OH 43537.
010163	Gowan Co, POBox 5569, Yuma, AZ 853665569.
011715	Speer Products Inc., 4242 B.F. Goodrich Blvd., Memphis, TN 381810993.
019713	Drexel Chemical Co, PO Box 13327, Memphis, TN 381130327.
033955	PBI/gordon Corp., Attn: James L. Kunstman, PO Box 014090, Kansas City, MO 641010090.
034704	Loveland Products, Inc., PO Box 1286, Greeley, CO 80632.
045735	Burlington Scientific Corp., 71 Carolyn Blvd., Farmingdale, NY 11735.
051036	Micro-Flo Co. LIC, 530 Oak Ct. Drive, Mem- phis, TN 38117.
054705	Lynne Zahigian Regu- latory Consulting, Agent For: Lawn and Garden Prod- ucts, Inc., PO Box 1566, Fallon, NV 89407.
055431	Rusty Millar, Agent For: Arizona Chem- ical Group Inc., 850 Micheltorena Street, Los Angeles, CA 900262702.
059623	California Dept of Food and Agri- culture, Office of Pesticide Consulta- tion and Analysis, 1220 N Street, Sac- ramento, CA 95814.
061282	Hacco, Inc., 110 Hop- kins Drive, Ran- dolph, WI 539561316.

TABLE 2.—REGISTRANTS REQUESTING VOLUNTARY CANCELLATION—Continued

EPA Company no.	Company Name and Address
062719	Dow Agrosciences LIC, 9330 Zionsville Rd 308/2e225, Indi- anapolis, IN 462681054.
066222	Makhteshim-Agan of North America Inc., 4515 Falls of Neuse Rd Ste 300, Ra- leigh, NC 27609.
068688	Speer Products Inc., 4242 B.F. Goodrich Blvd., Memphis, TN 38181.
080697	Tide International USA Inc., Agent For: Zhejiang Tide Cropscience Co., Ltd, 21 Hubble, Irvine, CA 92618.

III. What is the Agency's Authority for Taking this Action?

Section 6(f)(1) of FIFRA provides that a registrant of a pesticide product may at any time request that any of its pesticide registrations be canceled. FIFRA further provides that, before acting on the request, EPA must publish a notice of receipt of any such request in the **Federal Register**. Thereafter, the Administrator may approve such a request.

IV. Procedures for Withdrawal of Request

Registrants who choose to withdraw a request for cancellation must submit such withdrawal in writing to the person listed under **FOR FURTHER INFORMATION CONTACT**, postmarked before August 21, 2006. This written withdrawal of the request for cancellation will apply only to the applicable FIFRA section 6(f)(1) request listed in this notice. If the products have been subject to a previous cancellation action, the effective date of cancellation and all other provisions of any earlier cancellation action are controlling. The withdrawal request must also include a commitment to pay any reregistration fees due, and to fulfill any applicable unsatisfied data requirements.

V. Provisions for Disposition of Existing Stocks

The effective date of cancellation will be the date of the cancellation order. The orders effecting these requested

cancellations will generally permit a registrant to sell or distribute existing stocks for 1 year after the date the cancellation request was received. This policy is in accordance with the Agency's statement of policy as prescribed in the **Federal Register** of June 26, 1991, (56 FR 29362) (FRL-3846-4). Exceptions to this general rule will be made if a product poses a risk concern, or is in noncompliance with reregistration requirements, or is subject to a data call-in. In all cases, product-specific disposition dates will be given in the cancellation orders.

Existing stocks are those stocks of registered pesticide products which are currently in the United States and which have been packaged, labeled, and released for shipment prior to the effective date of the cancellation action. Unless the provisions of an earlier order apply, existing stocks already in the hands of dealers or users can be distributed, sold, or used legally until they are exhausted, provided that such further sale and use comply with the EPA-approved label and labeling of the affected product. Exception to these general rules will be made in specific cases when more stringent restrictions on sale, distribution, or use of the products or their ingredients have already been imposed, as in a Special Review action, or where the Agency has identified significant potential risk concerns associated with a particular chemical.

List of Subjects

Environmental protection, Pesticides and pests.

Dated: February 6, 2006.

Robert Forrest,

Acting Director, Information Technology and Resource Management Division, Office of Pesticide Programs.

[FR Doc. E6-2492 Filed 2-21-06; 8:45 am]

BILLING CODE 6560-50-S

FEDERAL COMMUNICATIONS COMMISSION

Notice of Public Information Collection(s) Being Submitted for Review to the Office of Management and Budget

February 8, 2006.

SUMMARY: The Federal Communications Commission, as required by the Paperwork Reduction Act (PRA) of 1995, Public Law 104-13, and as part of its continuing effort to reduce paperwork burden, invites the general public and other Federal agencies to take this opportunity to comment on the following information collection(s). An

agency may not conduct or sponsor a collection of information unless it displays a currently valid control number. No person shall be subject to any penalty for failing to comply with a collection of information subject to the Paperwork Reduction Act (PRA) that does not display a valid control number. Comments are requested concerning (a) Whether the proposed collection of information is necessary for the proper performance of the functions of the Commission, including whether the information shall have practical utility; (b) the accuracy of the Commission's burden estimate; (c) ways to enhance the quality, utility, and clarity of the information collected; and (d) ways to minimize the burden of the collection of information on the respondents, including the use of automated collection techniques or other forms of information technology.

DATES: Written Paperwork Reduction Act (PRA) comments should be submitted on or before March 24, 2006. If you anticipate that you will be submitting PRA comments, but find it difficult to do so within the period of time allowed by this notice, you should advise the contact listed below as soon as possible.

ADDRESSES: Direct all Paperwork Reduction Act (PRA) comments to Leslie F. Smith, Federal Communications Commission, Room 1-A804, 445 12th Street, SW., Washington, DC 20554 or via the Internet to Leslie.Smith@fcc.gov or Kristy L. LaLonde, Office of Management and Budget (OMB), Room 10236 NEOB, Washington, DC 20503, (202) 395-3087 or via the Internet at Kristy.L.LaLonde@omb.eop.gov.

If you would like to obtain or view a copy of this revised information collection, you may do so by visiting the FCC PRA Web page at: <http://www.fcc.gov/omd/prs>.

FOR FURTHER INFORMATION CONTACT: For additional information or copies of the information collection(s), contact Leslie F. Smith at (202) 418-0217 or via the Internet at Leslie.Smith@fcc.gov.

SUPPLEMENTARY INFORMATION:

OMB Control Number: 3060-0584.

Title: Administration of U.S. Certified Accounting Authorities in Maritime Mobile and Maritime Mobile-Satellite Radio Services, FCC Forms 44 and 45.

Form Number: FCC 44 and 45.

Type of Review: Extension of a currently approved collection.

Respondents: Business or other for-profit entities.

Number of Respondents: 25 respondents; 100 responses/annum.

Estimated Time per Response: 1-3 hours.

Frequency of Response: Recordkeeping; On occasion, semi-annual, and annual reporting requirements; third party disclosure.

Total Annual Burden: 150 hours.

Total Annual Cost: \$375,000.

Privacy Impact Assessment: No impact(s).

Needs and Uses: The FCC has standards for accounting authorities in the maritime mobile and maritime-satellite radio services under 47 CFR Part 3. The Commission uses these standards to determine the eligibility of applicants for certification as a U.S. accounting authority, to ensure compliance with the maritime mobile and maritime-satellite radio services, and to identify accounting authorities to the International Telecommunications Union (ITU). Respondents are entities seeking certification or those already certified to be accounting authorities.

Federal Communications Commission.

Marlene H. Dortch,

Secretary.

[FR Doc. 06-1527 Filed 2-21-06; 8:45 am]

BILLING CODE 6712-01-P

FEDERAL COMMUNICATIONS COMMISSION

Notice of Public Information Collection(s) Being Submitted to OMB for Review and Approval

February 9, 2006.

SUMMARY: The Federal Communications Commission, as part of its continuing effort to reduce paperwork burden invites the general public and other Federal agencies to take this opportunity to comment on the following information collection, as required by the Paperwork Reduction Act of 1995, Public Law 104-13. An agency may not conduct or sponsor a collection of information unless it displays a currently valid control number. No person shall be subject to any penalty for failing to comply with a collection of information subject to the Paperwork Reduction Act (PRA) that does not display a valid control number. Comments are requested concerning (a) whether the proposed collection of information is necessary for the proper performance of the functions of the Commission, including whether the information shall have practical utility; (b) the accuracy of the Commission's burden estimate; (c) ways to enhance the quality, utility, and clarity of the information collected; and (d) ways to minimize the burden of the collection of information on the respondents,

ENVIRONMENTAL PROTECTION AGENCY**[EPA-HQ-OPP-2006-0005; FRL-7757-5]****Pennsylvania and Virginia State Plans for Certification of Applicators of Restricted Use Pesticides; Notice of Approval****AGENCY:** Environmental Protection Agency (EPA).**ACTION:** Notice.

SUMMARY: In the *Federal Register* of October 28, 2005, EPA issued a notice of intent to approve amended Pennsylvania and Virginia Plans for the certification of applicators of restricted use pesticides. In this notice EPA solicited comments from the public on the proposed action to approve the amended Pennsylvania and Virginia Plans. The amended Certification Plans Pennsylvania and Virginia submitted to EPA contained several statutory, regulatory, and programmatic changes to their current Certification Plans. The proposed amendments establish new commercial categories for vertebrate pest control. One public comment was received that had no specific information relevant to the issues presented; therefore, no changes were made based on this comment. EPA hereby approves the amended Pennsylvania and Virginia Plans.

ADDRESSES: The amended Pennsylvania and Virginia Certification Plans can be reviewed at the locations listed under Unit I.B. of the **SUPPLEMENTARY INFORMATION**.

FOR FURTHER INFORMATION CONTACT: Fabiola Estrada, USEPA Region III, Pesticide/Asbestos Programs and Enforcement Branch (3WC32), 1650 Arch St., Philadelphia, PA 19103-2029; telephone number: (215) 814-2171; e-mail address: estrada.fabiola@epa.gov.

SUPPLEMENTARY INFORMATION:**I. General Information****A. Does this Action Apply to Me?**

This action is directed to the public in general. This action may, however, be of interest to those involved in agriculture and anyone involved with the distribution and application of pesticides for agricultural purposes. Others involved with pesticides in a non-agricultural setting may also be affected. In addition, it may be of interest to others, such as, those persons who are or may be required to conduct testing of chemical substances under the Federal Food, Drug, and Cosmetic Act (FFDCA), or the Federal Insecticide, Fungicide, and Rodenticide Act

(FIFRA). Since other entities may also be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Copies of this Document and Other Related Information?

1. *Docket.* EPA has established an official public docket for this action under docket identification (ID) number EPA-HQ-OPP-2005-0247. Publicly available docket materials are available either electronically in www.regulations.gov or in hard copy at the Public Information and Records Integrity Branch (PIRIB) (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. The docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number for the docket facility is (703) 305-5805.

2. *Electronic access.* You may access this *Federal Register* document electronically through the EPA Internet under the "*Federal Register*" listings at <http://www.epa.gov/fedrgstr/>.

In addition to the sources listed in this unit, you may obtain copies of the amended Pennsylvania and Virginia Certification Plans, other related documents, or additional information by contacting:

1. Fabiola Estrada at the address listed under **FOR FURTHER INFORMATION CONTACT**.

2. David Scott, Bureau of Plant Industry, Pennsylvania Department of Agriculture, 2301 North Cameron St., Harrisburg, PA 17110-9408; telephone number: (717) 772-5214; e-mail: dascott@state.pa.us.

3. Kathy Dictor, Virginia Department of Agriculture & Consumer Services, Office of Pesticide Services, 2221 Carbon Hill Drive, Midlothian, VA 23113; telephone number: (804) 786-0685; e-mail: kdicator@vdacs.state.va.us.

4. Michelle DeVaux, Field and External Affairs Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 308-5891; e-mail address: devaux.michelle@epa.gov.

II. What Action is the Agency Taking?

EPA is approving the amended Pennsylvania and Virginia Certification Plans. This approval is based upon the

EPA review of the Pennsylvania and Virginia Plans and finding them in compliance with FIFRA and 40 CFR part 171. Further, one public comment that had no specific information relevant to the issues presented was submitted to the *Federal Register* notice of October 28, 2005 (70 FR 62109) (FRL-7735-2), soliciting comments. No changes were made based on the comment received; therefore, the amended Pennsylvania and Virginia Certification Plans are approved.

List of Subjects

Environmental protection, Education, Pests and pesticides.

Dated: March 30, 2006.

William Early,

Acting Regional Administrator, Region III.

[FR Doc. E6-5326 Filed 4-10-06; 8:45 am]

BILLING CODE 6560-50-S

ENVIRONMENTAL PROTECTION AGENCY**[EPA-HQ-OPP-2006-0084; FRL-7772-3]****Notice of Receipt of Requests to Voluntarily Cancel Certain Pesticide Registrations; Technical Correction****AGENCY:** Environmental Protection Agency (EPA).**ACTION:** Notice.

SUMMARY: In accordance with section 6(f)(1) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, EPA issued a notice of receipt of request by registrants to voluntarily cancel certain pesticide registrations in the *Federal Register* of February 22, 2006. The notice announced that 90 pesticide registrations would be canceled unless a cancellation request was withdrawn by August 21, 2006. The 90 registrations were listed in Table 1. This notice corrects information in Table 1 for one of the registrations. EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) was erroneously included in the February 22, 2006 Notice, therefore with this technical correction EPA is removing EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) from Table 1 of the February 22, 2006 *Federal Register* Notice. A request to voluntarily cancel EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) was previously published in the *Federal Register* of October 28, 2005. The terms of the October 28, 2005 Notice take precedent over the erroneous inclusion of this registration

in the February 22, 2006 **Federal Register** Notice.

DATES: Unless the request to cancel EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) is withdrawn by April 26, 2006 an order will be issued canceling this registration. The Agency will consider withdrawal requests postmarked no later than April 26, 2006.

FOR FURTHER INFORMATION CONTACT: John Jamula, Information Technology and Resources Management Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 305-6426; e-mail address: jamula.john@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general. Although this action may be of particular interest to persons who produce or use pesticides, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the information in this notice, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Copies of this Document and Other Related Information?

1. **Docket.** EPA has established a docket for this action under Docket identification number (ID) [EPA-HQ-OPP-2006-0084; FRL-7772-3]. Publicly available docket materials are available either electronically at <http://www.regulations.gov> or in hard copy at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. This Docket Facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket telephone number is (703) 305-5805.

2. **Electronic access.** You may access this **Federal Register** document electronically through the EPA Internet under the "Federal Register" listings at <http://www.epa.gov/fedrgstr/>.

II. What Action is the Agency Taking?

In accordance with section 6(f)(1) of FIFRA, as amended, EPA issued a notice of receipt of request by registrants to voluntarily cancel certain pesticide registrations (71 FR 9118, February 22, 2006) (FRL-7762-4). The notice announced that 90 pesticide registrations would be canceled unless a cancellation request was withdrawn by

August 21, 2006. The 90 registrations were listed in Table 1. EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) was erroneously included in the February 22, 2006 Notice. In this technical correction, EPA is removing the entry for EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) from table 1 of the February 22, 2006 Notice (71 FR 9119). A request to voluntarily cancel EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) was previously published in the **Federal Register** of October 28, 2005 (70 FR 62112) (FRL-7743-6) and the terms of the October 28, 2005 Notice are applicable to EPA Registration Number 000100-01074 (Cyclone Concentrate Herbicide) and take precedent over the erroneous inclusion of this registration in the February 22, 2006 **Federal Register** Notice and the terms of that Notice.

In FR Doc. E6-2492, in the issued of February 22, 2006, page 9119, in Table 1, the entry for Registration No. 000100-01074, product name: Cyclone Concentrate Herbicide, and chemical name: Paraquat dichloride, is removed in its entirety.

List of Subjects

Environmental protection, Pesticides and pests.

Dated: March 28, 2006.

Robert Forrest,
Acting Director, Information Technology and Resources Management Division, Office of Pesticide Programs.

[FR Doc. E6-5112 Filed 4-10-06; 8:45 am]

BILLING CODE 6560-50-S

ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-OW-2004-0014; FRL-8056-3]

Guidelines Establishing Test Procedures for the Analysis of Pollutants Under the Clean Water Act; Notice of Data Availability

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of Data Availability.

SUMMARY: On August 16, 2005, EPA proposed to approve a number of new analytical methods for measuring *E. coli* and other microbiological pollutants in wastewater and sewage sludge. Today's notice announces the availability of new data supporting approval of an additional *E. coli* method. EPA is soliciting comment only on the data and method described in today's notice.

DATES: Comments must be received on or before May 11, 2006.

ADDRESSES: Submit your comments, identified by Docket ID No. EPA-HQ-2004-0014, by one of the following methods:

- <http://www.regulations.gov>: Follow the on-line instructions for submitting comments.

- E-mail: OW-

docket@epamail.epa.gov Attention Docket ID No. OW-2004-0014

- Mail: Water Docket, Environmental Protection Agency, Mailcode: 4101T, 1200 Pennsylvania Ave., NW., Washington, DC 20460.

- Hand Delivery: EPA Water Center, EPA West Building, Room B102, 1301 Constitution Avenue NW., Washington, DC, Attention Docket ID No. OW-2004-0014. Such deliveries are only accepted during the Docket's normal hours of operation, and special arrangements should be made for deliveries of boxed information.

Instructions: Direct your comments to Docket ID No. EPA-HQ-OW-2004-0014. EPA's policy is that all comments received will be included in the public docket without change and may be made available online at <http://www.regulations.gov>, including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through <http://www.regulations.gov> or e-mail. The <http://www.regulations.gov> Web site is an "anonymous access" system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through <http://www.regulations.gov> your e-mail address will be automatically captured and included as part of the comment that is placed in the public docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD-ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses. For additional information about EPA's public docket visit the EPA Docket Center homepage at <http://www.epa.gov/epahome/dockets.htm>.
Docket: All documents in the docket are listed in the www.regulations.gov



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
ARIEL RIOS BUILDING - 1200 PENNSYLVANIA AVENUE, N.W.
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OCT - 4 2006

Syngenta Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419

Dear Sir or Madam:

SUBJECT: Rescission of Cancellation Order Issued August 22, 2006

This letter rescinds the August 22, 2006 cancellation order and advises you that under Section 6(f)(1) of the Federal Insecticide, Fungicide and Rodenticide Act, as amended, EPA hereby restores to full active status the registration listed below.


<u>REG-NR</u>	<u>PRODUCT NAME</u>
100-1074	Cyclone Concentrate Herbicide

The August 22 cancellation order was issued in error. The August letter states that "EPA hereby cancels the registrations listed on the enclosure per your request for voluntary cancellation as listed in the Federal Register Notice dated February 22, 2006." As you may know, the Agency issued a notice on April 11, 2006, entitled Notice of Receipt of Requests to Voluntarily Cancel Certain Pesticide Registrations; Technical Correction. 71 Fed. Reg. 18328 (April 11, 2006). That notice removed EPA Registration Number 100-1074 from the list contained in the February 22 Federal Register Notice. The April notice clarified that the request to voluntarily cancel EPA Reg. No. 100-1074 was covered by the October 28, 2005 Federal Register Notice instead. Therefore, the issuance of the cancellation order based on the request contained in the February notice was in error.

OCT 09 2006

Your request for voluntary cancellation of your product with EPA Reg. No. 100-1074 continues to be covered by the October 28 Notice, and the Agency has not yet acted on that request. Please contact the Agency to let us know if you would like us to process that request. We regret any inconvenience that this error may have caused.

Sincerely,

POV 
Arnold E. Layne, Director
Information Technology and Resource Management Division



U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

EPA Reg.
Number:
82557-1

Date of Issuance:
OCT 4 2006

Date of Expiration:
09/01/2008

Term of Issuance: Unconditional

Name of Pesticide Product:
Paraquat SL Herbicide

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Sinon USA Inc.
1080 Carol Lane, Suite 264
Lafayette, CA 94549

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This Registration Notice replaces the original Registration Notice dated January 25, 2006.

This product is conditionally registered in accordance with FIFRA section 3(c)(5) provided that:

1. You submit the outstanding data requirements 830.6317 Storage Stability and 830.6320 Corrosion Characteristics by January 25, 2007.

Signature of Approving Official:

Dan Kenny, Branch Chief
Herbicide Branch, Registration Division (7505P)

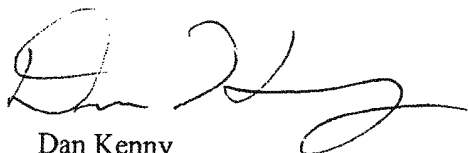
Date:

OCT 4 2006

2. This registration will expire, without hearing rights, on September 1, 2008, unless the registrant submits an amendment to remove the time limitation no earlier than six months before the expiration date.
3. Upon receipt of the amendment, the Agency will review all available information and will re-evaluate whether the registrant's product still differs only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment.
4. The Agency will issue its decision on the amendment request taking into account the determination described in paragraph 3 no later than the expiration date of the registration.
5. If the Agency fails to make the determination described in paragraph 3 by the expiration date, the registration will remain in effect until the Agency makes such a determination as described in paragraph 6.
6. If the Agency determines that the registration no longer meets the standard for registration as described in paragraph 3, the Agency will notify the registrant of this decision to deny the amendment. The Agency will initiate a Notice of Intent to Cancel the registration pursuant to section 6(e) of FIFRA.
7. If the Agency determines that the registration continues to meet the standard for registration, the amendment request will be granted and the time limitation will be removed or conditioned upon other terms that are necessary in light of the new information.

The basic formulation CSF [dated September 5, 2006] of the product referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act is acceptable. The basic CSF will be added to your file.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). If you have any questions, please contact Hope Johnson at 703-305-5410.

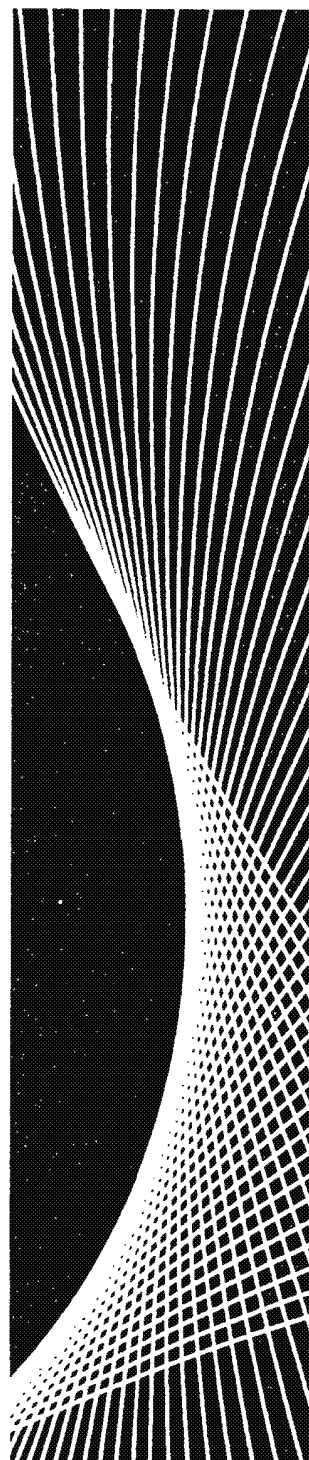


Dan Kenny
Branch Chief
Herbicide Branch
Registration Division (7505P)

Restricted Use Pesticide. Due to acute toxicity. For retail sale to and use only by certified applicators or persons under their direct supervision and only for those uses covered by the certified applicator's certification.

Firestorm™

Defoliant and desiccant herbicide for the control of weeds and grasses and as a harvest aid.



- NEVER PUT INTO FOOD, DRINK OR OTHER CONTAINERS.
- IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID.
- SYMPTOMS ARE PROLONGED AND PAINFUL.
- DO NOT USE OR STORE IN OR AROUND THE HOME.
- DO NOT REMOVE CONTENTS EXCEPT FOR IMMEDIATE USE.
- THE ODOR OF THIS PRODUCT IS FROM THE STENCHING AGENT WHICH HAS BEEN ADDED, NOT FROM PARAQUAT.

**Net
Contents:**

Active Ingredient:

paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride) 43.8%

Other Ingredients: 56.2%

Total: 100.0%

Contains 3.0 pounds paraquat cation per gallon as 4.143 pounds salt per gallon. Contains stench (odor) and emetic.

KEEP OUT OF REACH OF CHILDREN

DANGER/PELIGRO  **POISON**

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

EPA Reg. No. 82557-1-400

EPA Est. No.

001/012506

Product of Taiwan

Manufactured for:

Chemtura USA Corporation

Middlebury, Connecticut 06749

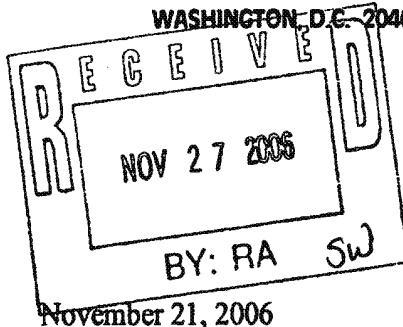


www.chemtura.com

Copy to Monty Dixon ✓



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
ARIEL RIOS BUILDING - 1200 PENNSYLVANIA AVENUE, N.W.
WASHINGTON, D.C. 20460



OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Dear Sir or Madam:

This letter is a final cancellation order, advising you that under Section 6(f)(1) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, EPA hereby cancels the registrations listed on the enclosure per your request for voluntary cancellation as listed in the Federal Register Notice dated October 28, 2005. The effective date of this cancellation order is the date of this letter.

As the basic registrant of the listed product(s) you may legally distribute or sell existing stocks of the canceled products until the disposition date listed on the enclosure. Existing stocks are defined as those stocks of a registered pesticide product which are currently in the United States and which have been packaged, labeled, and released for shipment prior to the effective date of the cancellation order.

It would be a violation of FIFRA for your or any supplementally registered distributor of your product(s) to distribute or sell any stocks currently in the United States which have been produced, packaged, labeled or released for shipment after the effective date of cancellation, or any existing stocks after the indicated disposition date. The Agency also expressly reserves the right to amend the existing stocks provisions of this Order if events should so warrant.

It is your responsibility as the basic registrant to notify any and all supplementally registered distributors of your product(s) that this cancellation order also applies to their supplementally registered products. You may be held liable for violations committed by your distributors.

Unless the provisions of an earlier order apply, existing stocks already in the hands of dealers or users can be distributed, sold or used legally until they are exhausted, provided that such sale and use comply with the EPA-approved label and labeling of the affected product(s).

Sincerely,

Arnold E. Layne, Director

Information Technology and Resource Management Division

NOV 27 2006

T

VOLUNTARY CANCELLATION ORDER (ENCLOSURE)

EPA CO NR: 000100

SYNGENTA CROP PROTECTION

P.O. BOX 18300

GREENSBORO, NC 27419

EPA PRODUCT
REGISTRATION

DISP
DATE

PRODUCT NAME

000100-01074

11/21/2006

CYCLONE CONCENTRATE HERBICIDE

66222-130

12/05/2006

128



U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

EPA Reg.
Number
66222-130

Date of Issuance
DEC - 5 2006

Date of Expiration
09/01/2008

Term of Issuance: Conditional

Name of Pesticide Product
Parazone 3SL

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Makhteshim Agan of North America, Inc.
4515 Falls of Neuse Road, Suite 300
Raleigh, NC 27609

Notar: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A) provided that:

1. You submit the outstanding data requirements 830.6317 Storage Stability and 830.6320 Corrosion Characteristics within one year from the date of this letter.
2. Revise the EPA Registration Number from 66222-RGN to 66222-130 on the label.
3. Add an appropriate EPA Establishment Number to the label.

Signature of Approving Official:

Date

James Tompkins, Product Manager (25)
Herbicide Branch, Registration Division (7505P)

12-5-06

EPA Form 8570-5

4. Remove the repeated "If Inhaled" section at the end of the FIRST AID section.
5. Remove "Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove contaminated clothing and wash clothing before reuse." from the section PRECAUTIONARY STATEMENTS.
6. On page 7, in the subsection "Spray Carrier," change "maximum" to "maximize" in the first sentence.
7. On page 8, in the section "Tank Mixing For Improved Burndown of Difficult Weeds and Residual Control," revise the statement "For best results, making a second application is recommended" to "For best results, make a second application."
8. On page 12, in the section CACAO, add the statement "Do not spray under windy conditions" in the Comments column.
9. On page 16, in the section FIELD CORN, POPCORN, SWEET CORN, SEED CORN, add "Post-emergence directed spray" under the heading.
10. On page 16, in the section FIELD CORN ONLY (grain, fodder, forage), remove the restriction "Do not apply within 7 days of harvest."
11. On page 17, in the section COTTON Harvest Aid, in the row "5.4 fl oz + 1 pt phosphate or 1 gal. chlorate (southern cotton), add "by broadcast application" after "Apply specified dosages"
12. On page 19, in the section GRASSES, revise "Repeat applications as necessary prior to grass emergence, but not exceed three applications per year" to "Repeat applications as necessary prior to grass emergence, but do not exceed three applications per year"
13. Revise the WARRANTY STATEMENT as follows:
 - a. Revise "To the extent allowed by law" to "To the extent consistent with applicable law"
 - b. Add "To the extent consistent with applicable law" before the statements:
 - i. "The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at Celsius' election, the replacement of product.
 - ii. "All such risks shall be assumed by the Buyer"
14. This registration will expire, without hearing rights, on September 1, 2008, unless the registrant submits an amendment to remove the time limitation no earlier than six months before the expiration date.
15. Upon receipt of the amendment, the Agency will review all available information and will re-evaluate whether the registrant's product still differs only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment.
16. The Agency will issue its decision on the amendment request taking into account the determination described in paragraph 15 no later than the expiration date of the registration.
17. If the Agency fails to make the determination described in paragraph 15 by the expiration date, the registration will remain in effect until the Agency makes such a determination as described in paragraph 18.
18. If the Agency determines that the registration no longer meets the standard for registration as described in paragraph 15, the Agency will notify the registrant of this decision to deny the amendment. The Agency will initiate a Notice of Intent to Cancel the registration pursuant to section 6(c) of FIFRA.

3/28

19. If the Agency determines that the registration continues to meet the standard for registration, the amendment request will be granted and the time limitation will be removed or conditioned upon other terms that are necessary in light of the new information.

NOTE: The statement "In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency" in the WARRANTY STATEMENT section is conditionally accepted exclusively due to the terms and conditions listed above in items 14-19. If at a later date, the Agency amends the terms of issuance of this registration to unconditional, the statement "In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency" must be removed or revised.

The basic formulation CSF [dated 9-20-06] of the product referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act are acceptable. The basic CSF will be added to your file.

You will submit one (1) copy of your final printed labeling before you release the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(c). A stamped copy of labeling is enclosed for your records. If you have any questions, please contact Hope Johnson at 703-305-5410.

James Tompkins
Product Manager (25)
Herbicide Branch
Registration Division (7505P)

RESTRICTED USE PESTICIDE

DUE TO ACUTE TOXICITY

FOR RETAIL SALE TO AND USE ONLY BY CERTIFIED APPLICATORS OR PERSONS UNDER THEIR DIRECT SUPERVISION AND ONLY FOR THOSE USERS COVERED BY THE CERTIFIED APPLICATOR'S CERTIFICATION.

Parazone™ 3SL

Herbicide

A Weed, Grass, and Harvest Aid Desiccant/Defoliant Herbicide

ACTIVE INGREDIENT:

Paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride)

43.8%

OTHER INGREDIENTS:

56.2%

Total 100.0%

Contains 3.0 pounds paraquat cation per gallon as 4.14 pounds salt per gallon.

Contains stench (odor) and emetic.

EPA Reg. No. 66222-RGN
EPA Est. No.

Mekhteshim Agan of North America, Inc.
4515 Falls of Neuse Road, Suite 300
Raleigh NC 27609

Net Contents: 2.5 gallons

KEEP OUT OF REACH OF CHILDREN**DANGER/ (Skull and Crossbones)
PELIGRO**

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

- NEVER PUT INTO FOOD, DRINK, OR OTHER CONTAINERS
- IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID. SYMPTOMS ARE PROLONGED AND PAINFUL.
- DO NOT USE OR STORE IN OR AROUND THE HOME.
- DO NOT REMOVE CONTENTS EXCEPT FOR IMMEDIATE USE.
- THE ODOR OF THIS PRODUCT IS FROM THE STENCHING AGENT WHICH HAS BEEN ADDED, NOT FROM PARAQUAT.

FIRST AID

Contains Paraquat, a Bipyridylum Herbicide

IF SWALLOWED:	<ul style="list-style-type: none">• SPEED IS ESSENTIAL. Immediate medical attention is required. If available, give an adsorbent such as activated charcoal, bentonite, or Fuller's Earth.• Call a poison control center or doctor immediately for treatment advice• Do not give anything by mouth to an unconscious person• Have person sip glass of water if able to swallow.• Do not induce vomiting unless told to by a poison control center or doctor.
IF INHALED:	<ul style="list-style-type: none">• Move person to fresh air.• The odor of this product is from the stenching agent, which has been added, not from the paraquat.• If person is not breathing, call 911 or an ambulance.• Call a poison control center or doctor for further treatment advice.
IF IN EYES:	<ul style="list-style-type: none">• Hold eye open and rinse slowly and gently with water for 15-20 minutes.• Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.• Call a poison control center or doctor for treatment advice
IF ON SKIN OR CLOTHING:	<ul style="list-style-type: none">• Take off contaminated clothing.• Rinse skin immediately with plenty of water for 15-20 minutes• Call a poison control center or doctor for further treatment advice

page 2

Does not appear on
EPA PPLS side as of
Jan 18, 2008.



U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

EPA Reg.
Number:
63558-5
93598

Date of Issuance:
DEC - 5 - 2006

Term of Issuance: Conditional

Name of Pesticide Product:
Paraquat Dichloride Technical

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Celsius Property BV (Neuhassch A RHP Branch)
c/o

Mecklenburg Agan of North America, Inc.
4515 Falls of Neuse Road, Suite 300
Raleigh, NC 27609

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, in his discretion, may at any time suspend or cancel the registration of a pesticide in accordance with the law. The acceptance of any needs in connection with the registration of a product under this Act shall not be construed as giving the registrant a right in exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A) provided you agree in writing to:

1. Submit the outstanding data requirements 830.6317 Storage Stability and 830.6320 Corrosion Characteristics within one year from the date of this letter.
2. Revise the EPA Registration Number from 83558-1 to 83558-5 on the label.
3. Add an appropriate EPA Establishment Number to the label.

Signature of Approving Official:

Date:

12-5-06

James Tompkins, Product Manager (25)
Registration Division (7505P)

Paraquat Litigation

- Revise the following statements of the label:
- Revise "To the extent allowed by law" to "To the extent consistent with applicable law"
 - Add "To the extent consistent with applicable law" before the statements:
 - "The exclusive remedy for any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, or negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at claimant's election, the replacement of product."
 - "All such costs shall be assumed by the Buyer."
 - Revise "Except as expressly provided herein" to "Except as warranted by this label"
 - Remove the statement "In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any trial, lawsuit, or as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency."

The basic formulation CSF, listed in 16 CFR of the product referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act is accurate. The basic CSF will be added to your file.

You will submit one (1) copy of your final printed labeling before you release the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). A stamped copy of labeling is enclosed for your records. If you have any questions, please contact Hope Johnson at 703-305-5410.

James Beardsley
Product Manager (25)
Herbicide Branch
Registration Division (7503P)

82542-3

10/11/2007

1148



U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:

☒ Registration
☐ Reregistration

(under FIFRA, as amended)

EPA Reg.

Number:

82542-3

Date of Issuance:

OCT 11 2007

Date of Expiration:

09/01/2008

Term of Issuance: Conditional

Name of Pesticide Product:

Paraquat Concentrate

Name and Address of Registrant (include ZIP Code):

Source Dynamics, LLC
10039 E. Troon North Drive
Scottsdale, AZ 85262

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. All any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A) provided that:

1. You submit the outstanding data requirements 830.6317 Storage Stability and 830.6320 Corrosion Characteristics within one year from the data of this letter.
2. Revise the EPA Registration Number from 82542-x to 82542-3 on the label.
3. Add an appropriate EPA Establishment Number to the label.

Signature of Approving Official:

James Tompkins, Product Manager (25)
Herbicide Branch, Registration Division (7505P)

Date:

OCT 11 2007

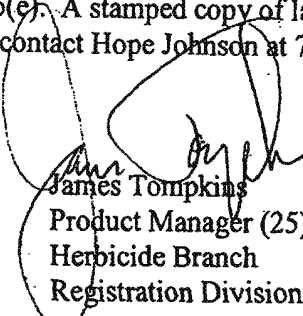
EPA Form 8570-6

4. The word POISON must appear in red on a contrasting background.. A Skull & Crossbones symbol must appear in close proximity to the word POISON.
5. Place the words "Manufactured for" before Source Dynamics, LLC; 10039 E. Troon North Drive; Scottsdale, AZ 85262
6. The "Net Contents" section on the first page must list the various container sizes you will market.
7. Add the following statement directly following the INGREDIENT STATEMENT: "This product contains the toxic ingredient methanol at 7%"
8. Revise the statement "Contains emetic" to "Contains emetic and stench (odor)" on page 1
9. Revise the PRECAUTIONARY STATEMENTS to the following: "May be fatal if swallowed. Fatal if inhaled. Corrosive. Causes irreversible eye damage. Wear protective eyewear. Do not breathe spray mist. Wear a dust mist respirator. Do not get in eyes or on clothing. Harmful if absorbed through skin. Avoid contact with skin. Prolonged or frequently repeated contact may cause allergic reactions in some individuals."
10. In the PPE section, replace "Dust mist NIOSH-approved respirator with any N, R, P, or HE filter" with "NIOSH approved particulate filtering respirator equipped with N, R, or P class filter media. The respirator should have a NIOSH approval number prefix TC-84A. It is recommended that you require that respirator wearer be fit tested, and trained in the use, maintenance, and limitations of the respirator" in the subsections "Applicators and other handlers (other than mixer mixers and loaders) must wear" and "Mixers and Loaders must wear"
11. On page 3, Move the statements "Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them. Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep separately from other laundry" from its current location to its own separate box.
12. On page 5 in the Spray Drift Information Section add the statement "Where states have more stringent regulations, they must be observed."
13. On page 8, remove the word "recommended" from the sections "Rates of Paraquat Concentrate" and "Spray Volume"
14. On page 7 in the section "Use of a Nonionic Surfactant or Crop Oil Concentrate"-subsection "Nonionic Surfactant" change "nonionic surfactant" to "nonionic surfactant cleared for the current use" Make the same change under "Crop Oil Concentrate"
15. On page 13, revise "ncluding" to "including" in the section Alfalfa-Dormant Season-Weeds.
16. On page 14, revise "high" to "higher" in the statement "If ryegrass, sheperdspurse, sowthistle, or groundsel are present, use high rate."
17. On page 17, in the section DRY PEAS and DRY BEANS, separate each commodity listed so that each commodity is on a separate line.
18. On page 19, in the section CHEMICAL FALLOW-Wheat-Annual Crop-Wheat Rotations (Spring applied prior to planting an annual crop), revise "recommendations" to "directions"
19. On page 20, revise "high" to "higher" in the statement "If ryegrass, sheperdspurse, sowthistle, or groundsel are present, use high rate."
20. On page 26, in the section COTTON-Desiccation of Regrowth, revise "recommended" to "listed" in the statement "Because regrowth is difficult to control, thorough coverage with the full recommended rate is necessary."
21. On page 28, separate "60" and "200 (CA only)" on different lines so that the grazing or preharvest interval days are clear.
22. On page 33, remove the word "recommended" from the section SOYBEANS

23. On page 37, in the section TREES AND VINES, separate each commodity listed so that each commodity is on a separate line.
24. On page 40, separate the additional precautions, restrictions and directions for the sections VEGETABLES-Tomatoes and VEGETABLES-(CA,WA,OR,ID only)-Lettuce, Melon, Sugar beets, Tomatoes, as currently they are all listed together and indistinguishable from each other. (i.e create a thick black line after the statement "To minimize drift, do not use nozzles or nozzle configurations which product fine spray droplets (mist), as that is the last statement in the section VEGETABLES-Tomatoes.
25. On page 44 under "Container Disposal" remove "?" Change "Minibulk containers: Return empty containers for reconditioning" to "Mini-Bulk Containers - Reseal container and offer for reconditioning, or triple rinse (or equivalent) and offer for recycling or reconditioning, or clean in accordance with manufacturer's instructions."
26. Add the following statements in the STORAGE AND DISPOSAL section, at the end of the Container Disposal subsection: Mini-Bulk Refillable Containers: "Before refilling, inspect thoroughly for damage, such as cracks, punctures, bulges, dents, abrasions and damaged or worn threads on closure devices. After filling and before transporting, check for leaks. Do not refill or transport damaged or leaking container."
27. This registration will expire, without hearing rights, on September 1, 2008, unless the registrant submits an amendment to remove the time limitation no earlier than six months before the expiration date.
28. Upon receipt of the amendment, the Agency will review all available information and will re-evaluate whether the registrant's product still differs only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment.
29. The Agency will issue its decision on the amendment request taking into account the determination described in paragraph 28 no later than the expiration date of the registration.
30. If the Agency fails to make the determination described in paragraph 28 by the expiration date, the registration will remain in effect until the Agency makes such a determination as described in paragraph 31.
31. If the Agency determines that the registration no longer meets the standard for registration as described in paragraph 28, the Agency will notify the registrant of this decision to deny the amendment. The Agency will initiate a Notice of Intent to Cancel the registration pursuant to section 6(e) of FIFRA.
32. If the Agency determines that the registration continues to meet the standard for registration, the amendment request will be granted and the time limitation will be removed or conditioned upon other terms that are necessary in light of the new information.

The basic formulation CSF [dated 9-10-07] of the product referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act are acceptable. The basic CSF will be added to your file.

You will submit one (1) copy of your final printed labeling before you release the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). A stamped copy of labeling is enclosed for your records. If you have any questions, please contact Hope Johnson at 703-305-5410.


James Tompkins
Product Manager (25)
Herbicide Branch
Registration Division (7505P)

SD label 2/4/07

4/48

Restricted Use Pesticide due to acute toxicity. For retail sale to and use only by certified applicators or persons under their direct supervision and only for those uses covered by the certified applicator's certification.

PARAQUAT CONCENTRATE

Defoliant and desiccant herbicide for the control of weeds and grasses and as a harvest aid.

NEVER PUT INTO FOOD, DRINK OR OTHER CONTAINERS.
IF SWALLOWED, TAKE IMMEDIATE ACTION AS PRESCRIBED IN FIRST AID.
SYMPTOMS ARE PROLONGED AND PAINFUL.
DO NOT USE OR STORE IN OR AROUND THE HOME.
DO NOT REMOVE CONTENTS EXCEPT FOR IMMEDIATE USE.
THE ODOR OF THIS PRODUCT IS FROM THE STENCHING AGENT WHICH HAS BEEN ADDED, NOT FROM PARAQUAT.

NET CONTENTS: _____

Active Ingredient:

paraquat dichloride (1,1'-dimethyl-4,4'-bipyridinium dichloride)	43.2%
Other Ingredients:	56.8%
Total:	100.0%

Contains 3.0 pounds paraquat cation per gallon as 4.14 pounds of dichloride salt per gallon. Contains emetic.

KEEP OUT OF REACH OF CHILDREN

DANGER/PELIGRO



POISON

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

EPA Reg. No. 82542-x
EPA Est. No.
Product of Taiwan

Source Dynamics, LLC
10039 E. Troon North Drive
Scottsdale, AZ 85262

ACCEPTED
with COMMENTS
in EPA Letter Dated

OCT 11 2007

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

82542-3

MRID	CITATION	SBMTR 1	SBMTR NAME 1	SUBJECT 1
45419900	Interregional Research Project No. 4 (2001) Submission of Residue Data in Support of the Petition for	959857	INTERREGIONAL RESEARCH	Residues in Food or Feed Commodities
45419901	Arsenovic, M. (2001) Paraquat: Magnitude of the Residue on Onion (Dry Bulb): Lab Project Number: 0	959857	INTERREGIONAL RESEARCH	Residues in Food or Feed - Residue/Recovery Data by Commodity
45439900	Interregional Research Project No. 4 (2001) Submission of Residue Data in Support of the Petition for	959857	INTERREGIONAL RESEARCH	Residues in Food or Feed Commodities
45439901	Arsenovic, M. (2001) Paraquat: Magnitude of the Residue on Okra: Lab Project Number: A1913: A1913	959857	INTERREGIONAL RESEARCH	Residues in Food or Feed - Residue/Recovery Data by Commodity
45493700	Griffin L.L.C. (2001) Submission of Product Chemistry Data in Support of the FIFRA 6(a)(2) Data Require	1812	GRIFFIN L.L.C.	Product/Manufacturing Chemistry & Analysis
45493701	Collier, R. (2001) FIFRA 6(a)(2) Report for Griffin Boa Concentrate, EPA Reg. No. 1812-424 and Griffin Boa	1812	GRIFFIN L.L.C.	Product Mfg - Formation of Unintentional Ingrid/Impurities
45526600	Griffin LLC (2001) Submission of Product Chemistry Data in Support of the Amended Registration of B	1812	GRIFFIN L.L.C.	Product/Manufacturing Chemistry & Analysis
45526601	Dowler, C. (2000) Griffin BOA Herbicide: Comparison of Emetic Content with Gramoxone Extra. Unpublished	1812	GRIFFIN L.L.C.	Product Mfg - Analytical Methods to Verify Limits
45565300	Griffin LLC (2001) Submission of Product Chemistry Data in Support of FIFRA 6(a)(2) Data Requirements fo	1812	GRIFFIN L.L.C.	Product/Manufacturing Chemistry & Analysis
45565301	Collier, R. (2001) FIFRA 6(a)(2) Report for Griffin Boa Concentrate and Griffin Boa Herbicide: (Produ	1812	GRIFFIN L.L.C.	Product Mfg - Formation of Unintentional Ingrid/Impurities
45648700	Griffin LLC (2002) Submission of Product Chemistry Data in Support of the Amended Registration of B	1812	GRIFFIN L.L.C.	Product/Manufacturing Chemistry & Analysis
45648701	Dowler, C. (2002) Griffin Analytical Method TM-1252: Emetic Content in BOA Formulated Product by G	1812	GRIFFIN L.L.C.	Product Mfg - Analytical Methods to Verify Limits
45658900	US EPA (2002) Submission of Published Documents from the Health Effects Division. Transmittal of 50 studi	989978	U.S. Environmental Protection Ag	Product/Manufacturing Chemistry & Analysis
45658942	Staiff, D.; Butler, L.; Davis, J. (1981) A Field Study of the Chemical Degradation of Paraquat Dichloride F	989978	U.S. Environmental Protection Ag	Fate in Soil - Transformation in/on Soil
46098800	Sinon Corporation (2003) Submission of Product Chemistry and Toxicity Data in Support of the Application for	70552	SINON CORP	Product/Manufacturing Chemistry & Analysis
46098801	Hauswirth, J. (2003) Paraquat Technical: Product Identity, Composition, and Analysis (Group A). Project Num	70552	SINON CORP	Product Mfg - Beginning Materials & Mfg Process
46098802	Hauswirth, J. (2003) Paraquat Technical: Physical and Chemical Properties (Group B). Project Number: SINON	70552	SINON CORP	Physical/Chemical - Color
46098803	Hutchinson, A. (2002) Paraquat Technical: Acute Dermal Toxicity (Limit) Test in Rats. Project Number: 50119	70552	SINON CORP	Acute Exposure - Dermal
46098804	Anderson, B. (2003) Paraquat Technical: Acute Inhalation Toxicity in Rats. Project Number: 661855. Unpubl	70552	SINON CORP	Acute Exposure - Respiratory/Inhalation
46098805	Hutchinson, A. (2002) Paraquat Technical: Acute Eye Irritation Test in Rabbits. Project Number: 501218. Un	70552	SINON CORP	Acute Exposure - Primary Eye Irritation
46098806	Hutchinson, A. (2002) Paraquat Technical: Acute Dermal Irritation Test in Rabbits. Project Number: 501202.	70552	SINON CORP	Acute Exposure - Primary Dermal Irritation
46098807	Hutchinson, A. (2002) Paraquat Technical: Buehler Test in Guinea Pigs for Delayed Skin Sensitization Potent	70552	SINON CORP	Subacute or Subchronic Exposure - Dermal Sensitization
46331200	Sinon Corporation (2004) Submission of Product Chemistry Data in Support of the Application for Registratio	70552	SINON CORP	Product/Manufacturing Chemistry & Analysis
46331201	Brown, E. (2004) Paraquat Technical: Product Identity, Composition, and Analysis (Group A). Project Number	70552	SINON CORP	Product Mfg - Beginning Materials & Mfg Process
46363600	Griffin Corporation (2004) Submission of Product Chemistry Data in Support of the Application for Registratio	81876	GRIFFIN CORPORATION	Product/Manufacturing Chemistry & Analysis
46363601	Dowler, C. (1999) Griffin BOA Concentrate: Product Identity and Composition. Project Number: P98/036. Un	81876	GRIFFIN CORPORATION	Product Mfg - Beginning Materials & Mfg Process
46363602	Dowler, C. (1999) Griffin Boa Concentrate: Analysis and Certification of Product Ingredients. Project Number:	81876	GRIFFIN CORPORATION	Product Mfg - Preliminary Analysis
46363603	Dowler, C. (2000) Storage Stability: Griffin Boa Concentrate. Project Number: P00/019, TM/1182, TM/1228.	81876	GRIFFIN CORPORATION	Physical/Chemical - Stability
46363606	Dowler, C. (2000) Griffin Analytical Method TM-1264: Paraquat Impurities: 2,2',6,6'-Tetrapyridine Content by G	81876	GRIFFIN CORPORATION	Analytical Methods - Chromatography
46364500	Syngenta Crop Protection Inc. (2004) Submission of Product Chemistry and Toxicity Data in Support of the Ap	100	SYNGENTA CROP PROTECTIO	Product/Manufacturing Chemistry & Analysis
46364502	Schilling, W. (2004) Physical and Chemical Properties of Paraquat Dichloride SL (A7813K): Paraquat Dichlor	100	SYNGENTA CROP PROTECTIO	Physical/Chemical - Color
46364503	Pooles, A. (2004) Paraquat 240 G/L SL Formulation (A7813K): Acute Oral Toxicity in the Rat - Up and Down	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46364504	Pooles, A. (2004) Paraquat 240 g/L SL Formulation (A7813K): Acute Dermal Irritation in the Rabbit: Final Rep	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Primary Dermal Irritation
46364505	Pooles, A. (2004) Paraquat 240g/L SL Formulation (A7813K): Acute Dermal Toxicity (Limit Test) in the Rat: Fir	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Dermal
46364506	Pooles, A. (2004) Paraquat 240 G/L SL Formulation (A7813K): Acute Eye Irritation in The Rat: Final Report. F	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Primary Eye Irritation
46364507	Merkel, D. (2004) Dermal Sensitization Study in Guinea Pigs (Buehler Method) with Paraquat (240 g/L) and P	100	SYNGENTA CROP PROTECTIO	Subacute or Subchronic Exposure - Dermal Sensitization
46364508	Merkel, D. (2004) Dermal Sensitization Study in Guinea Pigs (Buehler Method) with Alpha-Hexylcinnamaldehy	100	SYNGENTA CROP PROTECTIO	Subacute or Subchronic Exposure - Dermal Sensitization
46364509	Tisdell, M. (2004) Summary of Acute Toxicology Studies with Paraquat 240 g/L Formulation (A7813K): Summa	100	SYNGENTA CROP PROTECTIO	Subacute or Subchronic Exposure - Dermal Irritation
46364510	Brammer, A.; Heylings, J.; Swain, C. (2004) Paraquat 240 G/L SL Formulation (A7813K): Toxicokinetic Study	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46364511	Brammer, A.; Heylings, J.; Swain, C. (2004) Gramoxone 200 G/L SL Formulation (A3879D): Toxicokinetic Stu	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46364512	Johnson, I. (2003) Paraquat 200 g/L SL Formulation (A3879BU): Eye Irritation Study in the Rabbit: Final Repo	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Primary Eye Irritation
46364513	Johnson, I. (2003) Paraquat 200 g/L Formulation (A3879BU): Skin Irritation Study in the Rabbit: Final Report.	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Primary Dermal Irritation
46364514	Johnson, I. (2003) Paraquat 200 g/L SL Formulation (A3879BU): Acute Dermal Toxicity Study in the Rat: Final	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Dermal
46364515	Johnson, I. (2003) Paraquat 200 g/L SL Formulation (A3879BU): Acute Oral Toxicity Study in the Rat - Up and	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46364516	Johnson, I. (2003) Paraquat 200 g/L SL Formulation (A3879BU): Skin Sensitization Study in the Guinea Pig: F	100	SYNGENTA CROP PROTECTIO	Subacute or Subchronic Exposure - Dermal Sensitization
46364517	Brammer, A. (2004) Paraquat 200 g/L SL Formulation (A3879BU): Toxicokinetic Study in the Dog: Final Report	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46364518	Heylings, J.; Swain, C.; Brammer, A. (2004) Paraquat: Gramoxone 200 g/L Formulation - Toxicokinetic Study in	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46372400	Griffin Corporation (2004) Submission of Product Chemistry Data in Support of the Application for Registratio	81876	GRIFFIN CORPORATION	Product/Manufacturing Chemistry & Analysis
46372401	Dowler, C. (2000) Griffin Technical Paraquat: Analysis of 4,4'-Bipyridyl Content. Project Number: P00/035, TM	81876	GRIFFIN CORPORATION	Product Mfg - Preliminary Analysis
46372402	Dowler, C. (2000) Griffin Paraquat Technical: Analysis for Terpyridine Content. Project Number: P00/046, TM	81876	GRIFFIN CORPORATION	Product Mfg - Preliminary Analysis
46377400	Syngenta Crop Protection Inc. (2004) Submission of Product Chemistry Data in Support of the Application for	100	SYNGENTA CROP PROTECTIO	Product/Manufacturing Chemistry & Analysis
46377401	Schilling, W. (2004) Manufacturing Process Description and Supporting Data for Paraquat Dichloride SL (A78	100	SYNGENTA CROP PROTECTIO	Product Mfg - Formation of Unintentional Ingrid/Impurities
46613800	Sinon USA, Inc. (2005) Submission of Product Chemistry Data in Support of the Application for Registration of	82557	SINON USA INC.	Product/Manufacturing Chemistry & Analysis
46613801	Butz, R. (2005) Elixir (Paraquat 43.8% SL): Product Identity, Composition, and Analysis (Group A). Project N	82557	SINON USA INC.	Product Mfg - Beginning Materials & Mfg Process
46645900	Griffin Corp. (2005) Submission of Product Chemistry Data in Support of the Application for Registration of B	81876	GRIFFIN CORPORATION	Product/Manufacturing Chemistry & Analysis
46645901	Collier, R. (2005) BOA Concentrate: Response to Product Chemistry Questions. Unpublished study prepared	81876	GRIFFIN CORPORATION	Physical/Chemical - Boiling Point
46659500	Sinon USA, Inc. (2005) Submission of Product Chemistry Data in Support of the Application for Registration of	82557	SINON USA INC.	Product/Manufacturing Chemistry & Analysis
46659501	Su, H. (2005) Determination of Storage Stability of Paraquat Dichloride 43.8% SL. Project Number: D202, D2	82557	SINON USA INC.	Physical/Chemical - Corrosion Characteristics
46659502	Wang, S. (2005) Time Zero Evaluation for Paraquat Dichloride 43.8% SL Storage Stability Testing. Project N	82557	SINON USA INC.	Physical/Chemical - Corrosion Characteristics
46659503	Su, H. (2005) Determination of pH of Paraquat Dichloride 43.8% SL. Project Number: D202, D202/7. Unpubl	82557	SINON USA INC.	Physical/Chemical - pH
46659504	Su, H. (2005) Determination of Viscosity of Paraquat Dichloride 43.8% SL. Project Number: D202, D202/8. U	82557	SINON USA INC.	Physical/Chemical - Viscosity

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46659506	Su, H. (2005) Determination of Physical State/Color of Paraquat Dichloride 43.8% SL. Project Number: D202	82557	SINON USA INC.	Physical/Chemical - Physical State
46685100	Syngenta Crop Protection, Inc. (2005) Submission of Product Chemistry Data in Support of the Amended Reg	100	SYNGENTA CROP PROTECTIO	Product/Manufacturing Chemistry & Analysis
46685101	Schilling, W. (2005) Paraquat Concentrate ES (Also Known as Paraquat Technical and PP148 in this Volume	100	SYNGENTA CROP PROTECTIO	Product Mfg - Beginning Materials & Mfg Process
46726400	Griffin Corporation (2006) Submission of Product Chemistry Data in Support of the Application for Registrat	81876	GRIFFIN CORPORATION	Product/Manufacturing Chemistry & Analysis
46726401	Kaminsky, M. (2006) Preliminary Analysis of a Test Substance: BOA Concentrate: Amended Final Report. Pr	81876	GRIFFIN CORPORATION	Product Mfg - Preliminary Analysis
46778800	EDM Industries Inc. (2006) Submission of Product Chemistry and Toxicity Data in Support of the Registratio	68292	EDM INDUSTRIES INC.	Product/Manufacturing Chemistry & Analysis
46778801	Tieu, H. (2005) Product Chemistry: Paradox. Project Number: P/4. Unpublished study prepared by EDM Indu	68292	EDM INDUSTRIES INC.	Physical/Chemical - Color
46778802	Cerven, D. (2006) Acute Oral Toxicity - Up and Down Procedure (UDP): Paradox Herbicide: (Rat). Project Nu	68292	EDM INDUSTRIES INC.	Acute Exposure - Oral
46798300	Syngenta Crop Protection, Inc. (2006) Submission of Product Chemistry Data in Support of the Registratio	100	SYNGENTA CROP PROTECTIO	Product/Manufacturing Chemistry & Analysis
46798301	Schilling, W. (2006) Storage Stability at Ambient Temperature and Corrosion Characteristics of Paraquat SL	100	SYNGENTA CROP PROTECTIO	Physical/Chemical - Corrosion Characteristics
46829100	Sinon USA Inc (2006) Submission of Toxicity Data in Support of the Amended Registration of Paraquat SL He	82557	SINON USA INC.	Pesticide Effects on Non-target Animals (Including Man)
46829101	Butz, R.; Wilcke, J.; Putsavage, T.; et. al. (2006) Assessment of Paraquat SL Herbicide. Project Number: 200	82557	SINON USA INC.	Toxicological Effects by Route & Duration of Exposure
46830500	Sinon Corp (2006) Submission of Product Chemistry Data in Support of the Amended Registration of Paraque	70552	SINON CORP	Product/Manufacturing Chemistry & Analysis
46830501	Tsai, D. (2006) Paraquat Dichloride Technical: Storage Stability Testing. Project Number: D803. Unpublishe	70552	SINON CORP	Physical/Chemical - Corrosion Characteristics
46845000	Makhteshim Agan of North America, Inc (2006) Submission of Product Chemistry Data in Support of the Appli	66222	MAKHTESHIM-AGAN OF NORT	Product/Manufacturing Chemistry & Analysis
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46845002	Sun, G. (2006) Paraquat Technical Grade Active Ingredient Physical and Chemical Characteristics: Final Rep	66222	MAKHTESHIM-AGAN OF NORT	Physical/Chemical - Color
46845003	Everich, R. (2006) Paraquat Dichloride Technical - Product Properties. Project Number: RCE/050806, TAP/0	66222	MAKHTESHIM-AGAN OF NORT	Product Mfg - Beginning Materials & Mfg Process
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46845102	Everich, R. (2006) Parazone 3SL - Product Properties. Project Number: 050806E, TAP/01/0408/082. Unpubl	66222	MAKHTESHIM-AGAN OF NORT	Product Mfg - Beginning Materials & Mfg Process
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46865501	Swain, C.; Heylings, J. (2006) Gramoxone: Effects of Increased Emetic Levels on Toxicokinetics in the Dog: F	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
46906700	EDM Industries Incorporated (2006) Submission of Product Chemistry Data in Support of the Application for R	68292	EDM INDUSTRIES INC.	Product/Manufacturing Chemistry & Analysis
46906701	Tieu, H. (2006) Product Chemistry: Paradox. Project Number: P/5. Unpublished study prepared by EDM Indu	68292	EDM INDUSTRIES INC.	Physical/Chemical - Color
47019700	Sinon USA Inc. (2006) Submission of Product Chemistry Data in Support of the Registration of Paraquat SL H	82557	SINON USA INC.	Product/Manufacturing Chemistry & Analysis
47019701	Cheng, C. (2006) Determination of Storage Stability Testing of Paraquat Dichloride 43.8% SL. Project Numb	82557	SINON USA INC.	Physical/Chemical - Corrosion Characteristics
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47049201	Brammer, A. (2006) Paraquat 240G/L SL Formulation (A7813K): Supplement to Toxicokinetic Study in Dogs (100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
47049202	Brammer, A. (2006) Paraquat 200G/L SL Formulation (A3879BU): Supplement to Toxicokinetic Study in Dogs	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
47049203	Swain, C.; Heylings, J. (2006) Gramoxone: Supplement to Effects of Increased Emetic Levels on Toxicokinetic	100	SYNGENTA CROP PROTECTIO	Acute Exposure - Oral
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47091103	Garofani, S. (2006) Paraquat Technical: Validation of the Analytical Method for the Determination of the Cont	82542	SOURCE DYNAMICS, LLC	
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47091107	Durando, J. (2007) Paraquat 45.8 Percent Tech: Acute Oral Toxicity Up and Down Procedure in Rats. Project	82542	SOURCE DYNAMICS, LLC	Acute Exposure - Oral
47091108	Lowe, C. (2007) Paraquat 43.8 Percent Tech: Acute Dermal Toxicity Study in Rats-Limit Test. Project Numbe	82542	SOURCE DYNAMICS, LLC	Acute Exposure - Dermal
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47106702	Garofani, S. (2006) Paraquat Technical: Complete Analysis of Five Batch Samples: Final Report. Project Nur	82542	SOURCE DYNAMICS, LLC	Product/Manufacturing Chemistry & Analysis
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