

ZENECA

Ag Products*
Western Research Center

Report Series
RR 95-019B

PARAQUAT: WORKER EXPOSURE DURING MIXING, LOADING AND
APPLICATION OF GRAMOXONE® EXTRA TO PECANS USING
VEHICLE-MOUNTED, GROUND BOOM EQUIPMENT
(WRC-95-034) (WINO 18627)

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Category

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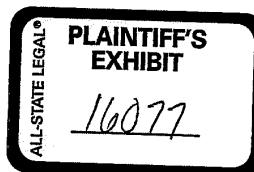
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Report Title

**Paraquat: Worker Exposure During Mixing, Loading and Application of GRAMOXONE® EXTRA to Pecans
Using Vehicle-Mounted, Ground Boom Equipment**

Data Requirement

Guideline-Subdivision U §235, 236

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Study Completion Date

April 28, 1995

Performing Laboratory

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Study Number

PARA-94-AE-01

Report Number

RR 95-019B

Page 1 of 104 Pages

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No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C).		
Company	<u>Zeneca Inc.</u>	
Submitter	<u>M. E. Rhodes</u>	Date <u>4-28-95</u>
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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study meets the requirements for 40 CFR Part 160 with the following exceptions:

1. Commercially available product was used, refer to section 3.4 of this report. Test substance containers were not retained. The test substance came from one batch and two sub-samples were taken, analyzed for purity and archived. The lack of keeping the containers should have no affect on study integrity.
2. Temperature and humidity were measured using a hygrometer/thermometer which was factory calibrated against National Bureau of Standards Traceable Instrumentation. Wind speed was taken using a Dwyer wind meter. Neither instrument can be re-calibrated. The information obtained from using these instruments is adequate and does not affect study integrity.

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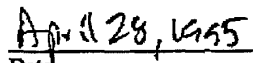
Report Title: Paraquat: Worker Exposure During Mixing, Loading and Application of GRAMOXONE[®]
EXTRA to Pecans Using Vehicle-Mounted, Ground Boom Equipment

QUALITY ASSURANCE STATEMENT

In accordance with Zeneca Ag Products, Zeneca Inc., policy and procedures for Good Laboratory Practice, the conduct of this study has been inspected/audited by the Quality Assurance Unit at the Western Research Center (WRC), Richmond, California, United States of America. So far as can be reasonably established, the methods described and results incorporated in this report accurately reflect the raw data produced during the study.

<u>Date</u>	<u>Inspection/Audit</u>	<u>Report Date</u>
September 27, 1994	Study conduct	April 12, 1995
September 28, 1994	Study conduct	April 12, 1995
April 27, 1995	Data and final report	April 28, 1995


Lance Sandvik
Quality Assurance Specialist


Date

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CERTIFICATION OF AUTHENTICITY

I, the undersigned, declare that this study was performed under my direction and that this report represents a true and accurate record of the results obtained.

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Study Number: PARA-94-AE-01

Report Title: Paraquat: Worker Exposure During Mixing, Loading and Application of GRAMOXONE® EXTRA To Pecans Using Vehicle-Mounted, Ground Boom Equipment

Author: Deborah J. Meier

Summary

A worker exposure study was conducted in the pecan growing area of Georgia and Alabama during September and October, 1994. The purpose of the study was to measure the systemic absorption of paraquat [formulated product name GRAMOXONE® EXTRA] resulting from the mixing, loading and application of GRAMOXONE® EXTRA with open cab, tractor - mounted spray equipment. The study was conducted to support label revisions related to the personal protective equipment (PPE) required for mixers, loaders and applicators as imposed by the Worker Protection Standard (WPS).

Specifically, seventeen subjects who mixed, loaded and applied GRAMOXONE EXTRA were monitored for their absorption of paraquat. A person who mixes, loads and applies a test substance using an open-cab tractor provides the maximum potential for exposure. Each subject had prior experience in pesticide applications to pecans. Applications were made using the maximum labeled rate of 3 pints per acre (0.94 lb active ingredient per acre). The trial period for each subject was seven days; a baseline or pre-exposure day followed by one day of exposure followed by five further days of urine collection. Subjects were asked to refrain from any potential exposure to paraquat for a minimum of six days prior to application and five days after the day of exposure. Urine samples were taken for each trial day including the baseline day. The urine samples were analyzed for paraquat.

Paraquat was detected in the urine of six subjects, and only in the exposure day samples. Paraquat was not detected in any of the samples taken the day following exposure or the second day following exposure. Thus, the urine samples from the remaining 3 post-exposure days were not analyzed. Under the conditions of the study, which provided the maximum potential for exposure, the amount of paraquat absorbed was estimated to be in the range of 0.0051 to 0.0378 mg. This equates to an absorbed dose range of 0.00007 to 0.00044 mg/kg bw/day.

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1 INTRODUCTION

This worker exposure study was conducted to develop data to support label revisions related to the personal protective equipment (PPE) required for mixers, loaders and applicators. The requirement for PPE was predetermined by the revised Worker Protection Standard (WPS) issued in August 1992, based on the toxicity classification of the formulated ion. Paraquat dichloride has been classified by the US Environmental Protection Agency (EPA) as Toxicity Category I based on acute oral, dermal, inhalation toxicity and eye irritation studies, and Toxicity Category III based on dermal irritation studies.

Based on the toxicity classification, the WPS now requires mixers, loaders and applicators to wear additional personal protective equipment compared to the pre-WPS label in order to be WPS compliant (Tables 1 and 2). The study was designed to fulfill the US EPA's requirements for Biological Monitoring for Outdoor Exposure (§ 235 and 236) as defined in the Pesticide Assessment Guidelines, Subdivision U; Applicator Exposure Monitoring.

Paraquat dichloride, a non-selective herbicide, is used for broad spectrum weed control and as a harvest aid. Paraquat dichloride is marketed by Zeneca Ag Products, a business unit of Zeneca Inc. The formulated products GRAMOXONE® EXTRA, GRAMOXONE® SUPER, CYCLONE®, CYCLONE® CF, CYCLONE® CONCENTRATE, and STARFIRE® are registered for use in a wide variety of crops, including tree and vine crops.

In 1994, Zeneca Ag Products carried out a study in pecan orchards in Georgia and Alabama to measure the systemic absorption of paraquat resulting from mixing, loading and application. Measurement of systemic absorption was accomplished by collecting complete 24-hour urine voids from seventeen subjects and analyzing the urine for paraquat. Georgia is the largest producer of pecans, representing 40% of US acreage. Alabama represents 7% of the US acreage. The study was conducted under typical use conditions.

The formulated product, GRAMOXONE® EXTRA, was applied to pecan orchards at the maximum single application rate of 3 pints per acre which equated to 0.94 lbs of active ingredient (ai) per acre. Subjects who mixed, loaded and applied the test substance driving an open cab tractor while using vehicle-mounted, ground boom spray equipment provided the maximum potential for exposure.

TABLE 1. COMPARISON OF PARAQUAT MIXER/LOADER PPE

CATEGORY	PARAQUAT PRE-WPS	PARAQUAT POST-WPS
Mixer/loader	NIOSH/MSHA-approved respirator	Dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)
	Disposable suit/coveralls or long-sleeved shirt and pants	Coveralls over long-sleeved shirt and long pants
	Full face shield	Protective eyewear
	Mid-forearm waterproof gloves	Waterproof gloves
	Waterproof apron	Chemical-resistant apron when cleaning equipment, mixing, or loading
	Waterproof footwear	Chemical-resistant footwear plus socks
		Chemical-resistant headgear for overhead exposure

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TABLE 2. COMPARISON OF PARAQUAT APPLICATOR PPE

CATEGORY	PARAQUAT PRE-WPS	PARAQUAT POST-WPS
Applicator	Disposable suit/coveralls or long-sleeved shirt and pants	Coveralls over long-sleeved shirt and long pants
	Wide-brimmed hat	Chemical-resistant headgear for overhead exposure
	Waterproof footwear	Chemical-resistant footwear plus socks
		Dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)
		Protective eyewear
		Waterproof gloves

2 STUDY DESIGN

Biological monitoring is an appropriate means of estimating absorbed dose because it measures the actual absorption from the three routes of exposure; dermal, inhalation, and oral ingestion. In addition, animal and human studies have demonstrated that paraquat is excreted unchanged in the urine (Ref. 1 - 3).

The biological monitoring period was 7 days, with the first day a pre-exposure, baseline day. Urine was also collected on the day of exposure and for 5 subsequent post-exposure days. Subjects were requested not to use or have contact with paraquat for six days prior to the exposure day and for five subsequent days following the exposure day. The activities of the subjects were observed and recorded on the exposure day.

A complete, 24-hour urine sample was collected from each subject on each monitoring day. The 24-hour period was from the second void of each day through to the first void the following day.

Seventeen subjects were requested to follow their normal agronomic practices associated with GRAMOXONE® EXTRA application according to the product label. To obtain maximum exposure, each subject was required to mix, load and apply GRAMOXONE® EXTRA to their fields of choice using their normal application equipment and open cab tractors.

3 FIELD PROCEDURES

3.1 Study Management

Seventeen subjects who mixed, loaded and applied GRAMOXONE® EXTRA were monitored for inhalation exposure to [see Appendix 2] and absorption of paraquat. During the field portion of the study, the study director, field manager and/or members of the study team were responsible for

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ensuring that all aspects of the field study were carried out to the required technical standards and in compliance with the standards of EPA's Good Laboratory Practices as stated in 40 CFR Part 160. At each field site, on the day of exposure, a member of the study team was present to document information required by the protocol and work practices (Tables 3 - 12).

3.2 Subject Details

Table 4 summarizes the age, height, weight, occupation, and years of experience for each of the monitored subjects. The subjects' ages ranged from 20 - 67. Their weights ranged from 161 to >300 lbs or 73 to >136 kg (scale only weighed up to 300 lbs). Each subject was experienced in pesticide application. Sixteen males and one female were monitored.

Prior to the initiation of the study, subjects were thoroughly briefed with regard to purpose and procedures of the study through written and verbal explanations. They were informed that they were under no obligation to start or continue participation in the study and could withdraw at any time. Each subject was supplied with a consent form, MSDS (Material Safety Data Sheet) and current GRAMOXONE® EXTRA label (note: the product used in this study was labeled with the pre-WPS use directions). Zeneca offered to supply any PPE as required by the label. All subjects were required to sign the consent form prior to the initiation of the study.

Subjects were asked to follow the GRAMOXONE® EXTRA label recommendations with respect to handling the product. In order to minimize bias, Zeneca did not interfere with any of the subjects' normal agronomic procedures.

The type of clothing worn during the exposure period varied from person to person. Details of the clothing worn throughout the exposure period are given in Table 6. Subjects 4211 and 4216 fully complied with the label with respect to wearing PPE. Due to the warm temperatures, many of the subjects wore short-sleeved shirts even while wearing other protective equipment. Eleven subjects wore short-sleeved shirts during the exposure period. Eight subjects wore protective gloves when mixing. Nine subjects did not wear gloves during mixing and loading, as specified on the label.

3.3 Trial Location, Weather and General Site Data

The trials were conducted at fifteen different farm sites during the period of September 20 through September 30, 1994. The sites were located in the pecan growing areas of south central and southwestern Georgia and southeastern Alabama. The sites spanned eleven counties and were sufficiently spaced apart to ensure a variety of environmental conditions. The location of the trial sites with the county and nearest town are listed in Table 11.

Weather data for each trial site were recorded approximately every hour during the exposure period. Temperature and relative humidity (RH) were measured using a Fisher hygrometer/thermometer certified using National Bureau of Standards Traceable Instrumentation. Wind speed was measured using a Dwyer Wind Meter. Table 12 lists the wind speed, wind direction, relative humidity and temperature throughout each exposure period. The temperature ranged from 63 °F to 93 °F. The relative humidity ranged from 34% to 91%. The weather was considered typical for the time of the year.

Tree maturity in the orchards varied from newly planted to mature trees. The fields generally were flat. Fall applications of GRAMOXONE® EXTRA at the maximum label rate in tree crops is a common weed control practice used 6 - 8 weeks prior to harvest.

3.4 Test Material

The active ingredient is paraquat dichloride [1,1'-dimethyl-4,4'-bipyridinium dichloride], CAS Registry No. 1910-42-5. Paraquat was applied as the formulated product GRAMOXONE® EXTRA (EPA

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Reg. No. 10182-280). GRAMOXONE® EXTRA contains 37.05% by weight of active ingredient equivalent to 2.5 lb of paraquat cation per US gallon.

The GRAMOXONE® EXTRA used throughout the study was commercially available product supplied by Zeneca. All containers used were from batch number TDF020149. Two samples (one from each inventory number) were taken during the study and shipped to the Zeneca Western Research Center (WRC) on October 3, 1994. The samples are being retained at the Zeneca Ag Products' GLR Archive for Test Substances, WRC, Richmond, California 94804. Paraquat analyses of the samples were conducted on Oct. 13, 1994 at WRC. One sample was 24.4 wt. percent pure and one was 23.3 wt. percent pure (analytical reference 15117-1) or 33.7 and 31.8 wt. percent paraquat dichloride, respectively. The technical grade active ingredient has been shown to be stable for a minimum of four years at ambient temperature (Ref. 4-5). Empty GRAMOXONE® EXTRA containers were not retained.

The amount of test material handled during mixing and loading is listed in Table 5. Applicators typically mix only enough product to treat a given acreage and thus the amount of product used for each tank mix can vary. The total amount of formulated product handled during mixing and loading ranged from 2.9 gallons to 27.6 gallons per day. The mean was 10.9 gallons per day. The amount of product handled was dependent upon type of application and acreage of field(s).

3.5 Mixing, Loading and Application Procedures

The application methods represented normal agricultural practices. The spray solutions were prepared by diluting the required quantity of product with water. The subject either poured the formulated product directly into the spray tank or measured the desired amount in a calibrated container prior to transferring the product to the spray tank. Water was added via a nurse truck or a well. Applications were made with typical commercial application equipment, which varied from site to site. Equipment descriptions are listed in Table 7. Application details are listed in Table 8.

Prior to the start of the exposure period, each tractor and spray rig used in the study was calibrated by the grower and the Zeneca observer or study director. Calibration details are listed in Table 9. For the majority of test sites, Zeneca provided new spray nozzles and screens for their spray booms. This reduced the amount of time spent calibrating and ensured a uniform distribution of test material.

GRAMOXONE® EXTRA was applied in the orchard by one of two methods (Table 7). One application method utilized a broadcast spray that eliminates plant growth from the base of the tree to approximately 6 to 8 ft on either side of the tree. This was accomplished by having a side mounted boom and spraying on both sides of the tree row. This method was used by ten subjects. The other application method was a broadcast spray designed to eliminate all plant growth between tree rows. Seven subjects used this method.

Sprayer output is listed in Table 9. Output ranged from 13.0 - 42.1 GPA (gallons per acre). The number of acres treated per day ranged from 8 to 74, with the mean being 29 acres (Table 9). Spray tank capacity ranged from 30 to 500 gallons (Table 7). The maximum label rate for a single application is 3 pints of formulated product per acre or 0.94 lb ai/acre. Fifteen subjects applied 0.94 lb ai/acre. Two subjects did not apply the target rate because of errors in calibration. In trial 4209 GRAMOXONE® EXTRA was applied at a rate of 0.74 lb ai/acre and in trial 4214 GRAMOXONE® EXTRA was applied at a rate of 0.98 lb ai/acre. All but one subject used a non-ionic surfactant at a rate of either 0.125 or 0.25% v/v (Table 5).

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4 MONITORING PROCEDURES

4.1 Systemic Absorption

The absorption of paraquat by workers was determined by measurement of the urinary excretion of paraquat. The compound is excreted as unchanged parent (Ref. 1-3). Urine samples were collected each day from the subjects over the entire monitoring period of each trial. Collection of urine samples started on the morning of the baseline or pre-exposure day after the first void in the morning and finished with the first void in the morning of the day after the last monitoring day.

Subjects were asked to make urine voids directly into clean polypropylene containers, which were available to the subject at all times to ensure that all urine would be collected. All subjects were instructed to exercise caution so that contamination of the urine with extraneous paraquat would not occur. To detect extraneous contamination that may have arisen during voiding of urine, when paraquat was being used, samples from the day of field exposure were collected in two parts: 1) second void of the day up until the subject changed clothing and washed hands following exposure; and 2) subsequent voids through first void of the next morning. The subjects were instructed to keep the polypropylene containers in the coolest place practical and protected from exposure to direct sunlight. On cessation of exposure, the subjects were instructed to exercise normal hygiene in terms of changing clothes and washing.

After receipt of the urine samples, the total volume of each 24 hour sample was measured and two 50 mL aliquots were taken and stored in polypropylene containers. Samples were frozen as soon as possible. The primary set of samples was shipped frozen to Zeneca Central Toxicology Laboratory (CTL) for analysis and the reserve set of samples was shipped frozen to Zeneca WRC as a contingency against loss of the primary set in transit.

4.2 Field Recovery and Storage Stability of Paraquat in Urine

Assessment of the recovery of paraquat from urine was conducted on each exposure day. Duplicate 50 mL urine samples from non-exposed subjects were fortified with paraquat at nominal concentrations of 0, 10, 20 and 50 nanograms (ng) per milliliter by addition of 100 μ L of fortification solution using a positive displacement pipette with a disposable polypropylene tip. The samples were fortified in the field lab just prior to the exposure period. The fortified samples accompanied the study personnel to the field each morning and were stored under the same ambient conditions as the 24 hour test samples from the subjects. After approximately 24 - 29 hours of storage under ambient conditions, samples were frozen and stored under identical conditions to those for the field study samples. Recovery and subjects' samples were analyzed concurrently.

The paraquat reference standard used was ASY20027-02S (Request #1994-1137). Its purity was 100% (wt/wt), and its expiration date was May 31, 1999. The weight percent of paraquat in paraquat dichloride was 72.4% (186.3/257.2). Fortification standards were refrigerated during the study except during use. Standards were removed from the refrigerator approximately one hour prior to fortification to allow them to reach ambient temperature. After fortification, the standards were returned to the field lab refrigerator. The field lab refrigerator temperature was monitored daily. The temperature range was 2 - 10 °C. A chain of custody was established for the field fortification standards.

4.3 Storage and Transport of Urine Samples

The 24 hour urine samples were delivered to the field laboratory at ambient temperatures. After aliquoting, the 50 mL samples were placed in a freezer located at the field laboratory site. Freezer temperature was monitored daily. The temperature range of the freezer was -18 to -28 °C.

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Primary urine samples were shipped from the field laboratory to CTL via Federal Express. The samples, stored in polypropylene containers, were placed inside plastic bags and then placed in a cardboard box. Boxes were placed in insulated shipping containers with dry ice added at a ratio of approximately 3:1.

After CTL confirmed the receipt of primary urine samples, reserve urine samples were shipped from the field laboratory to WRC via Federal Express or ACDS Trucking (freezer truck). All samples were received frozen and in good condition at CTL or WRC.

A chain of custody was established for each sample. The chain of custody included receipt of sample at the field laboratory from subjects or field study personnel, shipment to the analytical (CTL) or coordinating laboratory (WRC), and receipt and placement of shipments.

5 ANALYTICAL PROCEDURES

5.1 Sample Receipt

The primary urine samples were received frozen at CTL. Samples were stored frozen, until required for analysis. The temperature range of the freezer was -26 °C to -34 °C. Details of sample shipment and storage of the primary urine samples at CTL are described in Appendix 1, CTL/P/4588, section 2.1.

Reserve urine samples were received frozen at the WRC on September 29 and November 10, 1994. Samples were stored at <-15 °C in the Environmental Chemistry Section freezers.

5.2 Sample Analysis

Urine was analyzed for paraquat and creatinine at CTL between January 10 and February 9, 1995. Results are presented in Table 3 of this report and in Tables 1 and 3 of Appendix 1, CTL/P/4588. Analysis of creatinine was conducted using the Jaffe reaction (Ref. 6) on a Kone Specific Analyzer. Creatinine excretion is used as a marker to determine the completeness of a 24 hour urine collection. Paraquat was analyzed in urine by radioimmunoassay (Ref. 7) following solid phase extraction. A summary of the method, "Determination of Paraquat in Human Urine" is included in Appendix 1, CTL/P/4588. The limit of determination of the method is 5 ng/mL and the limit of quantitation is 10 ng/mL.

Back-up samples retained at the Zeneca WRC were not analyzed because of the successful analysis of the primary samples sent to CTL.

6. RESULTS

6.1 Statistical Methods

The statistical methods used in this study were the calculation of the arithmetic mean and percent recovery.

6.2 Field Recovery and Storage Stability

The field fortified samples were analyzed along with each sample set. Results of field fortifications are listed in Appendix 1, CTL/P/4588, Table 2. Paraquat was not detected in any of the control samples. The mean recoveries for fortifications at 10, 20 and 50.1 ng/mL were 108, 100, and 101%, respectively. No recovery correction was applied to the results of the test samples because the results of the fortified samples demonstrated the stability of paraquat in urine samples stored under identical conditions to the study samples.

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6.3 Systemic Absorption

A complete report detailing analytical methods and results and discussion related to biological monitoring is in Appendix 1, CTL/P/4588.

Daily creatinine excretion was consistent for all individuals and is considered to be confirmation of full 24 hour collections. Paraquat was detected in the urine of six subjects for only the exposure day samples. Paraquat was not detected in any of the samples taken from the day following exposure or the subsequent day. Thus, the urine samples from the remaining 3 days were not analyzed. The duration of exposure ranged from 230 to 660 minutes, the time spent mixing and loading ranged from 14 to 104 minutes (Table 3). Under the conditions of the study, the amount of paraquat absorbed was estimated to be in the range 0.0051 to 0.0378 mg (Table 3). This equates to an absorbed dose range of 0.00007 to 0.00044 mg/kg bw/day (Table 3).

Table 10 outlines the observations and any incidents that could have contributed to increased exposure.

7 Discussion

7.1 Field Recovery and Storage Stability

The nearly quantitative recoveries from the fortified field samples confirms analyte stability in the samples during storage from the times between collection in the field and final analysis in the laboratory.

7.2 Systemic Absorption

The study was conducted under actual use conditions. Two of the subjects' tractors (4203 and 4214) had their spray booms in front of the driver's seat and this may have resulted in some exposure. There was no clear correlation between duration of exposure, amount of product handled, or whether any PPE was worn, as it relates to paraquat absorption.

8 CONCLUSIONS

This study demonstrates that under conditions which are considered to have maximized the potential for exposure (one person who mixes, loads and applies paraquat in an open cab tractor using a vehicle-mounted sprayer) no more than 0.00044 mg paraquat/kg bw/day will be absorbed while wearing minimal protective equipment.

9 PERSONNEL AND TESTING FACILITIES

The following people performed work on this study:

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Field Conduct: Deborah Meier (Study Director), Malcolm Findlay (Field Manager), Mark Wiseman, Rae McCann

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Field Laboratory and Shipping: Pat Ryan (Field Laboratory Coordinator), Sabrina Leung, Barbara Buitrago, Malcolm Findlay, Deborah Meier, Anne Howell, Rae McCann, Tony Baza

Courier: Deborah Meier, Malcolm Findlay, Pat Ryan, Mark Wiseman, Neville Martin, Rae McCann

Urine Analyses: Jon Marsh (Principal Investigator)

Report Preparation: Deborah Meier, Catherine Grant

Study Management: James Markle

Technical Review: Malcolm Findlay, Graham Chester, M. E. Rhodes, James Markle

10 STUDY DATES

The experimental phase of the study covered these dates:

Study Initiation Date:	September 13, 1994 (protocol signed)
Study Experimental Start Date:	September 20, 1994 (first field application)
Study Experimental Termination Date:	February 9, 1995 (last urine sample analysis)

11 RETENTION OF RECORDS

The raw data and analytical report for the urine analyses are archived at the Central Toxicology Laboratory, CTL Reports Centre, Alderley Park, Macclesfield, Cheshire, SK10 4TJ, United Kingdom.

All other raw data (including field data), work practices, study protocol, and study report are located at Zeneca Ag Products, Western Research Center, 1200 S. 47th St., Richmond, CA 94804-0023. Reserves from each batch of the standard reference test substance are being retained as per GLP standards, at Zeneca Ag Products, Western Research Center, 1200 South 47th Street, Box 4023, Richmond, California 94804-0023.

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