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MEMORANDUM

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FROM: Tim Leighton

DATE: March 2, 1992

SUBJECT: Diquat - Draft Report

Enclosed are four copies of Paladin's draft report, **Review and Evaluation of Worker Exposure Studies and Individual Foliar Dislodgeable and Soil Residue Dissipation Studies**. Also enclosed is the registrant's submission (MRID Nos. 409174-01,02; 413772-00,02,03; and 413741-00).

DRAFT REPORT

DIQUAT

Review and Evaluation of Worker Exposure Studies and Individual
Foliar Dislodgeable and Soil Residue Dissipation Studies

USEPA Contract No. 68-D9-0166

Task No. 2-37

Prepared for:

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February 19, 1992

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CHAPTER 1. INTRODUCTION

- I. Purpose of study: The purpose of this report is to assess the validity of foliar dislodgeable residue dissipation data for diquat applied to bermuda grass and soil dissipation data following application of diquat applied to a potato field. Diquat was applied as Diquat Herbicide, which is diquat dibromide. The extent to which the data and the studies by which they were obtained meet the requirements specified in Subdivision K of the Pesticide Assessment Guidelines, Exposure:Reentry Protection was determined. Two separate studies are reviewed in this report.

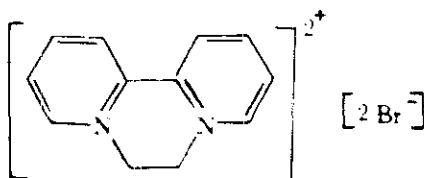
In addition, Chevron Chemical Company petitioned that existing worker protection requirements (reentry interval, protective clothing) for the diquat label be relaxed, based on discussions of worker exposure, residue dissipation, and product toxicity. A study on the rate of penetration of diquat and ethylene dibromide through several protective glove materials was also submitted for review. An analysis of this information is also contained in this report.

- II. Subdivision K: Subdivision K specifies the data requirements for residue dissipation and exposure studies on pesticides, and procedures by which the studies should be conducted. The purpose of Subdivision K is to obtain sufficient information to protect field workers from exposure to pesticides as a result of re-entering areas recently treated with pesticides that may present potential concerns for adverse health effects. This report is pertinent to this endeavor in that it contains an evaluation of the dissipation of foliar dislodgeable and soil residues of diquat for compliance with guideline data requirements. Thus, these studies provide the Agency with the opportunity to discern factors that may affect diquat residue dissipation.
- III. Executive Summary: Neither of the two studies fully met the requirements of Subdivision K. In the Bermuda grass study, the residue data were given in incorrect units (mass/turf area, not mass/leaf area). In the soil residue study, harvesting of potatoes on Day 7 of the study precluded using subsequent samples. Thus, an inadequate number of samples were collected and the study did not run long enough. Consequently, the Bermuda grass study should be considered supplemental, and the soil study unacceptable.

CHAPTER 2. BACKGROUND INFORMATION

I. Chemical Identity

- A. Chemical names: 6,7-Dihydrodipyrido[1,2-a:2',1'-c]pyrazinediium dibromide
1,1'-ethylene-2,2'-dipyridylum dibromide
(Budavari et al. 1989)
- B. Common name: Diquat (Farm Chemicals Handbook 1991)
- C. Trade name(s): Weedtrine-D
Aquacide
Dextrone (Farm Chemicals Handbook 1991)
- D. Molecular weight: 344.07 (Budavari et al. 1989)
- E. Empirical formula: $C_{12}H_{12}N_2Br_2$ (Budavari et al. 1989)
- F. CAS number: 85-00-7 (Farm Chemicals Handbook 1991)
- G. Chemical structure:



II. Physical and Chemical Properties

- A. Physical properties
1. Physical state (25°C): Yellow solid (pure salt monohydrate)
Dark, reddish-brown aqueous solution
(Herbicide Handbook 1989)
 2. Water solubility (20°C): 700 g/L (Farm Chemicals Handbook 1991)
 3. Solubility in organic solvents Slightly soluble in alcohols. Insoluble in non-polar organic solvents (Farm Chemicals Handbook 1991)
 4. Vapor pressure (20°C): Nonvolatile
(Herbicide Handbook 1989)

- B. Environmental behavior: The most important characteristic of diquat is its rapid and complete inactivation by soil constituents, especially clay. The negatively charged sites on clay react essentially irreversibly with the doubly positive diquat cation. Diquat can also be bound by soil organic matter such as humic acids. This adsorption is less strong than the clay binding process but is still sufficiently strong to inactivate the diquat. It is possible that diquat can photodegrade, but the evidence for this process is equivocal. Diquat, while persistent in the environment, is biologically unavailable (Herbicide Handbook 1989).

III. Regulatory information

- A. Test material: Diquat Herbicide.
- B. Purity of test material: No analytical determination of the purity of test material was made.
- C. Current registration and use distribution (if new use): Not applicable.
- D. Label information: A legible label was not provided in the registrant's report. However, the Herbicide Handbook (1989) provides information on application methods. For use as a dessicant, the product can be applied from the ground or the air for complete coverage of the aerial portions of plants. For aquatic weed control, diquat can be injected below the water surface or by pouring it directly from the container. Rates when used as a dessicant are 0.38-0.5 lb ai/acre, and for aquatic weed control are 2-4 lb ai/acre. Water is the usual carrier. Typical volumes range from 15-30 gallons/acre for ground spraying and 5-10 gallons/acre for aerial spraying.
- E. Other formulations: According to the Farm Chemicals Handbook (1991), the only commercial formulation of diquat is the dibromide (2 lb/gal).

CHAPTER 3 - BERMUDA GRASS

I. Description of Study

- A. Study identifier: 1988. "Dissipation of Dislodgeable Diquat Cation Residues on Bermuda Grass." Authored by G. H. Fujie, Chevron Chemical Company, Richmond, CA. EPA MRID No. 409174-02. HED No. 0-1615
- B. Geographical site description: The single site used to conduct this study was located in Gilroy, CA.
- C. Crop type: Bermuda grass.
- D. Meteorological data: Meteorological data were collected each sampling day at the site. These data are summarized below.

<u>Day</u>	<u>Air Temperature (°F)</u>	<u>Relative Humidity (%)</u>	<u>Time</u>
1	60	54	8:30
2	65	74	8:00
3	60	78	8:30
4	70	70	12:00
7	84	40	14:45
14	60	83	8:30
21	96	35	14:00
29	74	61	10:30

There were more data for the application day. On day 0, the air temperature was 78°F at 12:00 and 90°F at 16:00. The relative humidity at 12:00 was 54%, and at 16:00 was 41%. The soil temperature in the shade was 64°F and was 74°F in the sun. The wind speed was 0-2 mph out of the south. There was no cloud cover.

Additional data were collected at a weather station in San Jose, CA, north of the test site. These data are summarized below.

Week	Total Ppt (in)	Average values for the week								
		Air Temperature (°F)			Relative Humidity (%)			Dew Point (°F)	Wind Speed (mph)	Soil Temp (°F)
		Max	Min	Ave	Max	Min	Ave			
8/8/88	0	78	65	71	74	53	67	59	5.0	75
8/14/88	0	90	65	74	72	41	60	59	4.3	74
8/21/88	0	87	65	73	77	34	56	57	4.0	74
8/28/88	0.08	98	72	82	72	47	64	68	3.8	75
9/4/88	0	84	68	74	77	44	62	60	3.9	74

- E. Number of sites: A single treated plot was used. Two distinct sites within this single area were sampled at each sampling interval. There was no mention of a control plot.
- F. Number of replicates (total and per site): In each sampling period, 3 composite samples were collected from two randomly chosen subplots with the site. Thus, for the whole study, a total of 30 samples were generated. Six pretreatment composite samples were taken for use as control samples.
- G. Application rate(s): The application rate was stated to be 1.0 lb ai(active ingredient)/100 gallons. According to the registrant's report, this is the maximum application rate of Diquat. A treatment rate of 2.1 lb ai/acre was calculated based on the amount of spray applied to the test plot.
- H. Mixing/loading/application procedures: Diquat Herbicide was mixed with 100 gallons of water. Ortho x-77 Spreader (non-ionic) was added to the spray mix at a rate of 16 oz/100 gallons. The registrant's report stated that this mixture was broadcast applied with full coverage and thorough contact of the spray with the target species using a carbon dioxide backpack sprayer.
- I. Number of applications: One application of Diquat Herbicide was made to the site on August 8, 1988.
- J. Intervals between applications: This is not relevant as only one application was made.
- K. Sampling methodology: Leaf samples were collected as follows. At the single site, in each sampling period, three composite foliage samples from the single experimental plot were generated. Samples were collected at 1 hour, 4 hours, and 1, 2, 3, 4, 7, 14, 21, and 29 days post-application. A 20 x 20 cm area was sampled using a wooden template. Hand-held clippers were used to collect the samples. The samples were stored in plastic Nalgene bottles, removed from light, and stored in an insulated container with ice or Blue Ice. The samples were not frozen. Stored in this way, the samples were transported to the Residue Chemistry Laboratory of Chevron Chemical Company. Excluding the 4 hour sample, which was shipped simultaneously with the 1 day sample, all samples were shipped on the day of collection. Diquat residues were dislodged from all the samples within 24 hours of collection. Dislodging was achieved by mechanically shaking the samples for 15 minutes in 100 mL of a 0.01% aqueous solution of Aerosol OT-75. The dislodged residues were stored in the dark at ambient temperatures until the ion exchange clean-up step.
- L. Quality control data: No field recovery samples were generated. However, the residues were dislodged within 24 hours and diquat is not expected to degrade significantly in this time. Consequently, the lack of field recovery data does not appear to be a major omission in this submission. Laboratory recovery and storage stability samples were generated. Laboratory: Laboratory recovery samples were prepared by spiking detergent solutions with from 5-250 µg of diquat cation. The recoveries

ranged from 79-97% with an average value of 90%. The coefficient of variation for the laboratory recoveries is 8.3%.

Storage recovery: Storage stability samples were prepared by fortifying pretreatment sample extracts or blank detergent extracts with diquat cation at 1 $\mu\text{g/mL}$. The stability samples, like the dissipation sample extracts, were stored at ambient temperatures in the dark for 1 to 3 days prior to cleanup and analysis. Storage sample recoveries ranged from 79-101% with an average of 91%. The coefficient of variation is 6.3%.

M. Formulation analysis: No information was provided.

N. Recent history of pesticide use at the site: The only reference to this matter was a statement in the protocol that paraquat would not be used prior to the study, and that use of any pesticides to control insects and other pests would be approved by the Study Director. A list of specific products that were used was not provided.

O. Summary of results: The earliest post-application samples were collected at 1 hour on Day 1. The average result for this sample is 1.8 $\mu\text{g/cm}^2$. The complete set of average residue data has been compiled into Table 1. The data were apparently not corrected using recovery values.

II. Summary of Standard Evaluation Procedure

A. Summary of review procedure used

1. Review of protocol relative to Subdivision K Reentry Guidelines:

The submission was examined to determine the extent to which it meets the requirements of Subdivision K. The required elements include the following.

- a. A typical end-use product must be used.

This criterion was met by the use of Diquat Dibromide, which is a commercial formulation used on crop and non-crop species.

- b. The site at which the study was conducted must possess a climate similar to those in which the product is likely to be used.

The product is intended for use on golf courses, rights of way, and around residences. Consequently, this criterion was met by conducting the study in California, which, by virtue of its large number of golf courses, is an area in which the product most likely is used. Furthermore, the choice of California is acceptable since it is expected that the dry climate there will inhibit residue dissipation.

- c. The test substance must be applied in a manner consistent with the approved application methods specified for the end-use product and at the least dilution and highest permissible rate.

Since the copy of the label that was provided with the submission is illegible, it could not be determined whether or not the methods used adhered to the label requirements. However, the methods used appear to be typical commercial agricultural practices.

- d. The test period must coincide with the time of year or season during which the product will likely be used to satisfactorily control the pest.

The study took place in the summer. This is a likely time to spray turf.

- e. The study must include meteorological data obtained at or near the location of the test site.

This criterion was met.

- f. Duplicate foliage/soil samples must be collected periodically during the study.

This criterion was met.

- g. The first round of samples must be taken as soon as feasible following the final application (i.e., when the dust has settled or when the spray has dried).

This criterion was met.

- h. Sampling intervals must be short at first and may subsequently increase.

This criterion was met.

- i. Soil samples must be taken whenever there is the potential for human exposure to the product by virtue of its presence in the soil.

There was little potential for human exposure to soil residues of diquat in this study.

- j. Storage of samples must take place only when necessary, and must be performed in such a way as to minimize residue dissipation.

This criterion was met.

- k. Foliage residue data must be reported in units of $\mu\text{g}/\text{cm}^2$ of leaf surface, and soil residue data in units of ppm.

This criterion was not met. Instead of $\mu\text{g}/\text{cm}^2$ of leaf surface, results were reported in $\mu\text{g}/\text{cm}^2$. This is not an acceptable measure of the concentration since it depends on the turf thickness and height. These factors may vary from site to site, making comparisons impossible.

- 2. Review of Quality Assurance/Quality Control Procedures: These procedures were reviewed to ensure that the data were collected in accordance with GLPs and requirements outlined in Subdivision K of the Pesticide Assessment Guidelines. Among these elements are: proper blanks and recovery spike samples, appropriate replicate samples, maintenance of sample identity and integrity, proper chain of custody and documentation procedures, and a description of the quality assurance unit of the investigating organization and analytical laboratory.
- 3. Verification of calculations: Calculations explicitly presented or implicit in the presentation of data such as means, standard deviations, and correlation coefficients were checked. When available, chromatograms were spot checked (approximately 10% of chromatograms) to determine if the indicated concentrations agreed with any raw data that were presented. When raw data were included in the report, the extent of their agreement with the finished, tabulated data was determined.

III. Study Evaluation Summary

- A. Nature/purpose of study: This study was conducted by Chevron Chemical Company to generate dissipation data for foliar residues of diquat.
- B. Verification of calculations: Raw spectral data were not provided. However, analytical data sheets were included. Accurate transcription of these results to the finished data table was verified.

Table 1 contains the foliar residue dissipation data from the one test site. The dissipation data for diquat have been subjected to linear

regression analysis, and a diquat dissipation half-life has been calculated. The results are discussed below in Part IV.

- C. Adequacy of study protocol: The study protocol was evaluated by reviewing it for its adherence to the requirements of Subdivision K. Conformance with sound scientific practices was also assessed. The major flaws in the study design were the lack of field recovery data and presentation of the residue data in unacceptable units. Although the lack of field recovery data is not a major concern for this submission, the data presentation problem is potentially significant. Consequently, this study does not adhere to Subdivision K requirements.
- D. Adequacy of recovery data: The laboratory recovery and storage stability data are adequate. No field recovery data were generated.
- E. Acceptability of field and laboratory QA procedures: Based on a review of U.S. EPA GLP and other QA/QC requirements and standards, such as outlined in Subdivision K, Reentry Protection, of the Pesticide Assessment Guidelines, and minimal scientific standards, the laboratory QA/QC procedures followed in this study, and the results obtained from them are acceptable. As noted above, no field recovery samples were generated. Consequently, the field QA/QC procedures are not acceptable.
- F. Adequacy of analytical techniques: The detergent extracts containing the dislodgeable residues were adjusted to pH 3 and cleaned using an ion exchange column. The cleaned sample was reduced using sodium dithionate and the reduced diquat product was quantified using an HP 8451A spectrophotometer. The limit of detection was approximately 0.009 g/cm². No quantification limit was given. Reference and sample spectra were not provided, so no conclusions could be drawn concerning potential interference from other substances. No standard curves for the analyte were presented, and correlation coefficients were not given. However, it was stated that the linearity of the system was verified every two months using a minimum of five standards. Submission of data from the standardizations closest in time to the analyses is desirable. Without this information, the linearity of the relationship between diquat concentration and absorbance is in question as certain conditions exist which result in deviation from linearity for the relationship between concentration and absorbance. Laboratory recovery was adequate through the analytical procedures used. Although it is not possible to draw any conclusively determine the adequacy of the analytical technique from the available information, it is likely that the techniques were satisfactory.
- G. Data gaps: There were several data gaps in the registrant's report. First, there were no field recovery data. Second, no limit of quantification was provided. Also, there are no standardization data with which the linearity of the analytical method can be assessed. Finally, since a legible copy of the label was not provided, it could not be determined whether the application procedures were in accordance with the label directions.

H. Issues/items requiring submitter's clarification: No issues requiring clarification were observed by this reviewer.

IV. Summary and Discussion

Linear regression calculations were performed on the average foliar residue data for diquat from the single site. Since the dissipation data suggested an initial rapid phase followed by a slower phase, linear regression was performed on the data from the first seven days and on the entire data set (28 days). The natural logarithms of these data were plotted vs. time in days. The correlation coefficient for the first seven day's data was 0.939 and for the entire data set was 0.868. The half-lives calculated for the initial phase and the entire data set were 1.6 days and 5 days, respectively.

In summary, there are several instances in which this study fails to meet the requirements of Subdivision K and minimum scientific and technical standards. First, the residue data was not presented in Subdivision K specified units of $\mu\text{g}/\text{cm}^2$ of leaf surface. Units of $\mu\text{g}/\text{cm}^2$ of ground area were used instead. This use of ground area makes the data in the submission useful only to the extent that the product is used on turf that is very similar in thickness and height to the Bermuda grass tested. Large variation in height or thickness could conceivably have a significant effect on the rate of residue dissipation. Also, it is possible that the growth of leaves will result in residue dilution. Both of these factors could affect the safe reentry interval. Second, no field recovery data included in the submission. However, as previously discussed, due to the extraction of the samples within 24 hours, and the expected lack of diquat degradation, this is not a significant omission. Third, no calibration data and no limit of quantification were provided. Fourth, no tank spray characterization was provided. Finally, a legible copy of the label was not provided, making it impossible to determine whether the label directions were adhered to. This study should be considered supplemental at best.

TABLE 1

Diquat dislodgeable residue data following application of
Diquat Herbicide at 2.1 lbs ai/acre to Bermuda grass

Days post-application	Mean residue ($\mu\text{g}/\text{cm}^2$) ^a
0.042 (1 hour)	1.8
0.17 (4 hours)	0.95
1	1.3
2	0.62
3	0.20
4	0.17
7	0.092
14	0.049
21	0.036
29	0.028

^a It must be recalled that these data are in units of mass/area of turf, not mass/leaf area.

CHAPTER 4 - SURFACE SOIL

I. Description of Study

- A. Study identifier: 1988. "Diquat Cation Dissipation in Surface Soil." Authored by G. H. Fujie, Chevron Chemical Company, Richmond, CA. EPA MRID No. 409174-01. HED No. 0-1615.
- B. Geographical site description: The single site used to conduct this study was the Hulst Research Farm located in Hughson, CA.
- C. Crop type: The product was applied to a potato patch. Soil was the matrix analyzed.
- D. Meteorological data: Certain meteorological data were collected each day over the course of the study at the Hughson, CA weather station. These data are summarized below.

Month	Temperature Range (°F)						Relative Humidity (%)	
	Air		Soil 2"		Soil 6"			
	Min	Max	Min	Max	Min	Max	Min	Max
June	39	112	63	83	61	81	57	82
July	47	110	76	87	74	84	60	79
August	47	109	68	82	64	77	70	87

- There was no rainfall in July and August. On June 6, 0.06" of rain fell.
- E. Number of sites: A single treated plot was used. Soil from sixteen subplots was composited to yield each sample. There was no mention of a control plot.
 - F. Number of replicates (total and per site): At each sampling interval, 3 composite samples were collected from the site. As noted above, each sample was a composite of soil samples taken from 16 subplots. There were 10 sampling intervals. Thus, for the whole study, a total of 30 samples were generated. This number includes six pretreatment composite samples were also taken for use as control samples. It should be noted that only two of the three post-application samples were analyzed for diquat residues for the purpose of determining the dissipation rate. The remaining samples were kept frozen (-20°C) for an unspecified reason.
 - G. Application rate(s): The application rate was stated to be 0.25 lb ai(active ingredient)/acre. According to the registrant's report, this is the recommended maximum label application rate.

- H. Mixing/loading/application procedures: Diquat Herbicide was mixed with 100 gallons of water. Ortho X-77 Spreader (non-ionic) was added to the spray mix at a rate of 16 oz/100 gallons. The registrant's report stated that this mixture was applied using a tractor-mounted boom sprayer.
- I. Number of applications: Applications were made to the site on June 30, 1988 and July 5, 1988.
- J. Intervals between applications: The application interval was 5 days.
- K. Sampling methodology: Soil samples were collected as follows. At the single site, in each sampling period, three composite soil samples were collected from the single experimental plot. The samples were taken on 0, 1, 3, 7, 14, 21, and 28 days post-application. A total of 6 pretreatment samples were taken. All the samples were a composite of soil taken from 16 subplots in the single treated plot. A 18 x 25 cm area was sampled using a screened wooden template and a portable vacuum cleaner. The template consisted of a top layer of aluminum window screen, a middle layer of 100-mesh brass strainer cloth, and a bottom layer of 0.25 inch hardware cloth. The samples were stored in Nalgene bottles at -10°C. The samples were transported frozen on dry ice to the Residue Chemistry Laboratory of Chevron Chemical Company. The samples were stored at -20°C at the laboratory until analyzed. The maximum storage interval was stated to be 18 days. The samples were acid extracted by refluxing for 5 hours with 18 N sulfuric acid.
- L. Quality control data: No field recovery data were generated. Because samples were not extracted within 24 hours, this is potentially a significant omission. However, it must be noted that diquat is not expected to dissipate following adsorption to soil. Additionally, the storage recovery sample results listed below showed adequate recoveries. The laboratory and storage recovery data can be summarized as follows.
Laboratory recoveries: Three laboratory recovery samples were analyzed. The percent recoveries are 85%, 73%, and 85%. The mean recovery value is 81% and the coefficient of variation is 8.6%. Fortification levels were 0.15 and 3.7 ppm.
Storage recoveries: Six storage recovery samples were fortified with 0.10 ppm diquat and analyzed after 6 months storage at -20°C. The recoveries ranged from 75-95% with a mean recovery of 82%. The coefficient of variation is 10.8%.
- M. Formulation analysis: No information was provided.
- N. Recent history of pesticide use at the site: The only reference to this matter was a statement in the protocol that paraquat would not be used prior to the study, and that use of any pesticides to control insects and other pests would have to be approved by the Study Director. A list of specific products that were used was not provided.
- O. Summary of results: The earliest samples taken following the second application were collected on Day 0 (the same day as the second

application, after the spray had dried). The average result for this sampling interval is 8.74 ppm. Table 1 contains the complete set of average soil residue data.

II. Summary of Standard Evaluation Procedure

A. Summary of review procedure used

1. Review of protocol relative to Subdivision K Reentry Guidelines:
The submission was examined to determine the extent to which it meets the requirements of Subdivision K. The required elements include the following.

- a. A typical end-use product must be used.

This criterion was met by the use of Diquat Dibromide, which is a commercial formulation used on crop and non-crop species.

- b. The site at which the study was conducted must possess a climate similar to those in which the product is likely to be used.

This criterion was met by conducting the study in California, which, due to its intensive agriculture, is an area in which the product is likely to be used.

- c. The test substance must be applied in a manner consistent with the approved application methods specified for the end-use product and at the least dilution and highest permissible rate.

Since the copy of the label that was provided with the submission is illegible, it could not be determined whether or not the methods used adhered to the label requirements. It was stated in the submission that the product was applied at the maximum label rate.

- d. The test period must coincide with the time of year or season during which the product will likely be used to satisfactorily control the pest.

The study took place in the summer. To the extent that harvest of any agricultural commodities in this time in California require the use of a dessicant, this criterion was met.

- e. The study must include meteorological data obtained at or near the location of the test site.

This criterion was met.

- f. Duplicate foliage/soil samples must be collected periodically during the study.

This criterion was met.

- g. The first round of samples must be taken as soon as feasible following the final application (i.e., when the dust has settled or when the spray has dried).

This criterion was met.

- h. Sampling intervals must be short at first and may subsequently increase.

This criterion was met. However, it must be recalled that harvesting occurred on Day 7 of the study, invalidating all subsequent samples that were collected at the longer intervals.

- i. Soil samples must be taken whenever there is the potential for worker exposure to the product by virtue of its presence in the soil.

This criterion was met.

- j. Storage of samples must take place only when necessary, and must be performed in such a way as to minimize residue dissipation.

This criterion was met.

- k. Foliage residue data must be reported in units of $\mu\text{g}/\text{cm}^2$ of leaf surface, and soil residue data in units of ppm.

This criterion was met.

- 2. Review of Quality Assurance/Quality Control Procedures: These procedures were reviewed to ensure that the data were collected in accordance with GLPs and requirements outlined in Subdivision K

of the Pesticide Assessment Guidelines. Because this study was not conducted under Subdivision K, the Subdivision K requirements are not applicable. However, evidence of the scientific soundness of the study was sought. Elements relevant to this search include: proper blanks and recovery spike samples, appropriate replicate samples, maintenance of sample identity and integrity, proper chain of custody and documentation procedures, and a description of the quality assurance unit of the investigating organization and analytical laboratory.

3. Verification of calculations: Calculations explicitly presented or implicit in the presentation of data such as means, standard deviations, and correlation coefficients were checked. When available, chromatograms were spot checked (approximately 10% of chromatograms) to determine if the indicated concentrations agreed with any raw data that were presented. When raw data were included in the report, the extent of their agreement with the finished, tabulated data was determined.

III. Study Evaluation Summary

- A. Nature/purpose of study: This study was conducted by Chevron Chemical Corp. to generate dissipation data for soil residues of diquat.
- B. Verification of calculations: No raw data in the form of chromatograms were provided. There are typed raw data sheets, and these were compared to compiled data sheets to verify the accuracy of the transcriptions. There were no errors in transcription.

Table 1 contains the soil residue dissipation data. The dissipation data for diquat have been subjected to linear regression analysis, and diquat dissipation half-lives have been calculated for each site. The results are discussed below in Part IV.

- C. Adequacy of study protocol: The study protocol was evaluated by reviewing it for its adherence to the requirements of Subdivision K. Conformance with sound scientific practices was also assessed. There are two major flaws in the study design. The first is the selection of a test scenario in which the soil would necessarily be disturbed seven days following the second application. This limited the data to only seven days, which is insufficient. The entire study covered 29 days, but the later samples (collected past 7 days) are useless since harvest of potatoes on Day 7 disrupted the soil, obviously mixing contaminated soil with uncontaminated soil. The second problem is the lack of field recovery data. Consequently, this study neither adheres to Subdivision K requirements, or good scientific practices.
- D. Adequacy of recovery data: The laboratory and storage recovery data are adequate. There were no field recovery data.

- E. Acceptability of field and laboratory QA procedures: Based on a review of U.S. EPA GLP and other QA/QC requirements and standards, such as outlined in Subdivision K, Reentry Protection, of the Pesticide Assessment Guidelines, and minimal scientific standards, the laboratory QA/QC procedures followed in this study, and the results obtained from them are acceptable. There were no field QA/QC procedures.
- F. Adequacy of analytical techniques: Following the sulfuric acid extraction, the samples were subjected to ion exchange column cleanup. The eluates from this column were reduced using sodium borohydride. A series of organic and acidic extractions were performed ending with a methanol solution of the reduced product. The methanol solution was analyzed by gas chromatography using a Hewlett Packard 5890 or equivalent gas chromatograph equipped with a nitrogen/phosphorus-flame ionization detector. The quantification limit for the method was not provided. A detection limit of 0.01 ppm for a 50 g soil sample was presented. No sample chromatograms were presented, so no conclusions could be drawn concerning potential interference from other substances. However, a chromatogram of a standard solution of diquat was included that contains some extraneous peaks. This may indicate problems with the environmental sample chromatograms none of which are shown. Standard curves for the various analytes were not presented, and correlation coefficients were not given. Consequently, there is nothing to indicate to what extent the detector response was linear. There were few laboratory recovery data, but what was presented showed adequate recovery through the analytical procedures that were used. It is not possible to draw any conclusions regarding the adequacy of the analytical technique from the available information.
- G. Data gaps: There were several significant data gaps in the registrant's report. First, there were no field recovery data. No sample chromatograms or handwritten raw data were presented. Consequently, the derivation of the quantitative results from the chromatograms could not be verified. Finally, because a legible label was not provided, it could not be determined whether the application procedures were in accordance with the label.
- H. Issues/items requiring submitter's clarification: No issues requiring clarification were observed by this reviewer.

IV. Summary and Discussion

Linear regression calculations were performed on the average soil residue dissipation data for diquat. The natural logarithms of the average dissipation data were plotted vs. time in days. The correlation coefficient is 0.76. The half-life of diquat dissipation is 7.3 days. It must be recalled that this value was derived from through seven days.

In summary, there are several instances in which this study fails to meet the requirements of Subdivision K and minimum scientific and technical standards. First, the design of the study is flawed. The harvesting of potatoes at Day 7 renders useless data from the samples subsequently collected. The field work should have been organized to provide data for a more extended sampling time. A consequence of this is that too few samples were taken. Second, the submission contained no field recovery data. Third, there is no way to verify the results given the absence of representative chromatograms and handwritten raw data. This study should be considered unacceptable.

TABLE 1

Soil residues of Diquat cation following application
of Diquat Herbicide at 0.25 lb ai/acre

Sampling Day	No. of applications	Mean Diquat concentration (ppm)
Pretreatment	0	<0.01
0	1	2.06
0	2	8.74
1	2	9.26
3	2	4.94
7	2	5.37
7 ^a	2	0.39
14 ^a	2	0.77
21 ^a	2	0.44
28 ^a	2	0.41

^a These samples were collected post-harvest (harvesting occurred on day 7).

CHAPTER 5. EXPOSURE-RELATED STUDIES

Chevron Chemical Company has petitioned that existing worker protection requirements (reentry interval, protective clothing) for the diquat label be relaxed, based on discussions of worker exposure, residue dissipation, and product toxicity. In addition, a study on the rate of penetration of diquat and ethylene dibromide through several protective glove materials was submitted for review. The submitted data were reviewed in the context of this petition in the following sections.

I. Applicator Exposure Issues

- A. Review of Wojcik, G.A., J.F. Price, H.N. Nigg, and J.H. Stamper. 1983. Worker exposure to paraquat and diquat. Arch. Environ. Contam. Toxicol. 12: 65-70. MRID No. 413772-03. HED No. 0-0973

This monitoring study examined herbicide exposure to workers applying paraquat to tomato fields and citrus groves, or diquat to water hyacinths and hydrilla in waterways, in Florida. Total body and respiratory exposures were estimated by using dermal pads attached to applicators on clothing over ten different body areas, and either respirators (paraquat) or personal air monitors worn near workers' breathing zones (diquat). Dermal exposure to hands was estimated from residues rinsed from the hands or by analysis of cotton sampling gloves worn by each worker. Urine samples were taken from all workers within one week pre-application, and on each day the workers were monitored. Workers applying paraquat to tomato fields were monitored during one application period, and those applying paraquat to citrus groves or diquat to waterways were monitored during three separate application periods.

In the tomato fields paraquat was applied via a tractor-drawn sprayer with a drop boom. A 0.05% paraquat spray was applied by workers in normal clearance tractors without cabs (four replicates) or normal clearance tractors with air-conditioned cabs (two replicates), and 0.07% paraquat spray was applied by workers in high-clearance tractors without cabs (two replicates). Rates of a.i. applied per acre were not provided. Paraquat was applied to citrus groves from a tractor-drawn shielded boom sprayer, and all tractors were open and without canopies. Two different areas were treated with two different paraquat spray mixtures; either 0.11% (9 replicates) or 0.07% (6 replicates) (Locations I and II, respectively). Diquat was applied either using hand-operated spray equipment or by injection of diquat directly into the water with an invert system.

Laboratory recoveries of paraquat and diquat from pads averaged 77% and 93%, respectively. Average laboratory recoveries of both herbicides from air sampler foam plugs and respirator pads were 80% and 100%, respectively. However, loss studies under field conditions were not conducted for pads, plugs, or gloves. Urine assay limits ranged from 0.012 - 0.041 ppm for paraquat and 0.007 - 0.021 ppm (one at 0.047 ppm) for diquat urine assays.

Total potential dermal exposure was calculated by extrapolating data on the paraquat and diquat residues found on pads and gloves or rinsed from hands. For dermal and respiratory exposures, it was assumed that the residue found on the collection media represented contamination of the relevant body part. Exposures were given in terms of accumulation of residues on pads ($\mu\text{g}/\text{cm}^2\text{hr}$) and estimated total body exposure (mg/hr). Estimated exposure to each anatomic region (% total body exposure) was also given, and was based on data from Berkow (1931). The Berkow values (except for head, thighs, and upper arms) have been incorporated into those indicated for use by Subdivision U guidelines.

Exposure to paraquat applied to tomatoes was highest for a worker in an open tractor; although not statistically significant, use of an enclosed cab or a high clearance tractor reduced exposure by about 85%. Amounts of residue deposited on the pads differed significantly for three groups of body parts: hands - highest; chest, thighs, back, shins, and arms - intermediate; and shoulders - lowest (see Appendix A). Impermeable gloves and disposable coveralls were suggested as the most important means of protecting workers.

Workers in the two different areas of the treated citrus groves also produced pads with significantly different residue deposits, but the grouping of body part results differed from the tomato field results and also between the two areas. For Location I, residues were highest on the hands, intermediate on thighs, shoulders, and arms, and lowest on the shins, chest, and back. At Location II, the groupings were: hands - highest; thighs, arms and shins - intermediate; and chest, back, and shoulders - lowest (see Appendix A). The difference in results between the two areas was attributed to the different tank concentrations used; 0.11% at Location I and 0.07% at Location II.

For workers spraying diquat on water hyacinths, exposure was highest to hands, thighs and shins. Exposure was almost 10 times greater to applicators (who also were the mixers) than to drivers, who sat 3 ft above the applicators. Mixers of diquat for hydrilla treatment had hands and shins most highly exposed, and received approximately 3 times the

estimated total body exposure as the applicators. The estimated total body exposure of water hyacinth workers was calculated to be 3 times greater than that of hydrilla workers (see Appendix A).

Estimated total body exposures of workers to paraquat and diquat were significantly different for the three application scenarios, and were ranked as tomato>citrus>water hyacinth (waterway). Relative total body exposure ratios were given as 93:12:1, respectively, which the authors suggest is related to work practices; citrus and water hyacinth workers operated in relatively shielded environments, while tomato workers were in open fields subject to the wind.

Urine samples for all but one citrus worker were negative; he had positive results on one day. Respiratory exposure was less than 0.1% of the total body exposure, and the authors suggest this percentage may have been under-estimated because of comparison with the higher levels found on the pads. They also point out the dermal exposure might have been over-estimated since penetration of the herbicides through clothing was not measured.

The authors conclude the data indicate that there is little possible acute danger to applicators, mixers, or drivers from paraquat or diquat. They reiterate their recommendation for the use of gloves and disposable coveralls to reduce paraquat and diquat exposure to non-detectable levels. This study was not strictly reviewed relative to the Subdivision U guidelines as it was conducted and published prior to the promulgation of the guidelines. With two exceptions, the study appears to have been conducted in a valid manner and reported in a manner which allows an estimation of applicator exposure. Field recovery values were not measured, nor were application rates reported in a manner that would allow calculation of exposure in units of mass per pound of a.i. applied. The use of this study in exposure assessment is discussed below.

- B. Submission to EPA by Chevron Chemical Co., titled Permeation Study of Diquat/EDB Against Five Chemical Protective Gloves, by M. Conoley. 1989. 52 pp. MRID413741-00. HED No. 0-0973.

Permeation studies were conducted using a chemical mixture of diquat and ethylene dibromide (EDB) to determine breakthrough times and permeation rates of five commercially available gloves. These were: North Silvershield, Playtex Argus (neoprene/latex), Lab Safety (polyethylene), Travenol Vinyl, and Pioneer Nitrile. The mixture was spiked with additional EDB to raise the concentration to 132 ppm, which is

approximately 10 times the amount expected to be found in commercial diquat.

All permeation tests included a blank. Triplicate samples (8 x 8 cm) were taken from the palm of each glove type and bolted between two halves of an ASTM permeation cell (presumably as described in ASTM Method F 739-85). The cell was kept in a water bath maintained at a constant temperature ($23^{\circ}\text{C} \pm 1.0^{\circ}\text{C}$) and a constant volume of de-ionized water (100 ml/half cell). After waiting an initial 30 min for temperature equilibration of the cell, the diquat/EDB was added to one side of the cell, beginning the test time. The zero time sample was taken just before the diquat/EDB was added.

Samples (2 ml) were taken every 15 min for the first hour, and every 30 min after that up to 8 hrs, when the test was ended. A constant volume was maintained in the cell by adding 2 ml to each half after the sample was withdrawn. Each sample was split into two 1 ml fractions for separate diquat and EDB analyses, and stored (usually 48 hrs) at 5°C until analysis.

One microliter samples in hexane were injected into a Hewlett-Packard gas chromatograph equipped with an electron capture detector for analysis of EDB. The calibration curve based on EDB standards was given with an $r = 0.9999$, and the detection limit based on this curve was 7 ppb EDB. The percent recovery for the extraction of EDB from water samples with hexane averaged 96.7%.

A Cary UV-VIS spectrophotometer was used for analysis of diquat. Test samples were analyzed in 1 cm quartz cells, at 310 nm. The standard curve presented is linear with $r=0.9994$, and the detection limit for the method was given as 0.5 ppm diquat.

Results of analyses were presented in terms of permeation rate ($\mu\text{g}/\text{cm}^2 \text{ min}$) and breakthrough (min), although breakthrough was quantified only as $<15 \text{ min}$ or $>480 \text{ min}$. For diquat, no breakthrough was reported for any glove type for the duration of the test. Breakthrough of EDB was reported in three of the glove types in less than 15 minutes. The permeation rates measured were: Playtex Argus - $0.034 \mu\text{g}/\text{cm}^2$, Lab Safety - 0.15 cm^2 , and Travenol Vinyl - $0.12 \mu\text{g}/\text{cm}^2$. No EDB breakthrough was observed in the other two glove types for the duration of the test.

Sample chromatograms and % recoveries were presented for EDB analysis, but results from spectral and recovery analysis of diquat were not given. Other data gaps in the study report include the lack of raw data for breakthrough times and permeation rates, no description of the EDB

extraction method from the test samples, and no description of the volume of permeant added to the cell for each test.

The study protocol calls for measurement immediately after the permeant is charged into the test cell, but there is no evidence that this was done, nor does the applicant offer an explanation for this deviation. The protocol also states that the test method will be carried out in accordance with ASTM F 739-85, attached to the report as an appendix. However, several deviations or incomplete explanations of methodology chosen from the ASTM guidelines are evident in the study. The ASTM guidelines state that the sensitivity of the test method in detecting low permeation rates is determined by the analytical technique selected and the ratio of material specimen to collected medium volume. There is no discussion of whether this ratio was determined or used in the present study to assess the sensitivity of the test method (potentially important, since diquat was not detected in any test samples), nor was the concentration of the permeant (diquat/EDB) charged into the test cells given. Also, the guidelines state that samples of the test material should be random, but in the study all samples were taken from the palms of the gloves.

There is insufficient information given in the study method to determine whether several other ASTM method guidelines were followed. These include: 1. the test medium should be mixed continuously for the duration of the study to ensure homogeneity and minimization of concentration boundary layers. 2. the permeant should be brought to the temperature of the test cell before it is charged into the cell; and 3. the specimen's (in this case, glove sample) normal outer surface must contact the test chemical.

To conclude, the permeation study appears to have been conducted in a valid manner, although lack of reporting detail and several deviations from the standard ASTM methodology diminish the level of confidence of this conclusion. Diquat did not break through any of the test materials, although EDB, a contaminant of the diquat formulation did break through three of the materials.

II. Worker Protection Issues

- A. Summary of submittal to EPA titled "Basis for Removal of 24-Hour Reentry Restriction on Diquat Label" by K.K. Dougherty, January 11, 1989. 8 pp. MRID 413772-00. HED No. 0-0973.

An agent for the registrant, Valent U.S.A., requested a reassessment of the current 24 hour reentry interval for uses on golf courses, fields, and rights of way. The basis for the request is that "no adverse health hazard or risk would be expected even when reentry occurs immediately after the spray has dried and under the most extreme exposure conditions." Information about diquat's physical and chemical properties, dislodgeable residues, toxicity in animal studies, and skin penetrability is given to support this argument. The following is a summary of the presented information and reviewer response.

1. Physical and Chemical Properties

The diquat dibromide salt is a highly ionized water soluble salt. The diquat cation binds "tenaciously" to plant and soil material, so it is unavailable for dermal absorption.

Comment: The reference cited in the petition regarding the binding capacity (Tucker et al. 1967 J. Agric. Food Chem 15:1005) was reviewed for accuracy relative to the above quoted binding capacity of diquat. Although the study illustrates the well-documented soil binding capacity of bipyridylum herbicides, no mention was found of a similar binding capacity in plant material. Therefore, this argument on the lack of foliar availability for reentry exposures is invalid.

2. Dislodgeable Residues

The maximum dislodgeable diquat cation residue is cited from a study of Bermuda grass as $2.1 \mu\text{g}/\text{cm}^2$, one hour after treatment at the maximum rate directed by the label. At four hours post-application, the dislodgeable residue was approximately 65% of the initial measurement.

Comment: These data are utilized by the registrant to develop an exposure- and risk assessment, as discussed below. Based on the review presented in Chapter 3, this study has several deficiencies which limit its usefulness to support this intended purpose.

3. Animal Toxicity

Results of acute oral, dermal, and eye irritation toxicity tests in rats and rabbits place diquat in the FIFRA Toxicity Category II, while results of an acute inhalation test in rats places it in Category III and a skin irritant study in rabbits places it in Category IV. A NOEL of 5 mg diquat cation/kg/day was derived from a 21-day subchronic dermal study in rats. The applicant's review of medical and scientific literature revealed no substantiated reports of systemic diquat poisoning after skin contact.

Comment: Since the toxicological basis for the 24 hour reentry interval was not discussed, the merit of this argument cannot be judged.

4. Skin Penetration Studies

In vitro and in vivo studies conducted within animals and humans indicate that diquat has a low rate of percutaneous absorption, with humans having less permeable skin than other species. The human dermal absorption rate of 0.3%/10 hours was used (see 5) to estimate a worker margin of safety.

Comment: The referenced absorption factors have been submitted to the Agency and presumably have been found acceptable. However, as discussed below, the registrant's use of this value was invalid.

5. Margins of Safety

Margins of safety of 2800 were calculated using maximum measured turf dislodgeable residue (2.1 ug/cm^2), dermal absorption data, and a rat subchronic NOEL of 5 mg/kg/day. The exposure calculation assumed an individual entered a treated area one hour after application (i.e. the spray had dried), and contacted and transferred the maximum turf dislodgeable residue of 2.1 ug/cm^2 over the entire $20,000 \text{ cm}^2$ body surface area. Body weight was 70 kg., and dermal penetration rate (no clothing protective effect) of 0.3% per 10 hours. Therefore, daily exposure rate was estimated as $2.1 \text{ ug/cm}^2 \times 20,000 \text{ cm}^2 / (70 \text{ kg})(0.003)$, or 0.0018 mg/kg/day . Compared to a subchronic NOEL of 5 mg/kg/day was obtained, a margin of safety of 2,800 was calculated. The applicant therefore proposed the removal of the 24-hour re-entry interval required by the label, since there is no basis that reentry into a treated field after the spray has dried may potentially cause adverse health effects.

Comment: The exposure calculation approach used by the petitioner appears on the surface relatively conservative, but the assumption that

exposure is equivalent to complete body area cover contact with turf is undocumented. Therefore, the generic Zweig/Popendorf equation was used to confirm the exposure estimate, making the uncertain assumption (as did the registrant) that the 2.1 ug/cm^2 dislodgeable residue value is valid.

Therefore, $2.1 \text{ ug/cm}^2 \times 10,000 \text{ cm}^2 \text{ per hour} \times 8 \text{ hours} / 70 \text{ kg} = 2.4 \text{ mg/kg/day}$, approximately 4 times higher than the registrant estimate of external exposure (0.6 mg/kg/day).

However, the application of a dermal absorption factor to adjust human exposure estimates (internal dose) is invalid when the result is compared to a rat dermal study for the purpose of calculating a margin of safety. Thus, the MOS of 2800 calculated in the petition is actually 8. If the exposure estimate of this review is used instead, 2.4 mg/kg/day , the MOS is only 2. These margins of safety are insufficient to allow immediate reentry following the drying of the applied product.

- B. Summary of submittal to EPA titled "Basis for Changing the Diquat Label Protective Clothing Statement by K.K. Dougherty, January 11, 1989. 11 pp. MRID 413772-02. HED No. 0-0973.

The applicant also contends that the current label-required protective equipment for handling diquat: face shield or goggles; protective clothing; and rubber footwear for handling concentrate, and waterproof footwear and clothing for spraying (except aquatic subsurface) is unnecessary based on available exposure and toxicity data.

Instead, the following is recommended as label-required protection: "Wear long-sleeved shirt, long pants, face shield, rubber gloves, rubber apron and rubber boots when handling concentrate. When applying diluted material or when using aquatic subsurface application methods, wear long-sleeved shirt, long pants, rubber gloves, and rubber boots. When contacting vegetation wet with spray, wear long sleeved shirt, long pants, and rubber boots." In short, the applicant is requesting a waiver of the requirement for waterproof clothing when applying the diluted material. This request is based on the same toxicological and dermal absorption arguments forwarded in Section II.A above, and a discussion of applicator exposure drawn from the Wojek et al. paper review in Section I.A.

The highest mean non-aquatic applicator exposure rate measured by Wojek et al. was 168.59 mg/hr for application of paraquat to tomatoes via open cab boom equipment, translating into a rate of 0.0578 mg/kg/day for an 8 hour day and adjusting for dermal penetration. Using the paper's data on the proportion of exposure due to hands, use of impermeable

gloves would reduce exposure to 0.04335 mg/kg/day. Margins of safety presented in the submission thus are 115 for the use of gloves and 86 without gloves. These calculations assume complete penetration of the active ingredient through clothing. However, as discussed above, it is not valid to apply dermal absorption corrections to exposure estimates when calculating margins of safety relative to animal dermal no effect level data (as was done in the submission). Therefore, the margins of safety are actually 0.3 and 0.4 for the ungloved and gloved workers. Similarly, the reported margins of safety for the next highest exposure scenario, citrus open cab boom application of 1111 with gloves and 833 without gloves, are actually 3 and 2.5, when dermal absorption is not factored into the calculation. Finally, reported margins of safety for aquatic diquat application of 15151 with gloves and 11,363 without, are 45 and 32.

III. Summary

The arguments presented by the registrant with regard to elimination of reentry intervals and reduction in protective clothing requirements for non-aquatic uses based on adequate margins of safety are invalid. The primary reason is the adjustment of exposure estimates for dermal absorption prior to comparison to a rat dermal NOEL. This is an acceptable procedure when only oral toxicity data is available, but dermal NOELs are reported in terms of total external dosage. Recalculation of margins of safety to correct for this error gives values of less than 10 for all non-aquatic uses, which may not adequately protect worker health.

In addition, the usefulness of the submitted diquat foliar dissipation study on turf is limited at best for the purpose of determining reentry intervals, primarily due to deficient reporting of residue levels. Similarly, the Wojek et al. study used to characterize worker exposure is limited, primarily due to lack of information on application rate and inadequate study QA/QC relative to current Subdivision U standards.

It is suggested that the registrant submit a properly designed foliar dissipation study for consideration of elimination of the current reentry interval. In addition, the registrant may wish to estimate applicator exposure with generic data as contained in the Pesticide Handlers Exposure Data Base. The exposure rates reported by Wojek et al. (ca. 170 mg/hour) seem high based on this reviewer's experience. Basing exposure on a the larger sample size available in the data base, using the current maximum application rate, may provide a more accurate basis for determining the necessary level of protective clothing.

APPENDIX A

DERMAL EXPOSURE MEASUREMENTS

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Archives of Environmental Contamination and Toxicology 12, 65-70 (1983)