MEMORANDUM

TO: Al Nielsen EPA/OPP/OREB

cc: 2110.003 File
Tim Leighton
Jeff Evans

FROM: Jeff Dawson

DATE: September 14, 1993

SUBJECT: Summary Review of Chlorothalonil Storage Stability Data

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Storage stability data were submitted in support of the reregistration requirements for the broad-spectrum fungicide, chlorothalonil, specified by the U.S. Environmental Protection Agency (i.e., the Agency) under both Subdivisions K and U of the Pesticide Assessment Guidelines (U.S. EPA, 1984/U S. EPA, 1986/U.S. EPA, 1988). To summarize, the stability data were submitted in support of the following three exposure studies: (1)"A Tomato Harvester Exposure Study With Chlorothalonil"/EPA MRID 00147976, (2)"A Mixer, Applicator, and Mower Exposure Study With Chlorothalonil for Golf Course Maintenance - 1985"/EPA MRID 424338-10, and (3)"A Golfer Exposure Study With Chlorothalonil Used For Golf Course Maintenance - 1985"/EPA MRID 424338-11. [Note: Reviews of each of these companion studies are complete and have been submitted or will be submitted concurrently with this review.]

The following information can be used to identify the storage stability data submitted for review (i.e., 3 separate documents are included as part of the data which were reviewed):

Titles:	(1) Residues of 2,4,5,6-Tetrachloro- isophthalonitrile (chlorothalonil, SDS-2787) on Field Samples From The Method Development Pilot Tomato Harvester Exposure Study - 1984 (2) Same Title: Amendment to # (1) (3) Turf Study Memo Dated April 10, 1986
Sponsor/Performing Laboratory:	ISK Biotech Corporation 5966 Heisley Road P.O. Box 8000 Mentor, Ohio 44061
Authors:	C. King, P.M. Price
Report Dates:	(1) March 1, 1985 (2) August 22, 1988 (3) April 10, 1986
Identifying Codes: (No MRIDs Assigned To Date)	(1) 655-3MD-84-0024-001-001/ISK Doc. # (2) 655-3MD-84-0024-001-002/ISK Doc. # (3) 758-3HE-85-0051 & 0059/Activity File #

Most dosimeter/sample matrices used in each of the exposure studies were evaluated in the storage stability studies (i.e., "air tubes", "air filters", "gauze pads", "gloves", "socks"). [Note: Several matrices were not utilized/addressed in the storage stability studies including: work gloves from the mixer, applicator, mower study; no distinction was made between outer and inner sock materials used in both golf course studies; whole tomatoes from the harvester study; and leaf

dislodging solutions from the harvester study.] The first phase of storage stability data (i.e., 655-3MD-84-0024-001-001 & 002) involved all matrices except socks for storage intervals up to 120 days. The second phase of the study used "gauze pads and socks to cover the extended freezer storage time that was not covered in the previous stability study" (i.e., the first phase).

In the first phase, "the SDS Biotech randomization scheme from the SDS Biotech Integrated Statisitical Package was used to randomly select fortified control samples for storage at -20° ± 5°C. Samples from the stability study were generated from the lab. They were not samples sent in from the field study. Samples were fortified as follows: The air tubes were scored and broken to allow direct application of the standard to the chromsorb via 701N Hamilton Syringe. The filters were placed in 20 mL scintillation vials and fortified directly via 701N Hamilton Syringe. The gauze pads were fortified directly, folded and placed in 50 mL jars. The gloves were placed on a piece of aluminum foil, fortified directly, folded, cut, and placed in 200 mL jars. After being fortified, samples were stored until time of assay. At intervals varying from 0 to 120 days, selected samples were removed from storage, allowed to come to room temperature and assayed for chlorothalonil." In the second phase, "samples were prepared, randomized, and assayed as in the previous [phase of the] stability study. Socks and gauze pads were placed on a piece of aluminum foil, fortified directly, folded and placed in appropriate size jars. These samples were stored at -20° ± 5°C until the time of assay."

The analytical procedure for each matrix involved extraction (reciprocal shaking) of chlorothalonil residues with toluene (various volumes and extraction times depending upon matrix), followed by dilution if appropriate, then direct quantitation by GC. Additionally, it was indicated that "samples were quantitated as described under quantitation in report document number 655-3MD-84-0024-001." [Note: This number is the same ISK Document number which was assigned to phase 1 of the storage stability study (i.e., *Residues of Tetrachloroisophthalonitrile (chlorothalonil, SDS 2787), On Field Samples From The Method Development Pilot Tomato Harvester Exposure Study - 1984*).]

No other significant information was provided regarding the analytical aspects of the storage stability study except for the fact that some sort of quality control samples ("Amended Samples") were generated/analyzed and included in the report (i.e., no explanation was provided regarding the origin of these samples). The results for all "Amended" samples are presented below.

"Amended" Sample Results

Sample Matrix	Fortification Range	N	Recovery (%) Mean	Std. Dev.

Air Tubes	0.20 ug/sample	6	94.2	7.36
Air Filters	0.40 ug/sample	8	97.1	6.15
Gauze Patches	100.0 ug/sample	8	102.9	6.47
Gloves	1000.0 ug/sample	8	103.8	5.44
Gauze Patches[1]	1.0 to 100.0 ppm	8	104.0	4.27
Socks[1]	100.0 ppm	8	99.6	6.78

(1) Recovery values reported in phase 2 of the storage stability study.

All storage stability data which were reported are summarized below on an individual sample matrix basis (i.e., filters, tubes , etc.). For all storage stability samples in phase 1 of the study, the fortification levels were identical to those reported above for the "Amended Samples" and there were always 5 samples analyzed at each interval except for the gauze patches at the 90 day interval (i.e., N=4 for that interval). For phase 2 of the study, no specific fortification levels were identified in the report and 6 samples were always analyzed at each storage interval.

Storage Stability Data Summary

Storage Interval (Days)	Recovery/Standard Dev.					
	Gloves [1]	Filters [1]	Gauze Pads[1]	Air Tubes [1]	Gauze Pads [2]	Socks [2]
0	102.2/1.92	96.8/1.64	103.6/9.07	94.0/4.18	105.0/3.13	101.0/2.69
7	100.4/0.89	102.2/3.11	91.2/2.68	109.0/2.24	ND	ND
21	94.6/3.21	100.2/8.56	100.8/9.07	105.0/8.66	ND	ND
60	98.6/3.05	97.8/1.79	105.6/10.36	101.0/7.42	ND	ND
75	ND	ND	ND	ND	91.4/1.82	103.4/1.41
90	ND	ND	74.0/3.65	81.0/5.48	ND	ND
120	97.2/6.34	98.4/0.89	ND	ND	ND	ND
121	ND	ND	ND	ND	103.3/3.28	101.9/0.83
133	ND	ND	ND	ND	97.6/5.30	101.4/1.73

"ND" No data are available for storage interval.
(1) Samples generated and analyzed in phase 1 of the study. All values for phase 1 are presented as (%) recovery/std. dev..
(2) Samples generated and analyzed in phase 2 of the study. Also no fortification levels were specified for these samples. As such, the results are presented as (ppm) values. Evaluations of stability over time must be made based on comparisons to the results for the Day 0 sample analyses.

The field sample storage intervals for all matrices from each of the chlorothalonil exposure studies in which this storage stability study was referenced are summarized below. No other information was provided in the concurrent exposure studies outside of what has been already summarized above. The field phase of the tomato harvester study was conducted during the

interval ranging from June 18 to June 25, 1984. The "actual last assay dates for exposure samples" are reported below along with the sample storage interval (days) and a comparison with the stability sample storage intervals for each test matrix. [Note: All field sample storage intervals are maximums for each matrix at each study site.]

Storage Intervals/Tomato Harvester Study

Sample Matrix	Last Analysis Date	Field Sample Storage Interval (Days)	Field vs. Stability Comparison
Air Filters	7/10/84	22	Acceptable
Air Tube Adsorbents	7/13/84	25	Acceptable
Dermal Patches	8/17/84	60	Acceptable
Gloves	9/5/84	79	Acceptable

(1) "Acceptable" indicates stability sample storage interval exceeded or was equivalent to the field sample storage interval. "Unacceptable" indicates these criteria were not met.

The field phase of the mixer/applicator/mower study was conducted during the interval ranging from August 14 through August 28, 1985 at the Deer Lake golf course and from September 10 through September 25, 1985 at the Quail Hollow Golf Course. The "last assay dates" for the field samples for each study site are reported below along with the sample storage interval (days) and a comparison with the stability sample storage intervals for each test matrix.

Storage Intervals/Mixer, Applicator, Mower Study

Sample Matrix	Deer Lake Last Analysis Date	Field Sample Storage Interval (Days)	Field vs. Stability Comparison [1]	Quail Hollow Last Analysis Date	Field Sample Storage Interval (Days)	Field vs. Stability Comparison [1]
Air Filters	10/31/85	78	Acceptable	11/1/85	52	Acceptable
Air Tube Adsorbents	10/24/85	71	Acceptable	10/28/85	48	Acceptable
Dermal Patches	12/5/85	113	Acceptable	1/3/86	115	Acceptable
Gloves	12/19/85	119	Acceptable	1/17/86	129	Unacceptable
Socks	12/17/85	117	Acceptable	1/28/86	140	Unacceptable

(1) "Acceptable" indicates stability sample storage interval exceeded or was equivalent to the field sample storage interval. "Unacceptable" indicates these criteria were not met.

The field phase of the golfer study was conducted on August 20, 1985 at the Deer Lake Golf Course while the field phase of the study was conducted on September 17, 1985 at the Quail Hollow Golf Course. The "last assay dates" for the field samples for each study site are reported below along with the sample storage interval (days) and a comparison with the stability sample storage intervals for each test matrix.

Storage Intervals/Golfer Study

Sample Matrix	Deer Lake Last Analysis Date	Field Sample Storage Interval (Days)	Field vs. Stability Comparison [1]	Quail Hollow Last Analysis Date	Field Sample Storage Interval (Days)	Field vs. Stability Comparison [1]
Air Filters	10/31/85	72	Acceptable	11/1/85	45	Acceptable
Air Tube Adsorbents	10/23/85	64	Acceptable	10/25/85	38	Acceptable
Dermal Patches	11/27/85	99	Acceptable	1/20/86	125	Acceptable
Gloves	12/13/85	115	Acceptable	1/16/86	121	Unacceptable
Socks	12/6/85	108	Acceptable	1/28/86	133	Acceptable

(1) "Acceptable" indicates stability sample storage interval exceeded or was equivalent to the field sample storage interval. "Unacceptable" indicates these criteria were not met.

A Good Laboratory Practice Compliance Statement was provided in phase 1 of the storage stability study which was dated 3/1/85 and signed by Barbara L. Haley (Group Leader: Quality Assurance/Data Management Operations). The statement "concluded that this report accurately reflects the conduct of the study." The specific inspection dates were presented. However, the phases of the study which were audited were not identified.

Compliance with Subdivisions K and U of the Pesticide Assessment Guidelines (U.S. EPA, 1984/U.S. EPA, 1986/U.S. EPA, 1988) is critical if a study is to be considered acceptable. Storage stability data as well as any other analytical quality control data (i.e., laboratory and field recovery) are required as part of any acceptable human exposure monitoring study. Inadequacies and inconsistencies that were identified with the freezer storage stability study are presented below in an itemized fashion.

- The analytical data which were presented in the report are inadequate as no chromatograms were presented, the description of the analytical techniques used to extract the storage samples were incomplete (i.e., referenced the document number assigned to phase 1 of the study and no data/information were provided in the document), no explanantion was provided regarding the origin of the "Amended" samples, and no SOPs were provided/discussed regarding common laboratory issues (e.g., glassware prep and GC instrument operations/calibration).

- A specific rationale for issuing an amendment to phase 1 of the study (i.e., document 655-3MD-84-0024-002) was not provided. The type of error that precipitated the alteration of the reported results should be identified/detailed as the type of error may impact the reliability of the reported value (e.g., manipulation

of chromatographic data is more critical than a calculation error).

- Preparation of the sample matrices (i.e., dosimeters) for use in this study was not described in the study report. Additionally, it could not be determined if the same group/lot of dosimeters were used in the storage stability study as were used in the field phases of each of the studies; significant impacts on analytical processes can be caused due to varying matrix effects from dosimeters.

- The storage vessels used in the stability were not adequately described in the study. Additionally, it could not be determined if the same types of vessels were used in each of the field studies and the storage stability study.

- The duration of the stability sample storage interval met or exceeded the duration of the field sample storage interval except for three instances (i.e., gloves from Quail Hollow during the golfer and mixer/applicator/mower study and socks from Quail Hollow in the mixer/applicator/mower study). An explanation needs to be provided regarding this fact.

- Chlorothalonil storage stability was not evaluated on several matrices critical to the evaluation of exposure levels in the three exposure studies including the whole tomatoes and the foliar dislodgeable residue solutions/foliage samples (it is unclear from the study when the dislodging procedure was completed in relation to the remaining aspects of the analysis) and the work gloves worn by the mixers and applicators in the golf course study.

- It could not be determined from the available data if the storage stability study was conducted concurrently with the field studies. Additionally, it could not be determined if the stability samples were stored under identical conditions as the actual field samples (i.e., the same freezer) thereby allowing direct comparison of the results. Based on the available information it appears as though the samples were stored under at least similar conditions. However, the report did not definitively indicate that the storage conditions were constant or if any deviations from these conditions occured.

- Good Laboratory Practice requirements stipulate that the test material for any study that is conducted for FIFRA registration purposes be characterized. No such data/information were provided regarding the chlorothalonil used to fortify the

samples in this study.

- Storage stability samples for each matrix were only fortified at a single fortification level. Data generated using a range of fortification levels enhance the reliability of the results because it is more likely that a fortification level in the study may closely approximate actual residue levels in field samples.

- Environmental fate data were not provided to support the study design. Any metabolites/degradates of concern should have been included for evaluation in the study.

To summarize, the freezer storage stability study completed in support of the regulatory requirements for chlorothalonil should not be considered acceptable for regulatory purposes by the Agency. This rejection is based on several major criteria including, but not limited to the following: concurrent laboratory recovery samples were not clearly defined in the study report; the QA/QC regimen during routine analysis was inadequate; no environmental fate data were submitted to support the study design; some matrices from the exposure study were not evaluated; and the storage conditions for the stability study were not clearly defined/described. Additionally, several other inadequacies/inconsistencies were noted in the study results.

Should you have any additional questions please feel free to call at 703-750-3000.

Enclosures:

- Correspondence including pertinent study documents.

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R132833

Chemical: Chlorothalonil

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081901
HED File Code: 19050 Versar DER Warning: May not have been QAed by EPA--
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