**Data Evaluation Report on the acute toxicity of Penoxsulam on the Freshwater Diatom, *Navicula pelliculosa***
PMRA Submission #:{.....} EPA MRID #: 45831121

**Data Requirement:**

| | |
|---|---|
| PMRA DATA CODE | {.....} |
| EPA DP Barcode | D288160 |
| OECD Data Point | {.....} |
| EPA MRID | 45831121 |
| EPA Guideline | 123-2 |

**Test material:** Penoxsulam Purity: 97.5%
Common name: XDE-638
Chemical name: IUPAC: Benzenesulfonamide,2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[pyrimidin-2-yl)-6-(trifluoromethyl)
CAS name: Not reported
CAS No.: Not reported
Synonyms: Not reported

**Primary Reviewer**: Rebecca Bryan
Staff Scientist, Dynamac Corporation
**Signature:** Rebecca Bryan
**Date:** 12/29/03

**QC Reviewer:** Dana Worcester
Staff Scientist, Dynamac Corporation
**Signature:** Dana Worcester
**Date:** 12/29/03

**Primary Reviewer:** ~~Bill Erickson~~ J. GOODYEAR
**{EPA/OECD/PMRA}**
**Date:** {.....} Goodyear

**Secondary Reviewer(s):** {.....}
**{EPA/OECD/PMRA}**
**Date:** {.....}

**Company Code** {.....} [For PMRA]
**Active Code** {.....} [For PMRA]
**EPA PC Code** 1~~09031~~ 119031

**Date Evaluation Completed:** {dd-mmm-yyyy}

**CITATION:** H.D. Kirk, M.M Gilles, E.L. McClymont, and L.G. McFadden. 2000. XDE-638: Growth Inhibition Test with the Freshwater Diatom, *Navicula pelliculosa*. Unpublished study performed by Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan. Laboratory Project Identification No. 001001. Study submitted by Dow AgroSciences, LLC, Indianapolis, Indiana. Experimental start date March 23, 2000 and experimental termination date March 28, 2000. The final report issued June 9, 2000.

issued June 9, 2000.

**EXECUTIVE SUMMARY:**

In a 120-hour acute toxicity study, cultures of ***Navicula pelliculosa*** were exposed to Penoxsulam, as XDE-638, under static conditions. The nominal concentrations were 0 (negative control), 1.56, 3.13, 6.25, 12.25, 25, and 50 mg a.i./L. The mean measured concentrations were <0.12 (LOQ, negative control), 1.38, 2.65, 5.2, 10.7, 24, and 49.6 mg a.i./L. The 120-hour cell density percent inhibitions were 24.0, 28.5, 15.9, 28.0, 32.8, and 18.6% for the 1.38, 2.65, 5.20, 10.7, 24.0, and 49.6 mg a.i./L treatment groups, respectively. There were no significant effects on cell density. The $EC_{50}$ was >49.6 mg a.i./L, the $EC_{05}$: could not be determined, and the NOAEC was 49.6 mg a.i./L for cell density.

The study is scientifically sound; however, because the replicate number was lower than recommended and there was high cell density variability within and among the treatment groups, this study does not satisfy the U.S. EPA Guideline Subdivision J, §123-2 for an aquatic nonvascular plant study with *Navicula pelliculosa*. As a result, this study is classified as Supplemental, but it need not be repeated.

**Results Synopsis**

Test Organism: *Navicula pelliculosa*
Test Type: Static

**Cell Density:**
NOAEC: 49.6 mg a.i./L
$EC_{05}$: could not be determined
$EC_{50}$: >49.6 mg a.i./L 95% C.I.: N/A

Endpoint(s) Affected: None.

## I. MATERIALS AND METHODS

**GUIDELINE FOLLOWED:** The test was based on the following guideline: U.S. EPA-FIFRA Pesticide Assessment Guidelines, Subdivision J, Hazard Evaluation: Nontarget Plants Guideline 123-2, Growth and Reproduction of Aquatic Plants Tier 2. The following deviations from U.S. EPA Guideline, §123-2 are noted:

1. The values of pH at test initiation and termination were not specified, but a range was reported.

2. Three replicates per treatment group were tested, which is less than the recommended 4 replicates for *Navicula pelliculosa*. This deviation was considered to have affected the acceptability of this study because there was high cell density variability within and among treatment groups. The low replicate number resulted in low statistical power and, thus, contributed to the inability to detect potential differences from control.

3. Observations were not conducted every 24 hours. However, data was recorded at 0, 72, 96 and 120 hours.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance and No Data Confidentiality statements were provided.

**A. MATERIALS:**

**1. Test Material** Penoxsulam, XDE-638

**Description:** Pink, solid powder

**Lot No./Batch No. :** ND05167938

**Purity:** 97.5%

**Stability of Compound**
**Under Test Conditions:** The mean measured concentrations of XDE-638 were 79.9-95.8% of nominal at hour 0 and 82.4-102% of nominal at hour 120 (Table 3, p. 23).

*(OECD requires water solubility, stability in water and light, pKa, Pow, vapor pressure of test compound)*

**Storage conditions of test chemicals:** Not reported

**2. Test organism**:
**Name:** *Navicula pelliculosa*

*EPA requires a nonvascular species: For tier I testing, only one species, S. capricornutum, to be tested; for tier II testing, S. costatum, A. flos-aquae, S. capricorntum, and a freshwater diatom is tested*

*OECD suggests the following species are considered suitable: S. capricornutum, S. subspicatus, and C. vulgaris. If other species*

*are used, the strain should be reported*

**Strain:** Not reported
**Source:** Originally from Carolina Biological Supply Company, Burlington, NC. Current in-house laboratory cultures.
**Age of inoculum**: 4-5 days old
**Method of cultivation:** Supplemented Algal Assay Medium (Appendix B, p. 37).

**B. STUDY DESIGN:**

a) Range-finding Study: A 120-hour range-finding study with XDE-638 was conducted in order to estimate the nominal test concentrations for the definitive study. The range-finder test concentrations were 0.259, 2.59, and 25.9 mg a.i./L. The 120-hour $EC_{50}$ value and NOAEC were reported as >25.9 and 25.9 mg a.i./L, respectively.

b) Definitive Study

**Table 1 . Experimental Parameters**

| Parameter | Details | Remarks<br>*Criteria* |
|---|---|---|
| Acclimation period:<br>culturing media and conditions: (same as test or not) | Continuous<br>Supplemented Algal Assay Medium (Appendix B, p. 37); same as test, except for chelant used in cultures. | Inoculum used in test was taken from stock culture and transferred to fresh medium 4-5 days before testing.<br>*EPA recommends two week acclimation period.* |
| health: (any toxicity observed) | Not reported | *OECD recommends an amount of algae suitable for the inoculation of test cultures and incubated under the conditions of the test and used when still exponentially growing, normally after an incubation period of about 3 days. When the algal cultures contain deformed or abnormal cells, they must be discarded.* |
| Test system<br>static/static renewal:<br>renewal rate for static renewal: | Static | |
| Incubation facility | Incubator | |
| Duration of the test | 120 hours | *EPA requires: 96 - 120 hours* |

| Parameter | Details | Remarks<br>*Criteria* |
|---|---|---|
| | | *OECD: 72 hours* |
| Test vessel<br>material: (glass/polystyrene)<br>size:<br>fill volume: | Borosilicate Erlenmeyer flasks<br>250 mL<br>50 mL | *OECD recommends 250 ml conical flasks are suitable when the volume of the test solution is 100 ml or use a culturing apparatus.* |
| Details of growth medium<br>name:<br><br>pH at test initiation:<br>pH at test termination:<br>Chelator used:<br>Carbon source:<br>Salinity **(for marine algae):** | <br>Supplemented Algal Assay Medium<br>7.3-7.9 (during entire test)<br>Not reported<br>No<br>$NaHCO_3$<br>N/A | The values of pH at test initiation and termination were not reported.<br><br>*OECD recommends the medium pH after equilibration with air is ~8 with less than .001 mmol/l of chelator if used.*<br><br>*EPA recommends 20X-AAP medium.* |
| If non-standard nutrient medium was used, detailed composition provided (Yes/No) | N/A | |
| Dilution water<br>source:<br>type:<br>pH:<br>salinity **(for marine algae):**<br>water pretreatment (if any):<br>Total Organic Carbon:<br>particulate matter:<br>metals:<br>pesticides:<br>chlorine: | <br>Deionized water<br>Not reported<br>7.0-7.5<br>N/A<br>None<br>Not reported<br>Not reported<br>Not reported<br>Not detected<br>Not reported | *EPA pH: Skeletonema costatum= ~8.0 Others = ~7.5 from beginning to end of the test. EPA salinity: 30-35 ppt. EPA is against the use of dechlorinated water.*<br><br>*OECD: pH is measured at beginning of the test and at 72 hours, it should not normally deviate by more than one unit during the test.* |
| Indicate how the test material is added to the medium (added directly or used stock solution) | Stock solutions | |
| Aeration or agitation | Agitation, 75 rpm | *EPA recommends agitation only for Selenastrum at 100 cycles per min and Skeletonema at ~60 cycles per min. Aeration is not recommended.* |

| Parameter | Details | Remarks<br>*Criteria* |
|---|---|---|
| Initial cells density | Approximately 10,000 cells/mL (actual range: 14,007-15,226 diatoms/mL) | *EPA requires an initial number of 3,000 - 10,000 cells/mL. For Selenastrum capricornutum, cell counts on day 2 are not required.*<br><br>*OECD recommends that the initial cell concentration be approximately 10,000 cells/ml for S. capricornutum and S. subspicatus. When other species are used the biomass should be comparable.* |
| Number of replicates<br>control:<br>solvent control:<br>treated ones: | <br>3<br>3<br>3 | Three replicates with plants, one replicate without plants.<br><br>*EPA requires a negative and/or solvent control with 3 or more replicates per doses. Navicula sp.tests should be conducted with four replicates.*<br><br>*OECD preferably three replicates at each test concentration and ideally twice that number of controls. When a vehicle is used to solubilize the test substance, additional controls containing the vehicle at the highest concentration used in the test cultures should be included in the test.* |
| Test concentrations<br>nominal:<br><br>measured: | <br>0 (negative control), 1.56, 3.13, 6.25, 12.25, 25, and 50 mg a.i./L<br><br><0.12 (LOQ, negative control), 1.38, 2.65, 5.2, 10.7, 24, and 49.6 mg a.i./L | *EPA requires at least 5 test concentrations, with each at least 60% of the next higher one.*<br><br>*OECD recommends at least five concentrations arranged in a geometric series, with the lowest concentration tested should have no observed effect on the growth of the algae. The highest concentration tested should inhibit growth by at least 50% relatively to the control and, preferably, stop growth completely.* |

| Parameter | Details | Remarks<br>*Criteria* |
|---|---|---|
| Solvent (type, percentage, if used) | N/A | |
| Method and interval of analytical verification | HPLC; 0 and 120 hours | |
| Test conditions<br>temperature:<br>photoperiod:<br>light intensity and quality: | 22.6-23.3°C<br>Continuous<br>3220-4700 lux | *EPA temperature: Skeletonema: 20 °C, Others: 24-25 °C; EPA photoperiod: S. costatum 14 hr light/ 10 hr dark, Others: Continuous; EPA light: Anabaena: 2.0 Klux (±15%), Others: 4 - 5 Klux (±15%)*<br><br>*OECD recommended the temperature in the range of 21 to25°C maintained at ± 2°C and continuous uniform illumination provided at approximately 8000 Lux measured with a spherical collector.* |
| Reference chemical {if used)<br>name:<br>concentrations: | N/A | |
| Other parameters, if any | None | |

**2. Observations:**

**Table 2: Observation parameters**

| Parameters | Details | Remarks/Criteria |
|---|---|---|
| Parameters measured including the growth inhibition/other toxicity symptoms | Cell count | *EPA recommends the growth of the algae expressed as the cell count per mL, biomass per volume, or degree of growth as determined by spectrophotometric means.* |
| Measurement technique for cell density and other end points | Electron particle counting using a Coulter Multisizer. | *EPA recommends the measurement technique of cell counts or chlorophyll a*<br><br>*OECD recommends the electronic particle counter, microscope with counting chamber, fluorimeter, spectrophotometer, and colorimeter. (note: in order to provide useful measurements at low cell concentrations when using a spectrophotometer, it may be necessary to use cuvettes with a light path of at least 4 cm).* |
| Observation intervals | 0, 72, 96, and 120 hours | Observations were not conducted every 24 hours.<br>*EPA and OECD: every 24 hours.* |
| Other observations, if any | None | |
| Indicate whether there was exponential growth in the control | Yes, dilution water group cell densities at test termination was 68.6X greater than the dilution water control group cell densities at test initiation. | *EPA requires control cell count at termination to be ≥2X initial count or by a factor of at least 16 during the test.*<br><br>*OECD: cell concentration in control cultures should have increased by a factor of at least 16 within three days.* |
| Were raw data included? | Yes | |

## II. RESULTS and DISCUSSION:

### A. INHIBITORY EFFECTS:

The 120-hour cell density percent inhibitions were 24.0, 28.5, 15.9, 28.0, 32.8, and 18.6% for the 1.38, 2.65, 5.20, 10.7, 24.0, and 49.6 mg a.i./L treatment groups, respectively.

**Table 3: Effect of Penoxsulam, XDE-638, on freshwater diatom (*Navicula pelliculosa*)**

| Treatment mean measured and nominal concentrations [a] (mg a.i./L) | Initial cell density (cells/mL) | Mean Cell density (cells/mL) at | | |
|---|---|---|---|---|
| | | 72 hours | 120 hours | |
| | | | cell count | % inhibition |
| Dilution water control | 15,226 | 240,507 | 1,044,804 | -- |
| 1.38 (1.56) | 14,084 | 159,928 | 794,200 | 24.0 |
| 2.65 (3.13) | 14,007 | 169,763 | 746,774 | 28.5 |
| 5.2 (6.25) | 14,597 | 139,144 | 879,189 | 15.9 |
| 10.7 (12.5) | 14,510 | 173,329 | 752,137 | 28.0 |
| 24 (25) | 15,114 | 146,443 | 702,271 | 32.8 |
| 49.6 (50) | 14,979 | 183,188 | 850,834 | 18.6 |
| Reference chemical (if used) | N/A | N/A | N/A | N/A |

[a] The nominal test concentrations are presented in parentheses.

**Table 4: Effect of Penoxsulam, XDE-638, on the freshwater diatom *Navicula pelliculosa***

| Mean Measured and Nominal Treatment Concentrations [a] (mg a.i./L) | Initial cell density (cells/mL) | Mean Growth Rate per day | % inhibition (Mean Growth Rate per day) | Mean Area Under Growth Curve | % inhibition (Mean Area Under Growth Curve) |
|---|---|---|---|---|---|
| Dilution water control | 15,226 | Not reported | Not reported | Not reported | Not reported |
| 1.38 (1.56) | 14,084 | Not reported | Not reported | Not reported | Not reported |
| 2.65 (3.13) | 14,007 | Not reported | Not reported | Not reported | Not reported |
| 5.2 (6.25) | 14,597 | Not reported | Not reported | Not reported | Not reported |
| 10.7 (12.5) | 14,510 | Not reported | Not reported | Not reported | Not reported |
| 24 (25) | 15,114 | Not reported | Not reported | Not reported | Not reported |
| 49.6 (50) | 14,979 | Not reported | Not reported | Not reported | Not reported |
| Reference chemical | Not reported | Not reported | Not reported | Not reported | Not reported |

| Mean Measured and Nominal Treatment Concentrations [a] (mg a.i./L) | Initial cell density (cells/mL) | Mean Growth Rate per day | % inhibition (Mean Growth Rate per day) | Mean Area Under Growth Curve | % inhibition (Mean Area Under Growth Curve) |
|---|---|---|---|---|---|
| (if used) | | | | | |

[a] The nominal test concentrations are presented in parentheses.

**Table 5: Statistical endpoint values.**

| Statistical Endpoint | Biomass | Growth rate | Cell density |
|---|---|---|---|
| NOAEC or $EC_{05}$ (mg a.i./L) | Not reported | Not reported | 49.6 |
| $EC_{50}$ (mg a.i./L) | Not reported | Not reported | >49.6 |
| $IC_{50}$ or $EC_{50}$ (mg a.i./L) (95% C.I.) | Not reported | Not reported | Not reported |
| $IC_{25}/EC_{25}$ (mg a.i./L) (95% C.I.) | Not reported | Not reported | 46.9 (-313 - 407) |
| Reference chemical, if used NOAEC $IC_{50}/EC_{50}$ | N/A | N/A | N/A |

N/A = Not applicable.

**B. REPORTED STATISTICS:**

Statistical Method: The $EC_{25}$ and $EC_{50}$ values were calculated using least squares linear regression for algal cell counts. The NOAEC was determined using analysis of variance and the Dunnett's t-test. The $EC_{50}$ based on area under the growth curve could not be calculated. All statistical calculations were performed using the mean measured concentrations.

**Cell Density:**
NOAEC: 49.6 mg a.i./L
$EC_{05}$: 49.6
$EC_{50}$: >49.6 mg a.i./L 95% C.I.:

Endpoint(s) Affected: None.

**C. VERIFICATION OF STATISTICAL RESULTS:**

Statistical Method: Cell density data satisfied the assumptions of ANOVA. The NOAEC was determined using this test via TOXSTAT statistical software. The $EC_{05}$ value for cell density could not be determined using the Probit method via Nuthatch statistical software, given the variable nature of the response; the $EC_{50}$ value could be visually determined, because inhibition of cell density did not exceed 50%. The reviewer used the mean measured concentrations to calculate toxicity values.

**Cell Density:**

NOAEC: 49.6 mg a.i./L
$EC_{05}$: could not be determined
$EC_{50}$: >49.6 mg a.i./L 95% C.I.: N/A

Endpoint(s) Affected: None.

**D. STUDY DEFICIENCIES:**

Three replicates per treatment group were tested, which is less than the recommended 4 replicates for *Navicula pelliculosa*. This deviation was considered to have affected the acceptability of this study because there was high cell density variability within and among treatment groups. The low replicate number resulted in low statistical power and, thus, contributed to the inability to detect potential differences from control.

**E. REVIEWER'S COMMENTS:**

The reviewer's results were identical to those of the study authors; no significant adverse effects on cell density were detected. However, the low replicate number in this study resulted in low statistical power and, given the highly variable response of cell density, may have contributed to the inability to detect potential significant differences from control. US EPA guidelines, Subdivision J, §123-2 recommend the use of 4 replicates for *Navicula pelliculosa*, while only three replicates per treatment were tested in this study. This deviation was considered to have affected the results of this study and, so, it affected the acceptability. This study is classified as Supplemental, but it need not be repeated.

**F. CONCLUSIONS:** The study is scientifically sound, but it does not satisfy the guidelines for an aquatic nonvascular plant study with *Navicula pelliculosa* [§123-2] because of the low replicate number and highly variable response of cell density. This study is classified as Supplemental, but it need not be repeated. According to the results of this study, there were no significant effects on cell density. The $EC_{50}$ was >49.6 mg a.i./L and the NOAEC of was 49.6 mg a.i./L.

**Cell Density:**
NOAEC: 49.6 mg a.i./L
$EC_{05}$: could not be determined
$EC_{50}$: >49.6 mg a.i./L 95% C.I.: N/A

Endpoint(s) Affected: None.

## III. REFERENCES:

Holst, R.W. and T.C. Ellwanger, 1982, Pesticide Assessment Guidelines Subdivision J Hazard Evaluation: Non-target Plants, EPA 540/9-82-020, Washington, D.C.

Holst, R.W., 1986, Hazard Evaluation Division: Standard Evaluation Procedure Non-Target Plants: Growth and Reproduction of Aquatic Plants Tiers 1 and 2. EPA 540/9-86-134, Washington, D.C.

Environmental Protection Agency-FIFRA GLPs. Title 40 CFR, 160-Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards, Final Rule.

OECD Series on Principles of Good Laboratory Practice Compliance and Monitoring, Number 1. OECD Principles on Good Laboratory Practice (as revised in 1997) ENV/MC/CHEM(98)17.

EC Directive 99/11/EC of 8 March 1999 (OJ No. L 77/8-21, 23/3/1999).

A.J. Smith, Purity Report for XDE-638, FA &PC 993090, May 20, 1999.

Smith, A.J., "Certificate of Analysis for Test/Reference/Control/Substances Analytical Report FA & PC Number 993090. 20 May, 1999.

Miller, W.E., Green, J.C. and Shiroyama, T. (1978). The *Selenastrum capricornutum* Printz Algal Assay Bottle Test. EPA-600/9-78-018.

Kirk, H.D., M.M. Gilles, McClymont, E.L. and McFadden, L.G. XDE-638: Growth Inhibition Test with The Saltwater Diatom, *Skeletonema costatum*, The Dow Chemical Company, Toxicology & Environmental Research and Consulting Laboratory, Study # 001003, report in progress.

Neter, J., Wasserman, W. and Kutner, M.H. (1983). Applied Linear Regression Models. Richard D. Irwin Inc., Homewood, Illinois.

Winer, B.J. (1971). Statistical Principles on Experimental Design. 2nd Ed., McGraw Hill, Co. New York, New York.

Organisation of Economic Co-Operation and Development (OECD). OECD Guideline for Testing of Chemicals. Algal Growth, Inhibition Test. Number 201. Adopted 7 June, 1984.

**APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:**

**cell density**
File: 1121cd Transform: NO TRANSFORMATION

ANOVA TABLE

| SOURCE | DF | SS | MS | F |
|---|---|---|---|---|
| Between | 6 | 238062291019.250 | 39677048503.188 | 1.277 |
| Within (Error) | 14 | 434832187808.000 | 31059441986.281 | |
| Total | 20 | 672894478827.000 | | |

Critical F value = 2.85 (0.05,6,14)
**Since F < Critical F FAIL TO REJECT Ho:All groups equal**

cell density
File: 1121cd Transform: NO TRANSFORMATION

DUNNETTS TEST - TABLE 1 OF 2 Ho:Control<Treatment

| GROUP | IDENTIFICATION | TRANSFORMED MEAN | MEAN CALCULATED IN ORIGINAL UNITS | T STAT | SIG |
|---|---|---|---|---|---|
| 1 | control | 1044804.333 | 1044804.333 | | |
| 2 | 1.38 | 794200.333 | 794200.333 | 1.742 | |
| 3 | 2.65 | 746773.333 | 746773.333 | 2.071 | |
| 4 | 5.2 | 879189.333 | 879189.333 | 1.151 | |
| 5 | 10.7 | 752136.333 | 752136.333 | 2.034 | |
| 6 | 24.0 | 702271.000 | 702271.000 | 2.380 | |
| 7 | 49.6 | 850834.000 | 850834.000 | 1.348 | |

Dunnett table value = 2.53 (1 Tailed Value, P=0.05, df=14,6)

cell density
File: 1121cd Transform: NO TRANSFORMATION

DUNNETTS TEST - TABLE 2 OF 2 Ho:Control<Treatment

| GROUP | IDENTIFICATION | NUM OF REPS | Minimum Sig Diff (IN ORIG. UNITS) | % of CONTROL | DIFFERENCE FROM CONTROL |
|---|---|---|---|---|---|
| 1 | control | 3 | | | |
| 2 | 1.38 | 3 | 364058.953 | 34.8 | 250604.000 |
| 3 | 2.65 | 3 | 364058.953 | 34.8 | 298031.000 |
| 4 | 5.2 | 3 | 364058.953 | 34.8 | 165615.000 |
| 5 | 10.7 | 3 | 364058.953 | 34.8 | 292668.000 |

| | | | | | |
|---|---|---|---|---|---|
| 6 | 24.0 | 3 | 364058.953 | 34.8 | 342533.333 |
| 7 | 49.6 | 3 | 364058.953 | 34.8 | 193970.333 |

cell density
File: 1121cd Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

| GROUP | IDENTIFICATION | N | ORIGINAL MEAN | TRANSFORMED MEAN | ISOTONIZED MEAN |
|---|---|---|---|---|---|
| 1 | control | 3 | 1044804.333 | 1044804.333 | 1044804.333 |
| 2 | 1.38 | 3 | 794200.333 | 794200.333 | 806721.000 |
| 3 | 2.65 | 3 | 746773.333 | 746773.333 | 806721.000 |
| 4 | 5.2 | 3 | 879189.333 | 879189.333 | 806721.000 |
| 5 | 10.7 | 3 | 752136.333 | 752136.333 | 768413.778 |
| 6 | 24.0 | 3 | 702271.000 | 702271.000 | 768413.778 |
| 7 | 49.6 | 3 | 850834.000 | 850834.000 | 768413.778 |

cell density
File: 1121cd Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

| IDENTIFICATION | ISOTONIZED MEAN | CALC. WILLIAMS | SIG | TABLE P=.05 WILLIAMS | DEGREES OF FREEDOM |
|---|---|---|---|---|---|
| control | 1044804.333 | | | | |
| 1.38 | 806721.000 | 1.655 | | 1.76 | k= 1, v=14 |
| 2.65 | 806721.000 | 1.655 | | 1.85 | k= 2, v=14 |
| 5.2 | 806721.000 | 1.655 | | 1.88 | k= 3, v=14 |
| 10.7 | 768413.778 | 1.921 | * | 1.89 | k= 4, v=14 |
| 24.0 | 768413.778 | 1.921 | * | 1.90 | k= 5, v=14 |
| 49.6 | 768413.778 | 1.921 | * | 1.91 | k= 6, v=14 |

s = 176236.892
Note: df used for table values are approximate when v > 20.

**$EC_x$**

**!!!Failure#1: near-singular matrix, model possibly unsuitable.**