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

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

**MEMORANDUM**

**Date:** August 25, 2011

**SUBJECT:** **Picoxystrobin** Qualitative Risk Assessment Based On Crlj:CD1(ICR) Mouse and CD[Crl:CD(SD)] Rat Dietary Studies

| | |
|---|---|
| **PC Codes:** 129200 | **DP Barcode:** NA |
| **MRID Nos.:** 48457401 and 48457402 | **Registration No.:** NA |
| **Petition No.:** NA | **Regulatory Action:** NA |
| **Assessment Type:** NA | **Reregistration Case No.:** NA |
| **TXR No.:** 0055677 | **CAS No.:** 117428-22-5 |

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## I. CONCLUSIONS

There was a statistically significant negative trend in mortality, and a statistically significant negative pair-wise comparison of the high dose group with the controls, with increasing doses of Picoxystrobin in both male rats and male mice.

Male mice had a statistically significant trend in liver adenomas. There were no other statistically significant findings in male mice.

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Male rats had a statistically significant trend, and a significant pair-wise comparison of the 3500 ppm dose group with the controls, for testicular interstitial cell tumors.

## II. ACTION REQUESTED

Prepare a qualitative risk assessment of the male mouse liver and the male rat testicular tumors.

## III. BACKGROUND

A carcinogenicity study in Crlj:CD1(ICR) mice was conducted by Korea Institute of Toxicology, Daejeon, Republic of Korea, for E.I. du Pont de Nemours and Company, Wilmington, Delaware, on April 11, 2011 (Laboratory Study No. IG08070, MRID No. 48457401).

The study design allocated groups of 60 mice per sex to dose levels of 0, 100, 600, 2400 or 4800 ppm of Picoxystrobin for 78 weeks. Doses were equivalent to 0, 12, 71, 293 or 583 mg/kg bw/day in males. Only the male mice have been evaluated in this qualitative risk assessment. There was no evidence of carcinogenicity in female mice.

A chronic toxicity/carcinogenicity study in CD[Crl:CD(SD)] rats was conducted by MPI Research, Inc., Mattawan, Michigan, for E.I. du Pont de Nemours and Company, Wilmington, Delaware, on April 7, 2011 (Laboratory Project ID No. DuPont-26171, MRID No. 48457402).

The study design allocated groups of 70 rats per sex to dose levels of 0, 50, 200, 1000 or 3500 ppm of Picoxystrobin for 104 weeks. Doses were equivalent to 0, 2.2, 8.8, 45.3, or 162.1 mg/kg bw/day in males. An additional 10 rats per sex per dose were designated for interim sacrifice at week 52. Only the male rats have been evaluated in this qualitative risk assessment. There was no evidence of carcinogenicity in female rats.

## IV. RESULTS/DISCUSSION

### Survival Analyses

There was a statistically significant negative trend in mortality, and a statistically significant negative pair-wise comparison of the high dose group with the controls, with increasing doses of Picoxystrobin in both male mice (Table 1) and male rats (Table 3), all at $p < 0.01$.

### Tumor Analyses

Male mice had a statistically significant trend in liver adenomas at $p > 0.05$. There were no other statistically significant findings in male mice.

Male rats had a statistically significant trend at $p < 0.01$, and a significant pair-wise comparison of the 3500 ppm dose group with the controls at $p < 0.05$, for testicular interstitial cell tumors.

The statistical analyses of the tumors in the male rats and the male mice were based upon Peto's Prevalence Test (Tables 2 and 4).

Table 1. Picoxystrobin – Crlj:CD1(ICR) Mouse Study (MRID 48457401)

Male Mortality Rates[+] and Cox or Generalized K/W Test Results

| | Weeks | | | |
|---|---|---|---|---|
| Dose (ppm) | 1-26 | 27-52 | 53-79[f] | Total |
| 0 | 1/60 | 4/59 | 12/55 | 17/60 (28)**n |
| 100 | 0/59[a] | 4/59 | 14/55 | 18/59 (31) |
| 600 | 1/60 | 2/59 | 10/57 | 13/60 (22) |
| 2400 | 0/60 | 2/60 | 8/58 | 10/60 (17) |
| 4800 | 0/60 | 2/60 | 2/58 | 4/60 (7)**n |

[+]Number of animals that died during interval/Number of animals alive at the beginning of the interval.

[a]One accidental death at week 3, dose 100 ppm.

[f]Final sacrifice at weeks 78-79.

n: Negative trend or negative change from control.

( )Percent.

Note: Time intervals were selected for display purposes only.
Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

Table 2. Picoxystrobin – Crlj:CD1(ICR) Mouse Study (MRID 48457401)

Male Liver Tumor Rates[+] and
Peto's Prevalence Test Results

| | Dose (ppm) | | | | |
|---|---|---|---|---|---|
| | 0 | 100 | 600 | 2400 | 4800 |
| Adenomas (%) | 6/52 (12) | 5[a]/54 (9) | 9/56 (16) | 9/58 (16) | 13/58 (22) |
| p = | 0.03794* | 0.63074 | 0.27858 | 0.40703 | 0.12427 |
| Carcinomas (%) | 6[b]/49 (12) | 6/51 (12) | 6/54 (11) | 12/57 (21) | 9/57 (16) |
| p = | 0.14743 | 0.54436 | 0.65701 | 0.16942 | 0.26574 |
| Combined (%) | 12/52 (23) | 11/54 (20) | 15/56 (27) | 20[c]/58 (34) | 19[d]/58 (33) |
| p = | 0.06733 | 0.60579 | 0.39425 | 0.18677 | 0.18640 |

+Number of tumor bearing animals/Number of animals examined, excluding those that died before observation of the first tumor.

[a]First adenoma observed at week 56, dose 100 ppm.
[b]First carcinoma observed at week 64, dose 0 ppm.
[c]One animal in the 2400 ppm dose group had both an adenoma and a carcinoma.
[d]Three animals in the 4800 ppm dose group had both an adenoma and a carcinoma.

Note: Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

Table 3. Picoxystrobin – CD[Crl:CD(SD)] Rat Study (MRID 48457402)

Male Mortality Rates[+] and Cox or Generalized K/W Test Results

| | Weeks | | | | | |
|---|---|---|---|---|---|---|
| Dose (ppm) | 1-26 | 27-52 | 52[i] | 53-78 | 79-104[f] | Total |
| 0 | 0/79[a] | 2/79 | 10/77 | 11/67 | 39/56 | 52/69 (75)**n |
| 50 | 0/80 | 3/80 | 10/77 | 15/67 | 30/52 | 48/70 (69) |
| 200 | 0/80 | 5/80 | 10/75 | 10/65 | 37/55 | 52/70 (74) |
| 1000 | 0/80 | 4/80 | 10/76 | 13/66 | 33/53 | 50/70 (71) |
| 3500 | 2/80 | 2/78 | 10/76 | 10/66 | 22/56 | 36/70 (51)**n |

[+]Number of animals that died during interval/Number of animals alive at the beginning of the interval.

[a]One accidental death at week 13, dose 0 ppm.

[i]Interim sacrifice at week 52.
[f]Final sacrifice at week 104.

n: Negative trend or negative change from control.

( )Percent.

Note: Time intervals were selected for display purposes only.
Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

Table 4. Picoxystrobin – CD[Crl:CD(SD)] Rat Study (MRID 48457402)

Male Testicular Tumor Rates[+] and
Peto's Prevalence Test Results

| | Dose (ppm) | | | | |
|---|---|---|---|---|---|
| | 0 | 50 | 200 | 1000 | 3500 |
| Interstitial Cell Tumors (%) | 1/38 (3) | 1/44 (2) | 0/40 (0) | 2/43 (5) | 7[a]/52 (13) |
| p = | 0.00100** | 0.57349 | 0.84826 | 0.33201 | 0.03461* |

+Number of tumor bearing animals/Number of animals examined, excluding those that died before observation of the first tumor.

[a]First interstitial cell tumor observed at week 88, dose 3500 ppm.

Note: Significance of trend denoted at control.
Significance of pair-wise comparison with control denoted at dose level.
If *, then $p < 0.05$. If **, then $p < 0.01$.

References

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