US EPA ARCHIVE DOCUMENT
Data Evaluation Report on the Acute Oral Toxicity of GF-443 on Avian Species \textit{Colinus virginianus}

PMRA Submission Number

EPA MRID Number 45831001

Data Requirement:

<table>
<thead>
<tr>
<th>PMRA DATA CODE</th>
<th>EPA DP Barcode</th>
<th>OECD Data Point</th>
<th>EPA MRID</th>
<th>EPA Guideline</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>45831001</td>
<td>§71-1</td>
</tr>
</tbody>
</table>

Test material: GF-443

Purity: Not reported

Common name: Submitted to support registration for penoxsulam (not otherwise specified)

Chemical name: IUPAC: Not reported

CAS name: Not reported

CAS No.: Not reported

Synonyms: Not reported

Primary Reviewer: Rebecca Bryan

Staff Scientist, Dynamac Corporation

QC Reviewer: Christie E. Padova

Staff Scientist, Dynamac Corporation

Primary Reviewer: William Erickson - Biologist

OPP/EFED/ERB - III

Secondary Reviewer(s):

[EPA/OECD/PMRA]

Reference/Submission No.:

Date Evaluation Completed:

Acute Oral Toxicity of GF-443 (21.7% penoxsulam) to bobwhite quail

EXECUTIVE SUMMARY:

The acute oral toxicity of GF-443 (21.9% EUP of penoxsulam) to 21-week-old Northern Bobwhite quail (Colinus virginianus) was assessed over 14 days. GF-443 was administered to the birds via gavage at nominal concentrations of 0, 778, 1296, 2160, 3600, 6000, and 10,000 mg/kg bw of the EUP. The nominal concentrations of the active ingredient were 170, 283, 473, 778, 1314, 2190 mg ai/kg.

No mortalities or treatment-related sub-lethal effects were observed during the study. In addition, no significant differences in body weights were observed. A statistically-significant reduction in feed consumption was observed on Days 0-3 at the 2190 mg ai/kg bw dose group compared to the control (15 versus 19 g/bird/day). Feed consumption recovered for the remainder of the study. No treatment-related abnormalities were observed at terminal necropsy. The 14-day acute oral LD₅₀ is >2190 mg ai/kg bw, which categorizes GF-443 as practically nontoxic to Northern Bobwhite quail on an acute oral basis.

This toxicity study is scientifically sound and fulfills the guideline requirements for an acute toxicity study using the Northern Bobwhite quail (§71-1). This study is classified as CORE.

Results Synopsis

Test Organism Size/Age: 21-weeks old, 167-214 g (combined sexes)

LD₅₀: >2,190 mg/kg bw
NOAEL: 1,302 mg/kg bw
LOAEL: 2,190 mg/kg bw
Endpoint(s) Affected: Transient effects on feed consumption

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The study protocol was based on procedures outlined in the U.S. EPA Pesticide Assessment Guidelines, Series §71-1. The following deviation from guideline §71.1 were observed:

The identity and purity of the test substance were not reported. Although this study was submitted to support the registration of penoxsulam, it was unclear if GF-443 was a synonym for penoxsulam, a metabolite, or some other ingredient of a formulated or end-use product. Eventually it was determined that it is an EUP with 21.9% ai.

This deviation is considered significant, and as a result, this study does not fulfill guideline requirements.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

A. MATERIALS:

1. Test Material: GF-443 (21.9% ai)

    Description: Cream to light tan liquid

    Lot No./Batch No.: E-828-59
Acute Oral Toxicity of GF-443 (21.7% penoxsulam) to bobwhite quail
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Purity: Not specified

Stability of Compound Under Test Conditions: N/A

Storage conditions of test chemicals: Ambient

OECD requires water solubility, stability in water and light, $pK_a$, $P_{ow}$, and vapor pressure of the test compound. OECD requirements were not reported.

2. Test organism:

   Species: Northern Bobwhite quail (*Colinus virginianus*)

   Age at study initiation: 21 weeks old

   Weight at study initiation: 167-214 g

   Source: Dyes Quail Farm/Colorado Game Bird Ranch, Yuma, CO.

B. STUDY DESIGN:

1. Experimental Conditions

   a) Range-finding Study: No range-finding study was reported.

   b) Definitive Study:
# Table 1. Experimental Parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Details</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acclimation period:</td>
<td>17 days.</td>
<td><strong>EPA recommends that birds be pre-conditioned to the test facilities for at least 15 days.</strong></td>
</tr>
<tr>
<td>Conditions (same as test or not):</td>
<td>Same as test.</td>
<td><strong>OECD recommends that birds be pre-conditioned to the test facilities for at least 7 days.</strong></td>
</tr>
<tr>
<td>Feeding:</td>
<td>Dry, non-medicated Turkey and Gamebird Grower (Ranch-Way, Inc.) and tap water were provided, <em>ad libitum</em>, during acclimation and testing.</td>
<td><strong>EPA requires: pens must conform to good husbandry practices and should not create crowding stress.</strong></td>
</tr>
<tr>
<td>Health (any mortality observed):</td>
<td>General physical condition and suitability for testing were determined by a veterinarian prior to testing.</td>
<td><strong>OECD lists no criteria for pen construction other than stating that pens should be suitable for the captive rearing of that species.</strong></td>
</tr>
<tr>
<td>Pen size and construction materials</td>
<td>Steel wire pens; 51 x 25 x 25.5 cm (floor surface area of 1275 cm(^2)).</td>
<td><strong>EPA requires a day for dosing and at least 14 days observation.</strong></td>
</tr>
<tr>
<td>Test duration</td>
<td>14 Days</td>
<td></td>
</tr>
<tr>
<td>Dose preparation</td>
<td>A single dosing solution was prepared using GF-445 and HPLC-grade water.</td>
<td></td>
</tr>
<tr>
<td>Indicate method of confirmation of dose</td>
<td>The actual amount (mL) of test substance administered was determined (Appendix A1, pp. 22-24).</td>
<td></td>
</tr>
<tr>
<td>Mode of dose administration</td>
<td>Oral, via gavage.</td>
<td><strong>Gavage or gelatin capsule.</strong></td>
</tr>
</tbody>
</table>
### Table 2: Observations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Details</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose levels</strong></td>
<td></td>
<td><strong>Criteria</strong></td>
</tr>
<tr>
<td>nominal:</td>
<td>0 (vehicle control), 778, 1296, 2160, 3600, 6000, and 10,000 mg/kg bw EUP (21.9% ai).</td>
<td><em>EPA requires a minimum of 5 treatment levels unless LD&lt;sub&gt;50&lt;/sub&gt; is demonstrated to be greater than 2000 mg ai/kg.</em></td>
</tr>
<tr>
<td>measured:</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td><strong>Solvent/vehicle, if used</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>type:</td>
<td>HPLC-grade water</td>
<td><em>EPA recommends that the test material be administered without a vehicle if possible. Maximum vehicle should not exceed 0.1 to 1.0% of body weight.</em></td>
</tr>
<tr>
<td>amount/bw:</td>
<td>Approximately 1.0% bw</td>
<td></td>
</tr>
<tr>
<td><strong>Number of birds per groups/treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>for negative control:</td>
<td></td>
<td>5 males and 5 females/group</td>
</tr>
<tr>
<td>for solvent/vehicle control:</td>
<td></td>
<td><em>EPA recommends 10 birds per treatment group and 10 birds for each control and vehicle group.</em></td>
</tr>
<tr>
<td>for treated:</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>No. of feed withholding days before dosing</strong></td>
<td></td>
<td><em>EPA recommends that food should be withheld for at least 15 hours prior to dosing.</em></td>
</tr>
<tr>
<td><strong>Test conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature:</td>
<td>19-26°C (mean min. = 20°C; mean max. = 25°C)</td>
<td><em>EPA recommends that a 10 hr light/14 hr dark photo-period.</em></td>
</tr>
<tr>
<td>Relative humidity:</td>
<td>21-34% (mean min. = 23%; mean max. = 28%)</td>
<td></td>
</tr>
<tr>
<td>Photo-period:</td>
<td>10-hours light/14-hours dark.</td>
<td></td>
</tr>
<tr>
<td><strong>Reference chemical, if used</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>name:</td>
<td>None used.</td>
<td></td>
</tr>
<tr>
<td>concentrations tested:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Observations:
II. RESULTS AND DISCUSSION:

A. MORTALITY:

No treatment-related mortalities occurred during the study (Table I, p. 15).

Table 3: Effect of GF-443 on mortality of Collinus virginianus.

<table>
<thead>
<tr>
<th>Treatment (mg ai/kg bw)</th>
<th>No. of birds</th>
<th>Cumulative mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ποιες 6 οφ 10
**Acute Oral Toxicity of GF-443 (21.7% penoxsulam) to bobwhite quail**

<table>
<thead>
<tr>
<th>Reference chemical</th>
<th>mortality</th>
<th>LD&lt;sub&gt;50&lt;/sub&gt;</th>
<th>NOAEL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*One bird was found dead caught underneath the feeder (not included in number of birds tested).*

**B. SUB-LETHAL TOXICITY ENDPOINTS:**

No treatment-related signs of toxicity, or significant differences in body weights were observed during the study (Tables I and II, pp. 15-16). A statistically-significant reduction in feed consumption was observed on Days 0-3 at the 2,190 mg ai/kg bw dose group compared to the control (15 versus 19 g/bird/day; Table III, p. 17). Feed consumption recovered for the remainder of the study. No post-mortem abnormal findings were observed that could be attributed to treatment (Table IV, p. 18).
Table 4: Sub-lethal effects of GF-443 on *Colinus virginianus*.

<table>
<thead>
<tr>
<th>Treatment, mg ai/kg bw</th>
<th>Males and Females</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 3</td>
<td>Day 7</td>
<td>Day 14</td>
</tr>
<tr>
<td>Vehicle Control</td>
<td>187</td>
<td>195</td>
<td>197</td>
<td>195</td>
</tr>
<tr>
<td>178</td>
<td>186</td>
<td>192</td>
<td>193</td>
<td>194</td>
</tr>
<tr>
<td>283</td>
<td>188</td>
<td>194</td>
<td>195</td>
<td>192</td>
</tr>
<tr>
<td>473</td>
<td>193</td>
<td>197</td>
<td>198</td>
<td>197</td>
</tr>
<tr>
<td>778</td>
<td>186</td>
<td>192</td>
<td>193</td>
<td>191</td>
</tr>
<tr>
<td>1314</td>
<td>188</td>
<td>191</td>
<td>196</td>
<td>194</td>
</tr>
<tr>
<td>2,190</td>
<td>188</td>
<td>190</td>
<td>193</td>
<td>193</td>
</tr>
<tr>
<td>NOAEL</td>
<td>2,190 mg ai/kg bw</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EC₅₀</td>
<td>&gt;2,190 mg ai/kg bw</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reference chemical: NOAEL: N/A
### Mean Feed Consumption, g/bird/day

<table>
<thead>
<tr>
<th>Treatment, mg/kg bw</th>
<th>Days 0-3</th>
<th>Days 3-7</th>
<th>Days 7-14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle Control</td>
<td>19</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>170</td>
<td>19</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>283</td>
<td>17</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>473</td>
<td>17</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>778</td>
<td>17</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>1314</td>
<td>17</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>2,190</td>
<td>15*</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>NOAEL</td>
<td>1,314 mg/kg bw</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Significantly different from the control (ANOVA/Dunnett).

**C. REPORTED STATISTICS:**

Body weight and feed consumption data were analyzed by a Chi-square test for normality, followed by a Bartlett’s test for homogeneity of variance. All data sets passed these tests, and were analyzed by ANOVA, followed by Dunnett’s test to compare each treatment group with the control. All analyses were conducted using TOXSTAT, v 3.4. The LD<sub>50</sub> was estimated because there were no effects on mortality.

**D. VERIFICATION OF STATISTICAL RESULTS:**

Statistical analyses were not required, as there was no mortality in this study, and effects on food consumption and body weight could be visually determined.

- LD<sub>50</sub>: >2,190 mg ai/kg bw
- NOAEL: 1314 mg ai/kg bw
- LOAEL: 2,190 mg ai/kg bw

Endpoint(s) Affected: Transient effects on feed consumption

**E. STUDY DEFICIENCIES:**

This study is scientifically sound. However, the identity and purity of the test substance were not reported. Although this study was submitted to support the registration of penoxsulam, it was unclear if GF-443 was a synonym for penoxsulam, a metabolite, or some other ingredient of a formulated or end-use product. As a
Acute Oral Toxicity of GF-443 (21.7% penoxsulam) to bobwhite quail

result, this study does not fulfill the guideline requirement for an avian oral LD$_{50}$ test ($\S 71-1$) and is classified as SUPPLEMENTAL. This study may be upgraded to Core status if the appropriate identification data are provided.

F. REVIEWER’S COMMENTS:

The reviewer’s conclusions were identical to the study authors’.

G. CONCLUSIONS:

This toxicity study is scientifically sound, and fulfills the guideline requirements for an acute toxicity study for an End-Use Product (21.9%) using the Northern Bobwhite quail ($\S 71-1$). This study is classified as CORE. There were no treatment-related effects on mortality, sub-lethal effects, or body weight. A transient decrease in food consumption was observed in birds from the 2,190 mg ai/kg bw dose group between Days 0-3. Necropsy after 14 days revealed no treatment-related abnormalities. The 14-day acute oral toxicity LD$_{50}$ was >2,190 mg ai/kg bw, which categorizes GF-443 as practically nontoxic to Northern Bobwhite quail.

LD$_{50}$: >2,190 mg ai/kg bw
NOAEL: 1314 mg ai/kg bw
LOAEL: 2,190 mg /kg bw
Endpoint(s) Affected: Transient effects on feed consumption

III. REFERENCES:

No references were cited.