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EPA Registration Division contact: **[Evisabel Craig, 202-566-2572]**

INSTRUCTIONS: **Please utilize this outline in preparing the pesticide petition. In cases where the outline element does not apply, please insert "NA-Remove" and maintain the outline. Please do not change the margins, font, or format in your pesticide petition. Simply replace the instructions that appear in green, i.e., "[insert company name]," with the information specific to your action**

[Croda, Inc., 300-A COLUMBUS CIRCLE Edison, NJ 08837-3907]

[Insert Petition Number]

EPA has received a pesticide petition **([Insert Petition Number])** from **[Croda, Inc., 300-A COLUMBUS CIRCLE Edison, NJ 08837-3907], [c/o Exponent, Inc. Chemical Regulation and Food Safety, 1150 Connecticut Ave., NW, Suite 1100, Washington, DC 20036]** proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180.910 to establish an exemption from the requirement of a tolerance **[for Glycerol Ester of Rosin, CAS RN 8050-31-5.]**

EPA has determined that the petition contains data or information regarding the elements set forth in section 408 (d) (2) of FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.* **[Not Applicable]**

2. *Analytical method.* **[Not Applicable]**

3. *Magnitude of residues.* **[There is no specific crop residue information available for the Glycerol Ester of Rosin and this information is typically not available nor required for the establishment of a tolerance exemption for inert ingredients.]**

B. Toxicological Profile

1. *Acute toxicity.* **[Based on the available data, two acute oral toxicity studies in the rat have been conducted for glycerol ester of rosin (CAS RN 8050-31-5). The oral LD_{50} in rat was determined to be 5000 mg/kg bw in both studies with no mortality reported. The lack of acute oral toxicity supports the lack of systemic bioavailability for glycerol ester of rosin. Systemic bioavailability for glycerol ester of rosin is negligible, which is supported by the physical chemical properties, the mammalian metabolism, and the results of the acute**

and repeated dose toxicity studies. As such, inhalation and dermal toxicity are not expected.]

2. *Genotoxicity.* **[Glycerol Ester of Rosin, (CAS RN 8050-31-5) was not mutagenic in either the AMES *in vitro* bacterial reverse mutation assay or in the *in vitro* mammalian chromosome aberration assay.]**

3. *Reproductive and developmental toxicity.* **[While there are no developmental or reproductive toxicity studies conducted specifically on glycerol ester of rosin, there is an OECD 421 reproduction/developmental toxicity screening study for rosin, pentaerythritol ester (CAS # 8050-26-8) and an OECD 422 Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening for rosin, partially hydrogenated methyl ester (CAS # 8050-15-5). These two rosins are representative of rosin esters in general, including, glycerol ester of rosin.**

In the developmental and reproductive toxicity screening studies, effects were secondary to decreased food consumption due to the palatability of the test substance. No systemic toxicity was reported, supporting the lack of systemic absorption. The studies support that the overall NOAEL for developmental and reproductive toxicity is greater than the limit dose of 1,000 mg/kg/day.]

4. *Subchronic toxicity.* **[Multiple studies evaluating the subchronic toxicity of glycerol ester of rosin were located. In the subchronic toxicity studies conducted with glycerol ester of rosin, effects were limited to decreased food consumption secondary to the palatability of the test substance. No systemic toxicity was reported, supporting the lack of systemic absorption. The overall NOAEL for subchronic toxicity is greater than the limit dose of 1,000 mg/kg/day, set at 2,500 mg/kg/day.]**

5. *Chronic toxicity* **[No studies evaluating the chronic toxicity were located for glycerol ester of rosin specifically. However, chronic toxicity/carcinogenicity studies are available for rosin compounds in the same category and are relevant to evaluating the potential chronic toxicity for glycerol ester of rosin.**

Two EPA OPPTS 870.420 guideline equivalent studies using 60 Sprague-Dawley rats/sex/dose treated with rosin (CASRN 8050-09-7) and hydrogenated rosin (CASRN 65997-06-0) via the diet with 0, 0.05, 0.2, or 1% for two years (two control groups were used). The approximate doses were 0, 50, 200, 1000 mg/kg bw/day. The NOAEL was a dietary level of 0.2% (approximately 200 mg/kg bw/day) and the LOAEL was a dietary level of 1% (approximately 1000 mg/kg bw/day) due to decreased weight gain at this dose. Rosin, hydrogenated (CASRN 65997-06-0) showed no evidence of carcinogenicity in rats following dietary administration for 2 years at a dose of approximately 1000 mg/kg bw/day.

A 24-month oral toxicity study in which dogs fed a diet containing 0.05% or 1.0% (14 or 260 mg/kg bw/day) wood rosin was also conducted. No effects were seen in mortality, hematology, urinalysis, liver and kidney function tests, gross and microscopic pathological examinations, and behavioral changes. At the 1 % dose, some increase in liver and kidney size was noted. As no biochemical indications of liver or kidney toxicity were reported and

no histopathological findings were reported in the liver or kidneys, the increase in liver and kidney size were not considered to be adverse effects. As such, the overall NOAEL for this study is 260 mg/kg/day, the highest dose level tested.

When using chronic toxicity data from other slightly different test articles (other rosins and resins and their derivatives) as a surrogate for glycerin ester of rosin, no chronic toxicity or carcinogenicity effects are expected and the NOAEL of 260 mg/kg/day is expected to be protective of any potential chronic effects.]

6. *Animal metabolism.* **[Rosins are poorly absorbed by all routes of exposure and the data presented included single and repeated dose administration of glycerol ester of wood rosin at high dose levels in the diet (7,000 to 28,000 mg/kg diet (ppm)) resulting in >90% recovery of the glycerol ester of wood rosin in the feces. Additional ADME studies further supported the lack of potential systemic bioavailability of glycerol ester of wood rosin.]**

7. *Metabolite toxicology*. **[No metabolites of toxicological concern are expected based on the proposed metabolic pathways and metabolites for glycerol ester of rosin. Glycerol ester of wood rosin a long history of safe use as a food additive.]**

8. *Endocrine disruption*. **[Glycerol ester of rosin does not belong to a class of chemicals known or suspected of having adverse effects on the estrogen receptor or endocrine system.** Glycerol ester of wood **has been evaluated in acute, subchronic, and developmental repeated dose studies that would be capable of detecting effects on endocrine mediated events. The results of these studies did not give any indication of a treatment-related effect on the estrogen receptor or endocrine system.]**

C. Aggregate Exposure **[Based on the available ADME studies demonstrating a lack of absorption of rosins and rosin derivatives and the toxicological database further supporting a lack of systemic toxicity up to 2,500 mg/kg/day, which is above limit dose of 1000 mg/kg bw/day, across multiple repeat dose studies for glycerol ester of rosin, a qualitative approach to risk assessment is appropriate for all pathways of human exposure (food, drinking water, and residential).**

The lack of absorption and lack of systemic toxicity supports that "a reasonable certainty of no harm" will result to the general population, including infants or children, from glycerol ester of rosin. Therefore, the tolerance exemptions specified in this petition are supported under the auspices of 40 CFR 180.910.]

Acute Reference Dose
[NA-Remove]

Chronic Reference Dose
[NA-Remove]

1. Dietary exposure.

[NA-Remove]

2. *Non-dietary exposure.*

[NA-Remove]

PROPOSED EXEMPTION FROM TOLERANCE:

40 CFR Reference	Exemption
40 CFR §180.910	**Glycerol ester of rosin as an inert ingredient in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.**

D. Cumulative Effects

[Section 408(b)(2)(D) (9v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." Unlike pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not conducted a common mechanism evaluation or safety finding for glycerol ester of rosin or other related chemistries].

E. Safety Determination

1. U.S. population. **[Based on the available toxicology studies, there are adequate data to evaluate the toxicological profile of glycerol ester of rosin (CAS # 8050-31-5). The data on glycerol ester of rosin specifically, and rosins more broadly, clearly demonstrate that there is a lack of oral absorption and subsequent lack of systemic exposure to glycerol ester of rosin; therefore there is no potential for systemic oral toxicity. The results of the 90-day oral toxicity studies with glycerol ester of rosin support a NOAEL of 2,500 mg/kg/day, which is above the limit dose for toxicological studies (1,000 mg/kg/day). Effects reported in the toxicological database include decreased food consumption due to palatability issues and subsequent decreases in body weight gain. These are not systemic effects and are not adverse treatment-related effects attributable to the toxicity of glycerol ester of rosin. Additionally, no carcinogenicity, reproductive, or developmental effects were reported in any of the repeat dose studies summarized above.**

The toxicological database supports that there is no hazard based on the oral exposure to glycerol ester of rosin (CAS # 8050-31-5). As such, a quantitative human health risk evaluation is not necessary because there is no hazard. If EPA does conduct dietary or occupational risk evaluations, the appropriate point of departure for oral, dermal, and inhalation exposure is 2,500 mg/kg/day.]

2. Infants and children. **[The toxicological database for glycerol ester of rosin specifically, or rosins more broadly, is complete and includes studies evaluating the ADME, acute, subchronic, chronic, developmental, and reproductive toxicity, carcinogenicity, and**

genotoxicity. There is no potential for embryo, fetal, or offspring susceptibility and no neurotoxicological effects were reported. Based on this information, the Food Quality Protection Act (FQPA) Safety Factor can be reduced to 1X and the total uncertainty factors are 100X]

F. International Tolerances

[There are no known international tolerances for glycerol ester of rosin.]