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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: September 10, 2014

SUBJECT: **Dikegulac Sodium.** Human Health Scoping Document and Preliminary Risk Assessment.

PC Code: 109601	**DP Barcode:** D421171
Decision No.: 492549	**Registration Nos.:** 2217-932, 2217-776, 69117-7
Petition No.: NA	**Regulatory Action:** Registration Review
Case No.:	**Risk Assessment Type:** Single Chemical
TXR No.: NA	**CAS No.:** 52508-35-7
MRID No.: NA	**40 CFR: NA**

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Executive Summary

To determine the scope of work necessary to support Registration Review, Health Effects Division (HED) has considered updates to Agency's science policy and risk assessment methodologies and to the dikegulac sodium toxicity, exposure, and usage databases.

Dikegulac sodium is a plant growth regulator. It is registered to control foliar growth and suppress nuisance fruiting for greenhouse and outdoor landscaping ornamentals, as well as for tree farms. There are no agricultural uses associated with dikegulac sodium. The current toxicology and exposure databases for dikegulac sodium are considered complete to support a non-food use registration. No residue chemistry data are required for a non-food use pesticide. The most recent dikegulac risk assessment took a qualitative approach to assessing risk, since this chemical does not pose a hazard at doses relevant to human exposure.

Dikegulac sodium has low acute toxicity for oral, dermal, and inhalation toxicity (all Toxicity Categories IV). The primary eye irritation study (§81-4) is classified as Toxicity Category III. The chemical exhibits slight dermal irritation (Toxicity Category III) and is not a dermal sensitizer. No target organ toxicity is identified in dogs and rats following oral exposures and in rabbits following dermal exposures at doses including and up to the Limit Dose ($\geq$ 1,000 mg/kg/day). The Hazard and Science Policy Council (HASPOC) waived the study requirements for subchronic inhalation, neurotoxicity (acute and subchronic), immunotoxicity, and reproduction studies since there is no evidence of neuro-, developmental, immuno-, or reproductive toxicity. Long-term rodent information regarding the chronic or carcinogenic potential of dikegulac sodium are not required for a non-food use chemical. There is no concern for mutagenicity. HED has concluded that dikegulac sodium does not pose a hazard at doses relevant to humans; therefore a qualitative risk assessment is appropriate for this chemical.

There are no registered or proposed residential handler uses for dikegulac sodium. Occupational handler and post-application exposure as well as residential postapplication exposure are expected based on the registered use patterns, however, no endpoints of toxicological concern have been identified for risk assessment purposes since dikegulac sodium does not pose a human health hazard, there are no occupational risks or residential post-application risks associated with the registered use of this chemical.

No new data are required to support the registration review of this pesticide. There are no hazards associated with dikegulac sodium at doses relevant to humans; therefore, a qualitative approach to risk assessment is appropriate. This document constitutes the preliminary risk assessment for the purpose of registration review. HED concludes that there are no human health risks associated with the currently registered uses of dikegulac sodium.

Introduction

HED has evaluated the status of the human health assessment for dikegulac sodium to determine whether sufficient data are available and whether any updates are needed to support Registration Review. HED has considered the most recent human health risk assessment for dikegulac sodium. While risk and exposure assessment policies have been updated since the last risk

assessment (DP317256, Y. Barnes, 10/31/2006 and addendum DP317852, S. Recore, 02/06/2007), HED is not recommending a new risk assessment as part of registration review due to the qualitative approach taken to assess risk for dikegulac sodium

Dikegulac sodium is structurally similar to natural products involved in the synthesis or biosynthesis of L-ascorbic acid (vitamin C), naturally occurring plant cell wall components, and to naturally occurring carbohydrates. Dikegulac sodium is listed as a GRAS (Generally Recognized as Safe) chemical in 21 CFR §182 for use as a chemical preservative (§182.3013), a dietary supplement (§182.5013), and a nutrient (§182.8013). The chemical identity and physicochemical properties of dikegulac sodium are attached in Tables 1.

There are two end-use formulations for the growth regulator dikegulac sodium; soluble concentrates (2217-776 and 2217-932) and a Ready-To-Use (RTU) formulation (69117-7). The soluble concentrate is applied to landscape ornamentals and to tree foliage using mechanically pressurized handgun, backpack sprayers, airblast, manual pressurized handwand, bark banding, and tree injection systems. The maximum application rates range from of 0.035 pounds active ingredient (ai) per gallon to 0.835 lb ai/gallon. The corresponding dikegulac sodium acid equivalent (ae) rate ranged from 0.035 lb ae/gallon to 0.77 lb ae/gallon.

The current label for the soluble concentrate formulation of dikegulac sodium requires baseline dermal protection (long-sleeved shirt, long pants, shoes plus socks) and the addition of waterproof gloves. The RTU injection product requires the same PPE plus the protective eyewear. The injection product contain a requirement for protective eyewear due to the nature of the application and not due to the acute toxicity of the active ingredient. Worker protective standard (WPS) language for early entry includes coveralls, shoes, socks, chemical-resistant gloves (of any waterproof material), and protective eyewear.

Most recently, there was a registrant request reviewed which petitioned the Agency to reduce the 12 hour restricted entry interval (REI) which is based on the acute toxicity of the chemical. HED determined that the registrant would need to supply EPA with specific information about the end use product containing dikegulac sodium to qualify for a reduced 4-hour REI requirement. The REI remains 12 hours pending registrant submission of end use product hypersensitivity, adverse health effects, and incident information (D370143, A. Nielson, 02/04/2010).

Hazard Identification/Toxicology

The available toxicological data for dikegulac sodium are sufficient for hazard assessment. All submitted studies are detailed in the attached toxicology tables (Table 3 through 5).The database consists of acute toxicity battery, developmental toxicity studies in rats and rabbits, subchronic (oral) toxicity studies in dogs and rats, and a 21-day dermal toxicity study in rabbits. Mutagenicity studies are available include *Salmonella typhimurium*, micronucleus, and gene mutation assays. The HASPOC considered all of the available hazard and exposure information for dikegulac sodium and concluded that data requirements for subchronic inhalation toxicity, reproduction, neurotoxicity (acute and subchronic), and immunotoxicity studies are waived at this time (U. Habiba, TXR 0057022, 07/31/2014). Since it is a non-food use chemical, submitted

toxicity studies in combination of published literature are sufficient to assess the toxicity of dikegulac sodium.

The available acute toxicity studies indicate that dikegulac sodium has very low oral, dermal and inhalation toxicity (Toxicity Categories IV). In July, 2008, EPA reclassified the primary eye irritation study (§81-4) from Toxicity Category II to Toxicity Category III based on provided supporting documents and a re-evaluation of the submitted Dikegulac sodium exhibited slight dermal irritation (Toxicity Category III) and is not a skin sensitizer.

Acceptable/Guideline oral subchronic toxicity studies were conducted in dogs and rats. A 90-day rat subchronic study revealed no toxicity, the NOAEL is ≥ 2,000 mg/kg/day with no LOAEL being established. In a 13-week dog toxicity study, beagle dogs were dosed at 0, 500, 1200 (via gelatin capsules), or 3000 mg/kg/day (via stomach tubes), diarrhea (presumable caused osmotically) was observed in the first week of treatment and especially in the high dose groups (1200 and 3000 mg/kg/day). However, this had no effect on the weight development of the dogs. The NOAEL is 1,200 mg/kg/day and the LOAEL is 3,000 mg/kg/day based on the relatively mild effects of profuse watery diarrhea and occasional vomiting.

A rat developmental toxicity study revealed no developmental or embryotoxic effects based on fetal and maternal parameters. The maternal NOAEL is 700 mg/kg/day and the LOAEL is 2,000 mg/kg/day, based on clinical observations of light sedation following the first two treatments. The developmental NOAEL is > 2,000 mg/kg/day with no LOAEL being established**.** In a rabbit developmental study, no treatment-related developmental or embryotoxic effects were seen based on maternal clinical signs, liver enzymes, liver weights, gross pathology, litter size, numbers of live fetuses, dead fetuses, or resorptions, post implantation loss, sex ratio, fetal weight, or placental weight. The maternal NOAEL is 700 mg/kg/day and the LOAEL is 2,000 mg/kg/day, based on clinical observations of diarrhea and lack of body weight gain. The developmental NOAEL is > 2,000 mg/kg/day with no LOAEL being established.

A 21-day dermal toxicity study in rabbits resulted in slight erythema. However, no compound-related effects on mortality, body weight, body weight gain, food consumption, hematology, ophthalmology, or gross pathology were observed in the females. The dermal NOAEL is 600 mg/kg/day with no LOAEL being established.

Available genotoxicity and mutagenicity studies were negative for reverse gene mutations in *Salmonella typhimurium*, not mutagenic in mouse lymphoma cell assays with/without activation at levels ranging from 500 to 5,000 µg/ mL, and negative for micronucleus induction in bone marrow cells of male and female CD-1 mice harvested 24, 48, and 72 hours post-administration of a single dose of 1,250, 2,500 or 5,000 mg/kg. For a non-food use chemical, no long-term rodent information regarding the carcinogenic potential of dikegulac sodium is required.

Based on the available data, there is no evidence to suggest that dikegulac sodium causes increased susceptibility in infants and children. Furthermore, based on the low hazard concern from the available studies, no endpoints of toxicological concern have been identified for risk assessment purposes.

Dietary Exposure

Dikegulac sodium does not have any agricultural or food production uses, as such it is designated and classified as a "non-food" use chemical. Based on the low hazard concern from the available studies, no endpoints of toxicological concern have been identified. Due to the hazard profile drinking water assessments are not needed. In addition, because dikegulac sodium is not used on any agricultural food and/or feed commodities and is classified as a "non-food" use chemical and metabolized to non-toxic substances; a dietary risk assessment is not required.

Residential Exposure

Dikegulac sodium is used in small quantities by the professional landscaping industry, and is not marketed to homeowners. Residential post application exposure is possible from occupational application to residential use sites however, due to the (very) low systemic toxicity of dikegulac sodium, a residential quantitative risk assessment is not warranted for any type, or duration of exposure.

Spray Drift and Volatility

Since dikegulac does not pose a hazard, there are no risks associated with potential exposure to spray drift or exposure from volatility expected from this chemical.

Occupational Exposure

Dikegulac sodium is registered for use as two end-use product formulations (soluble concentrate and RTU injections). Table 6 summarizes the occupational handler use patterns and potential exposure scenarios. While there are uses that could result in occupational handler and post-application exposure, due to the (very) low systemic toxicity of dikegulac sodium, a quantitative occupational risk assessment is not warranted for any type, or duration of exposure.

Turf Transferable Residue (TTR) and Dislodgeable Foliar Residue (DFR) data are not required for dikegulac sodium based on the current use patterns for this chemical.

Public Health and Pesticide Epidemiology Data

Because there are no incident cases reported for dikegulac sodium in either the Main or Aggregate Incident Data System (IDS) module, Poison Control Centers (PCCs), California Department of Pesticide Regulation, National Pesticide Information Center(NPIC) and National Institute of Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR) there does not appear to be a concern at this time that would warrant further investigation (D317857, M. Hawkins, 07/25/2006).

Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf). As a part of every pesticide risk

assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the United States Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey (NHANES), What We Eat in America (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for children, youths, and adults entering or playing on treated areas following application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

Cumulative

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to dikegulac sodium and any other substances. Dikegulac sodium does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that dikegulac sodium has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's OPP concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

Human Studies

This assessment does not rely on any data from studies in which human subjects were intentionally exposed to a pesticide.

Data Requirements

Residue chemistry data are not required for a non-food use chemical however the UV/visible absorption spectrum study is still outstanding. There are no outstanding toxicological or exposure data requirements for the currently registered uses of dikegulac sodium.

Preliminary Human Health Risk Assessment

The qualitative assessment discussed herein constitutes the preliminary risk assessment for dikegulac sodium. HED concludes that there are no human health risks associated with the currently registered uses of dikegulac sodium.

References

Memoranda Relevant to Registration Review for Dikegulac Sodium			
Author	**DP or TXR Barcode**	**Date**	**Title**
Y. Barnes	D317256	10/31/2006	Dikegulac Sodium. Human Health Considerations for the Reregistration Eligibility Decision
S. Recore	D317852	02/06/2007	Dikegulac Sodium: Addendum to HED Risk Assessment
U. Habiba	TXR 0057022	07/31/2014	Dikegulac Sodium: Summary of Hazard and Science Policy Council (HASPOC): subchronic inhalation, neurotoxicity (acute and subchronic), reproduction, and immunotoxicity studies.
M. Hawkins	D317857	07/25/2006	Review of Dikegulac Sodium Incident Reports
A. Nielsen	D370143	02/04/2010	Dikegulac Sodium: HED's response to PBI/Gordon Corporation's request to permit a 4-hour restricted entry interval for the end use product Atrinal Plant Growth Regulator (EPA Reg. No. 2217-776)
S. Recore	D317852	02/06/2007	Dikegulac Sodium: Addendum to HED Risk Assessment Acid Equivalent Rates

Attachments

Table 1. Chemical Identity of Dikegulac Sodium
Table 2. Physicochemical Properties of Technical Grade Dikegulac Sodium
Table 3. Satisfaction of Dikegulac Sodium Toxicology Data Requirements
Table 4. Dikegulac Sodium Acute Toxicity Profile
Table 5. Dikegulac Sodium Subchronic, Chronic, and Other Toxicity Profiles
Table 6. Summary of Representative Occupational Use Patterns, Formulations, and App Rates

Attachments

Chemical Identity and Physicochemical Properties Tables

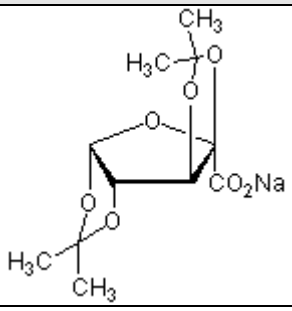
Table 1. Chemical Identity of Dikegulac Sodium	
Chemical Structure	
Common Name	Dikegulac Sodium
PC Code	109601
CAS Name	sodium 2,3:4,6-bis-*O*-(1-methylethylidene)-α-L-*xylo*-2-hexulofuranosonate
IUPAC Name	sodium 2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-2-hexulofuranosonate
CAS No.	52508 - 35 – 7
Registration Review Case No.	3061
Chemical Class`	Acid herbicide
Molecular weight	235.02 g/mol

Table 2. Physicochemical Properties of Technical Grade Dikegulac Sodium		
Parameter	**Value**	**Reference**
Molecular Weight	296.25 grams	MSDS
Melting range	> 300 ºC	MSDS
Density	9.12 lbs/gal	MSDS
Water solubility (20°C)	590 g/L, soluble	Merck Index 12th Edition
Solvent solubility (20°C)	methanol 390 g/L ; ethanol 230 g/L ; chloroform 60 g/L ; acetone <10 g/L ; hexane <10 g/L; cyclohexanone <10 g/L	Merck Index 12th Edition
Vapor pressure	$3.08E^{-12}$ mm Hg at 25 °C	SRC: Neely, WB & Blau, GE (1985)
Dissociation constant, pKa	Not reported	Data Required
Octanol/water partition coefficient, log K_{OW} (25°C)	Log P = -2.05	SRC: Meylan, Wm. Howard ,PH (1995)
UV/visible absorption spectrum	Not reported	Data Required

Table 3. Toxicology Data Requirements for Dikegulac Sodium		
Study	Technical	
	Required	Satisfied
870.1100 Acute Oral Toxicity	yes	yes
870.1200 Acute Dermal Toxicity	yes	yes
870.1300 Acute Inhalation Toxicity	yes	yes
870.2400 Acute Eye Irritation	yes	yes
870.2500 Acute Dermal Irritation	yes	yes
870.2600 Skin Sensitization	yes	yes
870.3100 90-Day Oral Toxicity in Rodents	yes	yes
870.3150 90-Day Oral Toxicity in Non-Rodents	CR[a]	yes
870.3200 21/28-Day Dermal Toxicity	yes	yes
870.3250 90-Day Dermal Toxicity	CR[a] (no)	---
870.3465 90-Day Inhalation Toxicity	CR[a] (yes)	waived[b]
870.3700 Prenatal Developmental Toxicity Study (Rodent)	yes	yes
870.3700 Prenatal Developmental Toxicity Study (Non-Rodent)	yes	yes
870.3800 Reproduction and Fertility Effects	yes	waived[b]
870.4100 Chronic Toxicity (Rodent)	CR[a] (no)	yes
870.4200 Carcinogenicity (Two Rodent Species; Rat and Mouse)	CR[a] (no)	yes
870.4300 Combined Chronic Toxicity/Carcinogenicity	---	---
870.5100 Bacterial Reverse Mutation Test	yes	yes
870.5300 *in vitro* Mammalian Cell Gene Mutation Test	yes	yes
870.5375 *in vitro* Mammalian Chromosome Aberration Test	yes	yes
870.5385 Mammalian Bone Marrow Chromosomal Aberration Test	yes	yes
870.5395 Mammalian Erythrocyte Micronucleus Test	yes	yes
870.6200 Neurotoxicity Screening Battery (Acute, Rat)	yes	waived[b]
870.6200 Neurotoxicity Screening Battery (Subchronic, Rat)	yes	waived[b]
870.6300 Developmental Neurotoxicity Study	CR[a] (no)	---
870.7200 Companion Animal Safety	CR[a] (no)	---
870.7485 Metabolism and Pharmacokinetics	CR[a] (no)	yes
870.7600 Dermal Penetration	CR[a] (no)	---
870.7800 Immunotoxicity	yes	waived[b]

a CR = conditionally required.

b Waived by Hazard and Science Policy Council (HASPOC) on (TXR).

Table 4. Acute Toxicity Data for Dikegulac Sodium				
Guideline No.	**Study Type**	**MRID**	**Results**	**Toxicity Category**
870.1100 81-1	Acute oral [rat] Acceptable/guideline	44093901	No deaths, no clinical signs LD50 >5000 mg/kg.	IV
	Acute oral [rat] Unacceptable/guideline	43064604		
		43064605		
		43064606		
		43064607		
		43064608		
870.1200 81-2	Acute dermal [rat] Acceptable/guideline	43064612	3 deaths, no clinical signs LD50 >2000 mg/kg	III
	Acute dermal [rabbit] Acceptable/guideline	43064610	LD50 >1000 mg/kg	II
		44093902	No deaths, no clinical signs. LD50 >5000 mg/kg	IV
870.1300 81-3	Acute inhalation [rat] Acceptable/guideline	43064613	No deaths. LC50 >2 mg/L	III
		44093903		IV
870.2400 81-4	Acute eye irritation [rabbit] Acceptable/guideline	43064614	Conjunctival redness was persistent for 48 and 72 hours.	IV
		44093904	No corneal effects were observed. Conjunctival redness, swelling or discharge returned to normal within 72 hours.	III[a]
870.2500 81-5	Acute dermal irritation [rabbit] Unacceptable/guideline	43064615	Slight dermal irritation/ slight erythema was apparent 72 hours after application	III
	Acute dermal irritation [rabbit] Acceptable/guideline	44093905	Slight erythema and edema observed	IV
870.2600 81-6	Acute dermal sensitization [guinea pig] Unacceptable/guideline	43064616	All animals survived. No adverse clinical signs. Not a dermal sensitizer	N/A
870.2600 81-6	Acute dermal sensitization [guinea pig] Acceptable/guideline	44093906	All animals survived. No adverse clinical signs. Not a dermal sensitizer	N/A
870.2500 81-5	Acute dermal irritation [rabbit] Acceptable/guideline	44093905	Slight erythema and edema observed	IV
870.2600 81-6	Acute dermal sensitization [guinea pig] Unacceptable/guideline	43064616	All animals survived. No adverse clinical signs. Not a dermal sensitizer	N/A
870.2600 81-6	Acute dermal sensitization [guinea pig] Acceptable/guideline	44093906	All animals survived. No adverse clinical signs. Not a dermal sensitizer	N/A

[a] The toxicity category on eye irritation was revised to III (TXR 0054936, 2008)

Table 5: Subchronic, Developmental, and Other Toxicity Profile on Dikegulac Sodium		
Guideline#/ Study Type	**MRID# (year)/ Classification /Doses**	**Results**
870.3100 82-1a 90-Day Subchronic toxicity (rat)	42957701 (1975) Acceptable/guideline 22 Fullinsdorf albino rats/sex/dose of 0, 200, 700, 2000 mg/kg/day for 13 weeks	Mortality, clinical signs, food consumption, body weight, hematology, urinalysis, organ weights, gross and microscopic pathology were unaffected by treatment. The NOAEL is ≥ 2000 mg/kg/day. The LOAEL was not established.
870.3100 82-1b 90-Day Subchronic toxicity (dog)	42957702 (1975) Acceptable/guideline 4 beagle dog sex/dose of 0, 500, 1200, 3000 mg/kg bw/day for 13 weeks	Mortality, clinical signs, body weight, hematology, urinalysis, organ weights, gross and microscopic pathology were unaffected by treatment. The NOAEL is 1200 mg/kg/day. The LOAEL is 3000 mg/kg/day based on relatively mild effects of profuse watery diarrhea and occasional vomiting.
870.3250 82-3 21-Day dermal toxicity	42957703 (1975) Acceptable/Guideline 5 New Zealand White rabbits/sex/ dose of 0, 3% or 30% seven days a week for 21 days.	Slight erythema occurred in three male and three female control rabbits during the treatment period. The dermal NOAEL is 600 mg/kg/day, no LOAEL being established.
870.3700a 83-3a Developmental Toxicity (rat)	43064617 (1977) Acceptable/Guideline 40 female Fullinsdorf albino rats/dose of (by gavage) 0, 200, 700 or 2000 mg a.i./kg/day (GD 7-16)	The maternal NOAEL is 700 mg/kg/day. The maternal LOAEL is 2000mg/kg/day, based on clinical observations of light sedation following the first two treatments. The developmental NOAEL is > 2000 mg/kg bw/day. No developmental LOAEL was established.
870.3700a 83-3a Developmental Toxicity (rabbit)	43064618 (1977) Acceptable/Guideline 20 female yellow-sliver rabbits/dose of 0, 200, 700 or 2000 mg a.i./kg/day (GD 7-19)	The maternal NOAEL is 700 mg/kg/day. The maternal LOAEL is 2000 mg/kg /day, based on clinical observations of diarrhea and lack of body weight gain. The developmental NOAEL is > 2000 mg/kg /day. No developmental LOAEL was observed.
Gene Mutation 84-2 870.5100 (*Salmonella typhimurium*)	440393907 (1995) Acceptable/Guideline 100, 333, 1000, 3330 and 5000 µg/ plate	Negative for reverse gene mutations in *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537 in presence or absence of S9 activation to doses from 100 to 5000 µg/plate. Cytotoxicity was not observed at any dose levels.
Gene Mutation 870.5300 84-2 (mouse lymphoma cells)	440393908 (1995) Acceptable/Guideline 500 to 5000 µg/mL	Not mutagenic in assays with/without S9activation. Cytotoxicity was not observed at any dose levels.
Micronucleus 870.5395 84-2 (mouse)	440393909 (1995) Acceptable/Guideline 1250, 2500, or 5000 mg/kg	Negative for micronucleus induction in bone marrow cells of Male and Female CD-1 mice harvested 24, 48, and 72 hrs. post-administration of single doses of 1250, 2500, or 5000 mg/kg/day. No overt toxicity in any treated animal or target organ in any treatment group.

Occupational Exposure Use Pattern Table

Table 6. Summary of Maximum Application Rates for Registered Dikegulac-Sodium Uses							
EPA Reg. No	Crop	Target	% ai.	Maximum Application Rate	Application Equipment	Amount Handled Daily	Use Directions and Limitations
Soluble Concentrate							
ATRINAL® NURSERY AND GREENHOUSE 2217-932	Greenhouse and nursery ornamentals, tree farms (chemical pinching)	Foliar Spray, bark banding, soil drench	18.5 %	0.052 lb ai/gallon (0.048 lb ae[1]/gallon)	Mechanically pressurized handgun	1,000 gallons	Not for use on green ash, red oak, conifers, trailing and weeping lantana, Christmas tree farms, and evergreens in California. Do not apply through any type of irrigation system. Do not use on food or fodder crops. PPE includes baseline dermal protection. Direct injections to trees, applicators must wear protective eyewear
					Manually pressurized handwand	40 gallons	
					Backpack		
ATRINAL® PLANT GROWTH REGULATOR 2217-776	Landscape Ornamentals -- shrubs, hedges, trees, and groundcover (growth control)			4.26 lb ai/A or 0.039 lb ai/gallon (0.035 lb ae/gallon)	Mechanically pressurized handgun	1,000 gallons	
					Manually pressurized handwand	40 gallons	
					Backpack		Use with medium or coarser spray nozzles. Do not apply through any type of irrigation system. Do not use on food or fodder crops. PPE includes baseline dermal protection. Direct injections to trees, applicators must wear protective eyewear
	Fruiting Landscape Trees and Shrubs (suppression of flower and fruit formation)			7.1 lb ai/A or 0.065 lb ai/gallon (0.060 lb ae/gallon)	Handgun	1,000 gallons	
					Manually pressurized handwand	40 gallons	
					Backpack		
	Broadleaf trees in rights-of-way, parks	Tree injection		0.09 lbs a.i./tree or 0.835 lb ai/gallon (0.77 lb ae/gallon)	Injection system	NA	
Ready to Use							
Pinscher® PGR 69117-7	Ornamental trees	Tree injection	18.5 %	0.0016 lb a.i./ tree	Injection system	NA	Apply in spring prior to flower. Do not apply to foo bearing plants

1 ae= acid equivalent.