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

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Scientific Review of Non-Target Organism Waiver Requests for Registration Application of **AG3 LIQUID** Containing 10.30% Mono and Dipotassium Salts of Phosphorous Acid and 0.15% Copper Sulfate (EPA Reg. Symbol 8622-AI)

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CONTENTS:

Non-target organisms waiver requests for guidelines §154-6 through -11 for AG3-Liquid (EPA Reg. Symbol 8622-AI) (Decision #: 336368; DP#: 305561).

ACTION REQUESTED:

On July 17, 2003, J. Michael Kelly, Ph.D. of toXcel, Authorized Representative for Ameribrom, Inc., submitted registration of this biochemical fungicide, a new agricultural use fungicide for the control of *Pythium* and *Phytophthora* of agronomic crops. The product contains 10.3% mono and dipotassium salts of phosphorous acid and 0.15% copper sulfate. Also included was a request for a waiver for the non-target organisms (§154-6 through -11). The waiver requests were denied in a letter from Sheryl K. Reilly, Ph.D., Chief of Biochemical Pesticides Branch.

On July 19, 2004, Dr. J. Michael Kelly submitted a revised response to EPA's letter on this issue.

CONCLUSIONS:

1. The waiver requests were addressed individually and in detail, and some supporting papers were provided for review. Unfortunately, much of the information provided were secondary sources which simply summarized data published elsewhere, and this requires going to the original to determine if it was valid. Most of the submitted articles in the Appendix referred to copper sulfate toxicity, and the waiver request response would have been better addressed by pulling out the relevant articles and including them in the specific guideline waiver request, instead of lumping them all in an Appendix, particularly when the Appendix has no toxicity information on the phosphorous acid salts. There was one paper, moreover, which seemed to be missing relevant pages: Hudson, Rick H., Tucker, R.K. and Haegele, M.A. (1984) Handbook of toxicity of pesticides to wildlife. USDI Fish and Wildlife Service Resource Publication Number 153. Washington, D.C. I could find nothing on either copper sulfate or the mono and dipotassium salts of phosphorous acid referred to in the article.
2. Each of the waiver requests was based on:
 - a. Low potential for exposure of the active ingredients to the organism, particularly compared to recommended use in fertilizers. Extensive information on the exposure potential is provided and useful, as well as vital in the risk assessment of the product.
 - i. Irrigation systems or sprays: dilute AG3-Liquid 1:150 in water, apply 2.5 to 5 gal (10-20 L)/acre at or near planting/sowing time, and at two week intervals within 2 months from time of planting/sowing.
 1. At this dilution, the mixture contains 0.007 lb/gal mono- and di-potassium salts of phosphorous acid and the application rate is 0.034 lb/acre. Seed-placed fertilizer phosphorous at rates up to 18 to 27 lb/acre are recommended for fertilizing cereal crops (McKenzie and Middleton, 1997).
 2. The concentration also contains 0.00016 lb/gal copper sulfate pentahydrate and the application rate is 0.00079 lb/acre (elemental copper content is approximately 0.00004 lb/gal and application rate is 0.0002 lb/acre).
 - ii. Foliar: dilute AG3-Liquid 1:27 in water, apply 1.5 gal (6 L)/acre. Apply diluted liquid to foliage with conventional sprayers at 2-3 weeks intervals, repeat as needed.
 1. The product as used (diluted 1:27 with water) contains 0.038 lbs/gal of mono- and di-potassium salts of phosphorous acid, and the application rate is 0.056 lb/acre.
 2. The foliar applications contain 0.00088 lb/gal sodium copper pentahydrate and the application rate is 0.00131 lb/acre, with elemental copper at 0.00022 lb/gal and applied at a rate of 0.00033 lb/acre).
 - b. Low toxicity of the active ingredients.
 - i. The toxicity referred to here is the toxicity obtainable from the public literature for copper sulfate and not for the copper sulfate pentahydrate which has 15% less elemental copper, and therefore are being proposed as suitable surrogates. Copper

is, in addition, a micronutrient ordained for copper deficiency, but the amount of copper in this product is 333-fold less than the elemental copper recommended for deficiency treatment.

- ii. There are no ecotoxicity data available on the phosphorous salts. There was a mention in a waiver that upon foliar application, the phosphite ions are taken up directly by the plant foliage and may undergo a degree of conversion to phosphate ions, or will be used directly by plants, as phosphite ions. The California fertilizer regulations (CDFA, 2003), which provided the information given above, also noted that placement close to seeds or root zones may be injurious to crops, and may be aggravated by a soil pH below 6.5. However, the use in fertilizer is much higher than the levels associated with this pesticide.
- c. Demonstrated low concern for exposure to small amounts of these chemicals based on EPA's decisions to grant exemptions from requirements of a tolerance for their existing fungicidal uses.

RECOMMENDATIONS:

4. The label provided with the submitted waiver requests is incorrect, in that it gives three active ingredients, adding [REDACTED] to the two listed on the CSF, mono and dipotassium salts of phosphorous acid and copper sulfate.

If the label is corrected, the product is ready for registration, as all toxicity studies and waiver requests are acceptable.

Inert ingredient information not included.

TOXICITY PROFILE

Acute oral toxicity	IV	MRID 460409-05
Acute dermal toxicity	IV	MRID 460409-06
Acute inhalation toxicity	IV	MRID 460409-07
Primary eye irritation	III	MRID 460409-08
Primary dermal irritation	IV	MRID 460409-09
Dermal sensitization	No	MRID 460409-10

LABELING: The Signal word is Caution from the Toxicity Rating of III for primary eye irritation.

Guideline 880.1100: Product identity and disclosure of ingredients (MRID 450319-01, CSF)

AG3 LIQUID contains 3.4% mono- and 6.9% dipotassium salts and 0.15% copper sulfate and 89.55% other ingredients. This product is to be used as a systemic fungicide for the control of *Pythium* Damping-Off and Root Rot, *Phytophthora* Root Rot and Downy Mildew diseases of agronomic crops.

The following table summarizes information submitted by the registrant regarding the active ingredients.

Chemical Names:	phosphonic acid, monopotassium salt phosphonic acid, dipotassium salt copper sulfate pentahydrate
Synonyms:	monopotassium salt of phosphorous acid, potassium dihydrogen phosphite, monopotassium phosphite, monopotassium phosphonate dipotassium salt of phosphorous acid, dipotassium hydrogen phosphite, dipotassium phosphite, dipotassium phosphonate
	CAS Registry Nos.: 13977-65-6 13492-26-7 7758-99-8
Molecular Formulae:	KH_2PO_3 K_2HPO_3 $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$
Chemical Family:	metallic salts
Source of Biochemical:	manufactured
Mode of Action:	fungicide

WAIVER REQUEST REVIEW FOR AVIAN ACUTE ORAL (QUAIL) TOXICITY TESTING (OPP §154-6)

Publicly available information regarding inorganic copper compounds indicates that copper sulfate poses less of a threat to birds than other animals. The lowest lethal doses (LD_{1,0}) for copper sulfate in pigeons and ducks are 1,000 mg/kg and 600 mg/kg, respectively (EXTOXNET, 2001; EXTOXNET, 2004)/ The oral LD₅₀ for Bordeaux mixture in young mallards dosed orally by capsule is >2,000 mg/kg (Pimentel, 1071). Bordeaux mixtures applied as foliar sprays contain approximately 0.016 lb elemental copper/gal, which is 67-fold greater than the AG3-Liquid recommended foliar spray for AG3-Liquid.

WAIVER REQUEST REVIEW FOR AVIAN DIETARY LC50 (MALLARD) TOXICITY TESTING (OPP §154-7)

Publicly available information regarding inorganic copper compounds indicates that copper sulfate poses less of a threat to birds than other animals. The lowest lethal doses (LD_{1,0}) for copper sulfate in pigeons and ducks are 1,000 mg/kg and 600 mg/kg, respectively (EXTOXNET, 2001; EXTOXNET, 2004)/ The oral LD₅₀ for Bordeaux mixture in young mallards dosed orally by capsule is >2,000 mg/kg (Pimentel, 1071). Bordeaux mixtures applied as foliar sprays contain approximately 0.016 lb elemental copper/gal, which is 67-fold greater than the AG3-Liquid recommended foliar spray for AG3-Liquid.

WAIVER REQUEST REVIEW FOR FRESHWATER LC50 (TROUT) TOXICITY TESTING (OPP §154-8)

Copper sulfate is very toxic to freshwater fish; however its toxicity to fish varies with the dose, species, and the physical state and chemical characteristics of the water (Pimentel, 1971). Copper compounds are approved of controlling algae in bodies of water occupied for food fish at rates of copper sulfate up to 2 ppm or 5.5 lbs/acres-foot. This is expected to not be toxic to fish, and is 4,231-fold greater than the maximum recommended foliar use rate of 0.0013 lb copper sulfate pentahydrate per acre in AG3-Liquid. The AG3-Liquid label prohibits use directly in water, in areas where surface water is present, or to intertidal areas below the mean high water mark, and copper is not expected to travel long distances through the soil, as copper ions are strongly adsorbed or precipitated to soil particles when applied to soil. The greatest concern for copper toxicity is in soft water because the toxicity of copper to fish increases as water hardness decreases (IFAS, 1988). Mayer and Ellersieck (1986) reported the following results for 96-hour LC₅₀ tests for several freshwater fish species: from 135 µg/L for rainbow trout to 3,510 µg/L for green sunfish.

Fish kills have resulted from anaerobic conditions when an overabundance of phosphorous in waterways causes algal blooms and die-offs followed by oxygen depletion from the decaying organic matter. Phosphorous acid has not been reported in published literature as being directly toxic to fish.

**WAIVER REQUEST REVIEW FOR ACUTE FRESHWATER INVERTEBRATES
(DAPHNIA) TOXICITY TESTING (OPP §154-9)**

Kim et al (1999) found that the toxicity of copper to freshwater invertebrates such as Daphnids is affected by the amount of dissolved organic matter (DOM) in the water. The 24-hour LC₅₀ of copper to *Ceriodaphnia dubia* was 75 µg/L when the DOM was 2.5 mg/L and ranged up to 270 µg/L when the DOM concentration was 10 mg/L. The toxicity of copper to *C. dubia* was closely related to the measured free-copper concentration (Cu⁺⁺) rather than to total copper concentrations. In another study in which the sensitivity to copper of *Ceriodaphnia* was compared to *Daphnia*, *Ceriodaphnia* were found to be more sensitive, with a 48-hour LC₅₀ of 4.16 µg/L compared with to 6.53 µg/L (Harmon et al., 2003). These results would indicate that relatively low levels of copper are toxic to *Daphnia*, however in another study, copper sulfate applied at a rate of 0.05 - 0.08 ppm in ponds to control algae resulted in an increase in cladocerans and other zooplankton (Crane, 1963 in Pimentel, 1971).

**WAIVER REQUEST REVIEW FOR NON-TARGET PLANT TOXICITY
TESTING (OPP §154-10)**

Copper compounds have the potential for phytotoxicity or poisonous activity in plants by disrupting photosynthesis. However, copper also is an essential element which plants need in very low concentrations and is necessary for photosynthesis and for metabolizing nutrients into usable energy sources. Use rates that control algae without damaging aquatic plants and that control fungi without damaging crops have been established. Furthermore, use of the TGAs in fertilizers is 2 to 3 orders of magnitude greater than proposed use as a fungicide in AG3-Liquid,

**WAIVER REQUEST REVIEW FOR NON-TARGET INSECT
(HONEYBEE ACUTE CONTACT) TOXICITY TESTING (OPP §154-11)**

One source stated that bees are endangered by strong water-based copper compounds, such as a Bordeaux mixture of copper sulfate, lime and water (Hartley and Kidd, 1983), however, the amount of copper sulfate pentahydrate in AG3-Liquid is so small in comparison to approved uses of copper containing compounds that it is not expected to affect bees under recommended use conditions.