

Methoprene

New York State Department of Environmental Conservation

Division of Solid and Hazardous Materials

50 Wolf Road, Albany, New York 12233-7250

Phone: (518) 457-6934 • FAX: (518) 457-0629



March 23, 2000

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ms. Catherine Elmi
State Regulatory Manager
Wellmark International
1000 Tower Lane, Suite 245
Bensenville, IL 60106

Dear Ms. Elmi:

Re: Application to Remove the Label Restriction "Do Not Apply to Known Fish Habitats" from Three Products:
Zoecon Altosid Briquets, EPA Reg. No. 2724-375
Zoecon Altosid XR Extended Residual Briquets, EPA Reg. No. 2724-421
Zoecon Altosid Pellets, EPA Reg. No. 2724-448

The New York State Department of Environmental Conservation (This Department) has completed review of the subject application, including supplemental information submitted. The request to remove the label restriction "Do Not Apply to Known Fish Habitats" from the subject products is **denied**.

The review identifies concerns regarding potential teratogenicity of methoprene degradates to aquatic vertebrates. We conclude that no definitive risk assessment is possible for these extended release products due to the lack of information on the formation and decline of methoprene degradation products, and their effects on non-target aquatic organisms continuously exposed to them for extended periods during sensitive life stages.

Application Chronology

Application was submitted June 22, 1999. The application was determined to be incomplete, and a letter sent July 14, 1999. After required information was submitted, the application was determined to be complete and a completeness letter sent August 25, 1999. A decision date of January 19, 2000 was established at that time. In a letter dated December 21, 1999, we notified you of our concerns regarding potential teratogenicity of methoprene degradates and afforded you the opportunity to provide any additional information to alleviate those concerns. On January 18, 2000 you submitted additional information and waived the decision date to allow time to review the information.



Current Status of Altosid Products

The three subject products:

Zoecon Altosid Briquets, EPA Reg. No. 2724-375
Zoecon Altosid XR Extended Residual Briquets, EPA Reg. No. 2724-421
Zoecon Altosid Pellets, EPA Reg. No. 2724-448

are extended residual products and are currently registered for use in small bodies of water such as: storm drains, catch basins, roadside ditches, artificial water holding containers, cess pools & septic tanks, waste treatment & settling ponds, freshwater swamps & marshes, salt & tidal marshes, etc. The only areas prohibited are areas of known fish habitat. In addition, there are other Altosid products:

Zoecon Altosid Mosquito Growth Regulator, EPA Reg. No. 2724-392
Zoecon Altosid Liquid Larvicide Conc., EPA Reg. No. 2724-446
Zoecon Altosid XR-G, EPA Reg. No. 2724-451

which do not have the extended residual of the subject products and which are currently allowed for use in fish habitat. These products with shorter residual activity are not expected to present the same risk to aquatic organisms, specifically fish, as the subject products which maintain residual concentrations of methoprene for an entire mosquito breeding season. **Because there are methoprene products that are registered for use in waters that are known fish habitat, it has been determined that no critical need exists for the subject products to be allowed for this same use.**

Ecological Risk Assessment

Review of the materials submitted indicate that the risk posed to aquatic vertebrates, particularly fish, by continuous exposure to methoprene degradates remains unacceptable. A number of issues with respect to both exposure to and the toxicity/teratogenic potential of the degradates are unresolved.

One potential cause postulated for the recent increase in deformities in frog populations is increased exposure to exogenous compounds which disrupt the embryonic retinoic acid signaling system, interfering with normal development (Burkhart, J.G et al 2000. Strategies for Assessing the Implications of Malformed Frogs for Environmental Health, Environmental Health Perspectives, Vol. 108, No. 1). Methoprene degradation products and metabolites have been shown to exhibit retinoid-like activity and to be teratogenic in amphibians. There is evidence that photolyzed methoprene is more teratogenic than the parent compound and that *Xenopus* larvae exposed to the mixture of degradates had deformities similar to those being found in wild frog populations (LaClair, J.J., Bantle J.A., Dumont, J.1998. Photoproducts and metabolites of a common insect growth regulator produce developmental deformities in *Xenopus*. Environmental Science & Technology 32 (10): 1453-1461).

Recent research attempting to determine causal factors in the highly publicized deformed frog phenomenon identified residues of several pesticides in pond water from Michigan that induced developmental abnormalities in *X. Laevis*. Methoprene or its environmental degradation products were not identified in any of the sites at biologically relevant concentrations. Because they were not felt to be contributory in those instances, however, does not alleviate concern for effects to embryonic aquatic vertebrates exposed to methoprene degradates. The research has involved only amphibians, thus far; no similar work with fish seems to have been conducted. However, zebrafish eggs exposed for one hour to concentrations of retinoic acid ranging from 10^{-9} to 10^{-6} M (roughly .31 ppb to 310 ppb) at 4.3, 5.2, and 8.5 hours post fertilization, resulted in malformation of the brain and cranial ganglia beginning at 3 ppb. (Holder, N., Hill, J., 1991. Retinoic Acid Modifies Development of the Midbrain-Hindbrain Border and Cranial Ganglion Formation in Zebrafish Embryos. *Development* 113 1159-1170). While retinoic acid mimics do not tend to exhibit effects at concentrations as low as retinoic acid, these very short exposures demonstrate a high sensitivity and suggests that the use of the extended release methoprene products in fish bearing waters may prove deleterious to developing fish.

The full Ross microcosm water concentration study paper submitted by Wellmark was also reviewed. Your conclusion that, since the methoprene water concentration in the microcosm tanks is below levels of concern the degradate levels are also similarly low, is not supported by the information provided. No data for degradate identification, quantification, or fate were reported (Ross, D.H., Judy, D., Jacobson, B., and Howell, R., Methoprene Concentrations in Freshwater Microcosms Treated With Sustained -Release Altosid Formulations, *Journal of the American Mosquito Control Association*, Vol. 10, No. 2, 1994). Since neither methoprene nor the identified degradation products seem to dissipate through volatilization, the mass of the parent compound released into the water column will either remain in solution, or adsorb to organic carbon in the water column or sediments. If the methoprene content of an Altosid XR Extended Residual briquet were applied to the volume of water in the study tanks, the resulting water concentration would be roughly 542 ppb. The slow methoprene release from the briquet and the high photolysis rates in the six to seven inch water depth resulted in the low parent compound concentrations observed. The mass of the released parent becomes distributed among the degradation products.

In our initial review it was erroneously stated that hydrolysis doesn't contribute to methoprene dissipation. This was based on the statement in the United States Environmental Protection Agency Reregistration Eligibility Document (RED) for methoprene, "Methoprene does not appear to be susceptible to hydrolysis under normal environmental conditions." Further review of the methoprene RED, MSDS, and literature indicates otherwise. While photolysis is the primary degradation pathway when exposed to sunlight, methoprene is also subject to hydrolysis, at slow rates, and microbial metabolism. Under field conditions in deeper, darker, or vegetation shaded waters photodegradation rates will be reduced. Limited information on hydrolysis degradates and microbial metabolites has been submitted. This shift in degradation pathways will result in a slower overall dissipation rate of parent compound and degradates and also affect which degradates are produced.

A study paper by Ankley et al. was submitted by Wellmark to support your assertion that the subject methoprene products pose little or no risk to non-target organisms. However, in the discussion section the author cautions that "It is impossible from our data to calculate meaningful effect and no effect methoprene concentrations. Basing effect and no effect estimates upon the parent compound may not even be appropriate, if indeed metabolites or break-down products are responsible for adverse effects. Further work concerning the mechanisms and specific chemicals responsible for the observed pathology in our study, as well as measurement of these chemicals in relevant environmental settings, is required before it is possible to estimate the potential teratogenic risk of methoprene to wildlife, including amphibians." (Ankley, G.T., Tietge, J.E., DeFoe, D.L., Jensen, K.M., Holcombe, G.W., Durham, E.J., and Diamond S.A. 1998. Effects of Ultraviolet Light and Methoprene on Survival and Development of Rana Pipiens, Environmental Toxicology and Chemistry, Vol. 17, No. 12, 2530-2542.)

Regulatory Action

Based on existing information, we believe that the Department should take no action at this time that could expand the use of the Altosid products, nor the active ingredient, methoprene, in general. Therefore, the application is denied. In addition, we intend to continue to monitor emerging information to determine if methoprene presents any unreasonable risk to non-target organisms which are exposed as a result of existing uses.

If you wish to re-apply, a new application and fee are required. Data should be provided with any new application that will allow a complete characterization of the degradates in order for an adequate risk assessment to be performed.

Article 33-0711 of the New York State Environmental Conservation Law (copy enclosed) provides options that may be pursued when registration is denied. Please be aware that any product without the New York State accepted label may **not** be sold, offered for sale, distributed, or used in New York State.

If you have any questions, please contact Maureen Serafini, Chief of our Pesticide Product Registration Section, at (518) 457-7446.

Sincerely,



Stephen Hammond
Director
Division of Solid & Hazardous Materials

Enclosure

cc: w/o enc. - Janet Anderson/Willie Nelson
Biopesticides and Pollution Prevention Division
U.S. EPA