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TO: Board Members
FROM: Lebelle Hicks PhD DABT
RE: Dow AgroSciences Request for a 24(c) Label for GoalTender™ (EPA# 62719-447) on Broccoli

March 9, 2009

Dow AgroSciences Request for a 24(c) Label for GoalTender™

The petition currently being considered is a 24(c) for the use of GoalTender (EPA# 62719-447) herbicide for post-emergent treatment on broccoli. The product is a 41% emulsifiable concentrate containing 4 lbs oxyfluorfen ai/gal (Dow AgroSciences 2008). The proposed use rates are between 4 to 8 fl oz/A (0.125 to 0.25 lbs ai/A) (Dow AgroSciences 2009). *Note: All use rates below have been calculated in terms of lbs ai/A.*

The current Section 3 label has directions for pre-transplant–pre-emergent broccoli at double the rate (0.25 to 0.5 lbs/A), as proposed for the post-emergent use (0.125 to 0.25 lbs ai/A). Broccoli may be planted in rotation with potatoes. Under the “use on fallow beds” section there is a requirement for 60-day treatment to planting interval for potatoes (Dow AgroSciences 2008).

Tolerance and Food Residue Information

The existing tolerance for oxyfluorfen on broccoli is 0.05 ppm (CFR 180.381). There is a 35-day pre-harvest interval and the data submitted in the request indicate that residues from the post-emergent use will not exceed this tolerance. EPA reviewed oxyfluorfen for human health risks in 2002 (EPA 2002a) and issued a Re-registration Eligibility Decision (RED) later that year (EPA 2002b). EPA reported that all of the residues from existing uses reported by the USDA Pesticide Data Program were non-detect (EPA 2002b). IR-4 investigated the residues from the proposed post-emergent use on broccoli. Their report is included in the 24(c) request. The IR-4 reported two detectable residues: 0.0163 and 0.0168 ppm following post-emergent use on broccoli at the higher rate of 0.25 lbs/A (IR-4 2005). These residues levels are considerably below the tolerance level of 0.05 ppm.

Mammalian Toxicity and Risks Overview

Oxyfluorfen is a diphenyl ether herbicide that interferes with heme biosynthesis in plants resulting in a decrease in chlorophyll (Roberts 1998). It is a contact herbicide absorbed by the foliage, specifically the shoots (Tomlin 2003). Susceptible plants show chlorosis, necrosis and desiccation (Roberts 1998).

Oxyfluorfen has low acute toxicity by the oral, dermal and inhalation routes of exposure (EPA 2002b). Following subchronic and chronic exposure inhibition of heme synthesis and resultant anemias are observed in laboratory animals. Similar to chlorophyll in plants, heme is the iron-containing pigment that binds oxygen in mammals. In mammals it is the heme in the hemoglobin whose function is to transport oxygen to cells.



When looking at non-cancer toxicological endpoints, EPA calculates a chronic Reference dose (RfD). The RfD is equal to the lowest No Observable Adverse Effect Level (NOAEL) from the animal studies divided by uncertainty factors of 10 for extrapolating from lab animals to humans (interspecies extrapolation) and 10 for the variability in the human population (intraspecies variability). The greater the NOAEL, the less toxic the compound is following subchronic or chronic exposure. If there is evidence of sensitivity in the developing fetus or pup compared to the dam, another factor of 10 is added. This is the Food Quality Protection Act Safety Factor (FQPA SF).

Chronic exposure levels from the diet and drinking water are then calculated and compared to the RfD. If the daily exposure dose (mg/kg/day) is less than the RfD (mg/kg/day), this use is within the acceptable risk level.

The most sensitive NOAEL for oxyfluorfen is 3.0 mg/kg/day from the mice and dog studies. The Lowest Observable Adverse Effect Level (LOAEL) from these studies was 33 mg/kg/day (dogs and male mice) and 42 mg/kg/day (female mice). Effects observed at the LOAEL were liver toxicity. There was no evidence of sensitivity in the developing animal, resulting in a decrease of the FQPA SF to 1X (EPA 2002b).

Using the 3.0 NOAEL and the uncertainty factors of 100 for inter and intra species extrapolation the resulting RfD is 0.03 mg/kg/day (EPA 2002a). The dietary exposure estimated by EPA for US population, for infants < 1 yr old and for children between 1 to 6 yrs old was less than 1% of the RfD.

With regard to drinking water, EPA estimates from their models for estimated environmental concentrations (EEC) are 7.1 ppb for surface water and 0.08 ppb for ground water. If the drinking water levels of concern (DWLOC) is greater than the EEC then the risk is acceptable. The DWLOCs for chronic effects for US population, for infants < 1 yr old, children between 1 to 6 yrs old and women of child bearing age (13 to 50) range from 300 to 1,050 ppb. The DWLOCs are much greater than the estimated EECs indicating acceptable risks from potential drinking water exposure (EPA 2002b).

Oxyfluorfen is a “C” possible human carcinogen based on increases in combined hepatocellular adenomas and carcinomas in mice (EPA 2002b). Because of this, in addition to the RfD for non-carcinogenic effects, EPA also performed a cancer risk assessment. EPA’s acceptable risk level resulting from exposure to carcinogens is 1×10^{-6} (EPA 2002b).

Dietary cancer risks have been estimated at 3.8×10^{-7} . Cancer risks from drinking water were estimated based on an EEC of 5.7 and a DWLOC of 0.315 ppb. EPA considered that the inputs for the model, 2 lbs ai/A per year **every year** by broadcast makes this model-generated figure most conservative (EPA 2002b). This rate is 8 times the proposed use rate of 0.25 lb ai/A for this 24(c) application.

Environmental Fate

USDA Exttoxnet and EPA characterize oxyfluorfen as moderately persistent in soil (USDA 1996, EPA 2002c). Oxyfluorfen is slightly mobile in sandy soils and immobile in other soil types (EPA 2002c). It also readily binds to soil and is not readily desorbed from soils with high clay or organic matter and is also practicably insoluble in water at 0.1 ppm (USDA 1996, EPA 2002c). The Pesticide Manual reports K_{oc} s of 2,891 in sand to 32,381 in silt clay loam, indicating negligible leaching (Tomlin 2003). Oxyfluorfen is stable to hydrolysis at pH of 5, 7 and 9, over

28 days. It is rapidly photo-degraded in aqueous solutions (Roberts 1998, EPA 2002c). Laboratory evidence indicates that oxyfluorfen will persist in deep or turbid surface water when not exposed to sunlight.

Sediment sampling in California resulted in average levels between 1.0 and 27.2 ppb. Using a soil sediment coefficient of 100, water levels at 0.01 to 0.27 ppb can be estimated. EPA modeled EECs following aerial and ground applications at 0.25 lbs/A (the proposed 24[c] use rate) on cole crops in California. The resulting levels in surface water were 1.58 ppb by air and 1.33 ppb by ground. These levels are much lower than the estimated surface water concentration of 7.1 ppb that was calculated at the maximum label rate for non-cole crops.

Aquatic Toxicity and Risks Overview

Aquatic risks are calculated differently than human health risks. EPA defines the risk quotient (RQ) as the ratio of the EEC to the LC₅₀ (median lethal concentration) for acute risks and the ratio of the EEC to the No Observable Effect Concentration (NOEC) for chronic risks. The risks to aquatic species from exposure to oxyfluorfen were summarized in Environmental Fate and Effects Division (EFED) memo (EPA 2002c). The classic EPA levels of concern (LOC) for aquatic risks are: 0.5 for acute risks, 0.1 for restricted uses, 0.05 for endangered species and 1 for chronic risks.

Oxyfluorfen is highly to very highly acutely toxic for fish, invertebrates and aquatic plants. The lowest LC₅₀s for fish, freshwater invertebrates, marine invertebrates and aquatic plants are 200, 80, 32, 0.27 ppb, respectively. EPA assumed, based on existing data (NOEC of > 170 ppb), that marine fish are equally sensitive to oxyfluorfen as are freshwater fish. The resulting RQs are presented in Table 1.

Species	EEC ppb		Lowest LC ₅₀ ppb	Risk Quotient	
	Ground	Air		Ground	Air
Fish	1.33	1.58	200	0.01	0.01
Fresh water invertebrates	1.33	1.58	80	0.02	0.02
Marine invertebrates	1.33	1.58	32	0.04	0.05 ^(a)
Plants	1.33	1.58	0.29	4.59 ^(b)	5.49 ^(b)

(a) RQ exceeds the LOC for endangered species

(b) RQ exceeds the LOC for all endpoints

Regarding chronic risks to aquatic species, the LOCs were not exceeded for fish or invertebrates. Oxyfluorfen is practically non-toxic to birds (chronic and acute) and bees (acute > 100 ug/bee).

References	
40CFR180.381	40CFR180.381 Code of Federal Regulations Tolerances for 2-Chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene (Oxyfluorfen) 2007
Dow AgroSciences 2009	Dow AgroSciences 2008 Goal Tender (EPA# 62719-447) proposed 24c label for Maine
Dow AgroSciences 2008	Dow AgroSciences 2008 Goal Tender (EPA# 62719-447)
EPA 2002a	EPA 2002a Oxyfluorfen. Revised Human Health Risk Assessment. HED Chapter for the Re-registration Eligibility Decision (RED) Registration Case # 2490. Chemical # 111601. DP Barcode D281831.
EPA 2002b	EPA 2002b Re-registration Eligibility Decision (RED) Registration Case # 2490
EPA 2002c	EPA 2002c Environmental Fate and Effects Division (EFED) Risk Assessment for Oxyfluorfen Re-registration Decision Document. PC Code 111601 DP Barcode 282182
IR-4 2005	IR-4 2005 Analytical Summary Report PR #08806; Oxyfluorfen: Magnitude of the Residues on Broccoli IR-4 Western Regional Laboratory, University of California, Davis, CA.
Roberts 1998	Roberts ed. (1998) Metabolic Pathways of Agrochemical Royal Society of Chemistry Cambridge UK.
Tomlin 2003	Tomlin ed. (2003) The Pesticide Manual 13 th edition British Crop Protection Council Hampshire UK.
USDA 1996	USDA Exttoxnet Factsheet Oxyfluorfen