warfarin

Review Date: 11/01/2011

CAS #: 81-81-2

Type	Rodenticide that requires multiple feedings.
Controls	Rodents - mice and rats.
Mode of Action	Anticoagulant - slows or stops blood clotting resulting in hemorrhaging and death 5-7 days after feeding.

Thurston County Review Summary:

Warfarin products are rated high in hazard and fail Thurston County's pesticide review criteria. Warfarin is rated high in hazard due to its potential to cause toxicity or death to non-target animals that eat bait products containing warfarin. Warfarin is also rated high in hazard because it is a reproductive and developmental toxicant.

MOBILITY

Property	Value	Reference	Value Rating
Water Solubility (mg/L)	267	4	Moderate
Soil Sorption (Kd=mL/g)	Value not found		
Organic Sorption (Koc=mL/g)	2.96	6	High

Mobility Summary:

Warfarin is moderately soluble in water and adheres poorly to soil. If warfarin baits are not placed in secured bait stations the potential to be moved is dependent on the size of the bait and its availabilty to be carried off by wildlife. The overall hazard of warfarin products to move from where they are placed is rated moderate until all products are sold in secured bait stations that limit accessibility to children, pets, and non-target wildlife.

PERSISTENCE

Property	Value	Reference	Value Rating
Vapor Pressure (mm Hg)	0.0000225	4	Moderate
Biotic or Aerobic Half-life (days)	5	4	Low
Abiotic Half-life (days)	Value not found		
Terrestrial Field Test Half-life (days)	Between 14 to 42 days	3	Moderate
Hydrolysis Half-life (days)	Stable	3	High
Anaerobic Half-life (days)	Value not found		
Aquatic Field Test Half-life (days)	Value not found		

Persistence Summary:

The rate at which warfarin breaks down or degrades is largely dependent on the product formulation (parrafin block or pellets, grain-based, etc.) and not not necessarily the chemical properties of warfarin. The hazard of chemical persistence for warfarin alone is rated moderate because it wil likely break down to half of the applied concentration within 60 days if left out in the environment. When products are formulated into parrafin (wax-like) pellets or blocks or used in a bait station, it is rated high in hazard for persistence.

BIOACCUMULATION

Property	Value	Reference	Value Rating
Bioaccumulation Factor	Value not found		
Bioconcentration Factor	Value not found		
Octanol/Water Partition Coefficient	log Kow = 2.37	1	Low

Bioaccumulation Summary:

Ninety percent (90%) of warfarin injected into rats was eliminated from their bodies in urine and feces within 14 days. The low octanol/water partition coefficient value (log Kow is less than 2.5) also indicates that warfarin is not expected to accumulate in fish or animals. The hazard for warfarin to bioaccumulate is rated low.

ACUTE WILDLIFE TOXICITY VALUES and Risk Assessment

Test Subject	Value	Reference	Value Rating
Mammalian (LD50)	1 mg/kg	6	High
Avian (LD50)	>120 mg/kg	6	Moderate
Honey bee or insect (LD50)	"non-toxic as a bait"	6	Low
Annelida -worms (LC50)	Value not found		
Fish (LC50)	65 mg/L	4	Moderate
Crustacean (LC50)	>105 mg/L	4	Low
Mollusk (LC50)	Value not found		
Amphibian (LD50 or LC50)	Value not found		

Acute Toxicity Testing and Ecotoxicity Summary:

Single-dose toxicity testing indicates that warfarin is highly toxic to mammals, moderately toxic to fish and certain birds, and in its bait form it is considered low in toxicity to bees. The low solubility of warfarin will limit its concentration in waterbodies to below the level of concern for fish and other aquatic organisms (Reference 1).

Warfarin is considered a first-generation anticoagulant rodenticide which requires a rat or mouse to eat bait multiple times to get a dose that kills. Second-generation anticoagulant baits only require a single feeding to cause death. Both first and second-generation baits require over 12 hours to several days before it kills the animal. The EPA believes that there is concern for wildlife that directly consume any anticoagulant bait or that eat animals that have consumed bait (although the risk of secondary poisoning is less for warfarin than it is for second-generation anticoagulant baits). The risk of toxicity to non-target animals from the use of warfarin bait products is rated high in hazard.

ACUTE HUMAN TOXICITY - Risk Assessment

Subject and Scenario	Route	Dose of Concern	Exposure	Margin of Safety	Reference	Value Rating
Short-term risk assessment was not performed						
Short-term risk assessment was not performed						
Short-term risk assessment was not performed						
Short-term risk assessment was not performed						

Acute Toxicity Risk Assessment Summary:

The EPA did not perform any human risk assessments for warfarin. Lack of a risk assessment is considered a data gap.

CHRONIC HUMAN TOXICITY HAZARDS

Property	Value	Adverse Effect	Reference	Rating
Carcinogenicity	Not listed	- -	7 and 8	Data gap
Mutagenicity	Data gap			
Neurotoxicity - (NOAEL)	Value not found			
Endocrine Disruption	Value not found			
Developmental Toxicity (NOAEL)	LOAEL = 0.03 - 0.14 mg/kg/day	Chondrodysplasia punctata	8	High
Reproductive Toxicity (NOAEL)	Value not found	Stillbirths	1	High
Chronic Toxicity (NOAEL)	LOAEL = 0.029 mg/kg/day	Increased prothrombin time	8	Check risk

Chronic Toxicity Hazard Summary:

Warfarin is a known reproductive and developmental toxicant and exposures during pregnancy can cause birth defects, abortion, or stillbirth (Reference 1). The EPA has not evaluated or made a determination on the carcinogenic potential of warfarin and neither has the International Agency for Research on Cancer. Toxicity testing data for mutagenicity, neurotoxicty, and endocrine disruption could not be found and is considered a data gap for this review.

CHRONIC HUMAN TOXICITY - Risk Assessment

Subject and Scenario	Route	Dose of Concern	Exposure	Margin of Safety	Reference	Value Rating
Long-term risk assessment was not performed						
Long-term risk assessment was not performed						
Long-term risk assessment was not performed						
Long-term risk assessment was not performed						

Chronic Toxicity Risk Assessment Summary:

The EPA did not perform any human risk assessments for warfarin. Lack of a risk assessment is considered a data gap.

Metabolites and Degradation Products:

Metabolites of warfarin have been identified as 4-, 6-, 7-hydroxycoumarin and 8-hydroxycoumarin (Reference 6).

Comments:

Warfarin is not considered a skin allergen or a skin sensitizer (Reference 1).

References

1. USEPA. Office of Prevention, Pesticides and Toxic Substances. "Reregistration Eligibility Decision (RED) Warfarin and its Sodium Salt. May 1991.
2. USEPA. Office of Prevention, Pesticides and Toxic Substances. "Risk Mitigation Decision for Ten Rodenticides." May 28, 2008.
3. Health Canada. "Proposed Acceptability for Continuing Registration: Re-evaluation of brodifacoum, bromadiolone, chlorophacinone, diphacinone and warfarin." July 14, 2004.
4. International Union of Pure & Applied Chemistry. Pesticide Properties Database. Warfarin. Accessed 11/1/2011. http://sitem.herts.ac.uk/aeru/iupac/
5. Ward, Stone, Okoniewski, and Stedelin. "Poisoning of Wildlife with Anticoagulant Rodenticides in New York." Journal of Wildlife Diseases 35 (2), 1999.
6. EXTOXNET. Pesticide Information Profile: Warfarin. Publication Date 9/95.
7. International Agency for Research on Cancer. Agents Classified by the IARC Monographs, Volumes 1-102. (Accessed 10/20/2011). http://monographs.iarc.fr
8. USEPA. Integrated Risk Information System. Warfarin; CASRN 81-81-2. 03/31/1987.