

PROBLEM FORMULATION SUMMARY

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National Academy of Sciences (NAS) Review

- In 2013, DPR contracted with NAS to peer review DPR's risk assessment practices
- Completed in 2015 with several recommendations to DPR
- One recommendation: DPR conduct a “**Problem Formulation/Scoping Phase**” prior to drafting risk assessment

NEW RISK ASSESSMENT PROCESS



What is the Problem Formulation Phase?

- Process to determine the scope of the Risk Characterization Document (RCD)
- Risk Assessors and Risk Managers meet to identify what information the RCD will include



PROBLEM FORMULATION SUMMARY

PROVIDES INFORMATION TO MAKE DECISIONS ABOUT:

1. ENDPOINTS TO CONSIDER
2. EXPOSURE SCENARIOS TO INCLUDE OR EXCLUDE
3. MITIGATION OPTIONS TO BE INCLUDED OR EXCLUDED
4. DESCRIPTION OF UNCERTAINTIES
5. OTHERS?

Other Considerations

- Information and data provided by stakeholders – registrants, users, CAC, etc.

Primary Uses in California

- Treatment in and around structures for termites, roaches, ants
- Treatment of pets for fleas and ticks
- One registered product for agricultural use in California - turf

Identify & Prioritize Fipronil Toxic Endpoints

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Justification for Initiating Risk Assessment

- Fipronil registrants notified DPR of large number of alleged adverse effects in humans (2002-2015) from use of spot-on flea and tick control
- Potential for human exposure
- Concerns regarding toxicity in animals studies



Acute toxicity

- **Acute neurotoxicity** in rats (convulsions)

Chronic toxicity

- **Convulsions** and other neurological disturbances in rats and dogs
- **Oncogenicity** in rats (thyroid) and mice (liver)

No-Observed-Effect Levels (NOELs)

- **Low NOELs** 0.02 – 0.05 mg/kg/day
(The lower the NOEL, the greater the concern is for adverse effects in humans)

No Observed Effect Levels

Duration (route)	DPR NOEL mg/kg/day	Critical Endpoint
Acute (all routes)	0.03	Decreased body weight gain in pregnant rabbits
Subchronic (all routes)	0.05	Decreased body weight gain of rat pups; delay in preputial separation in male rats pups
Chronic (all routes)	0.02	Increased incidence and severity of progressive nephropathy in rats

Identify & Prioritize Fipronil Exposure Scenarios

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Eric Kwok, Ph.D., D.A.B.T., Senior Toxicologist

Objectives:

With National Research Council (NRC)'s comments in mind,

- Identify fipronil exposure scenarios at different lifestages of humans
- Screen and prioritize these scenarios based on their significance to California



Identify Exposure Scenarios

- Only consider fipronil products that are **actively registered in California**.
- Only consider exposure from **legal** fipronil use as described in the product labels **registered in California**.

TERMIDOR® SC
TERMITICIDE/
INSECTICIDE

ACTIVE INGREDIENT:
fipronil: 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((1R,S)-(trifluoromethyl)sulfinyl)-1H-pyrazole-3-carbonitrile 9.1%

OTHER INGREDIENTS: 90.9%

TOTAL: 100.0%

One gallon of Termidor® SC termiticide/insecticide contains

It is a violation of federal law to use this product in a manner inconsistent with its labeling.

• For sale to, use and storage only by individuals/firms licensed or registered by the state to apply termiticide and/or general pest control products.

Fipronil Products in California

Target site	Formulation	Application	Licensed user only?	PPE?	Outdoor only?
Turf	RTU granule	Broadcast	Yes	Yes	Yes
Dog/cat	RTU solution	Spot-on	No	No	No
Dog/cat	RTU solution	Spray	No	Yes	No
Structure	RTU dust/powder	Injection	Yes	No	Yes
Structure	Liquid concentrate	Spray	Yes	Yes	Yes
Structure	RTU bait station	Placement	No	No	No
Structure	RTU gel	Cracks/Crevices	No	No	No

RTU: ready-to-use; PPE: personal protective equipment; Outdoor only?: whether this group of products will be applied to indoor living space, such as living room, bedroom, etc.

Potential Human Receptor

Handler: people mix, load, transfer and/or apply fipronil

- Adult

Re-entry: people enter fipronil-treated area or contact treated objects

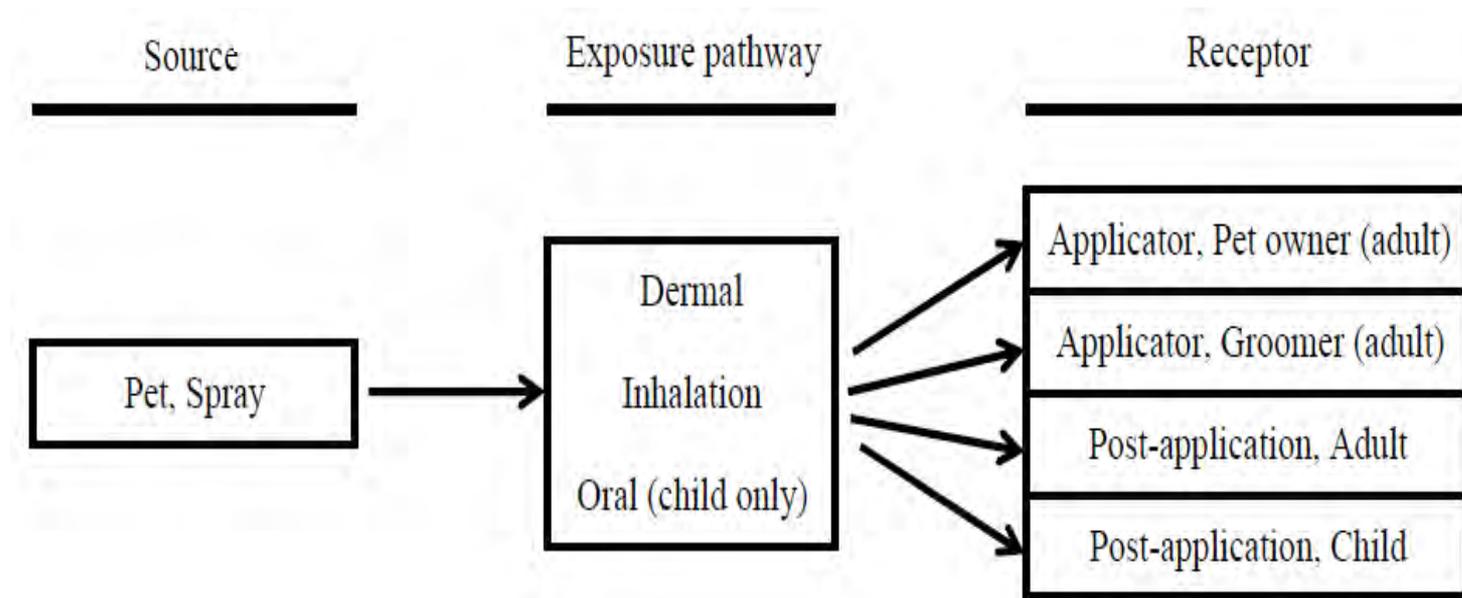
- Adult
- Child

General population: people get exposure from contaminated air, soil and/or water

- Adult
- Child

Exposure Conceptual Model

A conceptual model illustrates the sources, receptors and exposure pathways, and clarifies steps needed for exposure calculation.



Prioritize Individual Exposure Scenario

- Screen all exposure scenarios and identify those with high potential exposure to humans at different lifestages (i.e., children and adults)
- Prioritize resources by focusing on the exposure scenarios that are most significant to California
- Methods:
 - Exposure-based criteria
 - Use and Illness-based adjustments

Methods for Scenarios Prioritization

- **Exposure-based criteria:** scenarios will be classified based on their exposure potential

Exposure potential evaluation is based on:

- * U.S. EPA SOP for Residential Pesticide Exposure Assessment
 - * Surrogate Handler Exposure Estimates for Use in Assessments (HS-1826)
 - * Exposure assessment document of other pesticide(s) with similar uses
 - * Peer-review literature and professional judgements
- **Use and Illness-based adjustments:** scenarios with significant use/sales in California, or with illness cases reported, will be assigned higher prioritization.

Example

Product	Human receptor	Exposure-based criteria	Adjustments		Final priority decision
			Significant use/sales in CA?	Reported illness in CA?	
Pet, spray	Handler, pet owner	Medium	No	Yes	High
Structure, liquid concentrate	Re-entry, adult	High	Yes	Yes	High

Potential Mitigation Measures

Mike Zeiss, PhD, Senior Environmental Scientist

Include a mitigation measure in the RCD for evaluation if the measure is:

- 1) **Efficacious**: *probably* the mitigation measure would help reduce an exposure of concern
- 2) **Feasible**: *probably* DPR would be able and willing to implement such a measure



Even if included, the RCD might determine not efficacious, or not feasible

Next 5 slides: possible mitigation by application site, and by receptor

All intended to reduce dermal exposure

Application site	Receptor
Turf (granules)	Bystander (adult or child after the application)
Structural (dust or liquid concentrate, outdoors or in voids)	Applicator (licensed only)
	Bystander (adult or child after the application)
Dog / cat (spot-on or spray)	Applicator (pet owner or pet groomer)
	Bystander (adult or child after the application)





Potential Mitigation Measures (1 of 5): Turf Products, Post-Application

Increase restricted entry interval (REI)

Require warning signs be posted





Potential Mitigation Measures (2 of 5): Structural Products, Applicators/Handlers

Require additional PPE

(labels already require “waterproof gloves”, long sleeves and long pants)

Engineering controls for mixing/loading

(such as waterproof packaging)

Reduce amount applied per structure

(by reducing product concentration, or area treated per structure, or both)

Reduce frequency of application

(only effective for chronic exposure)



Potential Mitigation Measures (3 of 5): Structural Products, Post-Application

Increase reentry interval for residents

Termidor label: “Do not allow residents . . . to reoccupy contaminated areas of the structure until the cleanup is completed.”

Require warning signs be posted



Reduce amount applied per structure

(by reducing product concentration, or area treated per structure, or both)



Potential Mitigation Measures (4 of 5): Pet Products, Applicators/Handlers

Require PPE

(spray-product labels require “rubber gloves”, but not spot-on)

Reduce amount applied per animal

(by reducing product concentration, or area treated per animal, or both)

Reduce frequency of application

(effective only for chronic exposure)

Restrict use to certified applicators

(**new DPR license category** for pet groomers / vets , analogous to Maintenance Gardeners?)

DPR Enforcement says, might be pre-requisite for any measures for pet products



Potential Mitigation Measures (5 of 5): Pet Products, Post-Application

Require time between treatment and **children contact with pet**

Require time when **children excluded from treatment room** (to protect against transfer from contaminated surfaces in room)

Reduce amount applied per animal
(by reducing product concentration, or area treated per animal, or both)

Reduce frequency of application
(effective only for chronic exposure)

Restrict use to certified applicators
(**new DPR license category** for pet groomers / vets , analogous to Maintenance Gardeners?)

DPR Enforcement says, might be pre-requisite for any measures for pet products

If risks from pet products cannot be mitigated, then consider cancellation.

Potential Data Gaps

Turf granule products

Structural liquid concentrate products

Structural bait gel products

Structural dust products

Pet spray and spot-on products

Developing mitigation options

Structural liquid concentrate and dust products

How DPR will Address Data Gaps?

Analysis Plan

Evaluate potential exposure to applicators/handlers & residents



Data sources to estimate human exposure



Data sources for toxicology profile and hazard identification



Risk Characterization – estimate non-cancer margins of exposure and cancer risk

Analysis Plan continued

Risk Appraisal – Inform the Risk Manager the confidence the Risk Assessor has in the risk estimates

Respond to comments from US EPA and OEHHA reviewers

Timeline for RCD Completion

Complete draft by December 2016.

Written comments can be sent to:

Attn: Ann Hanger

Pesticide Registration Branch

Department of Pesticide Registration

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