PROBLEM FORMULATION DOCUMENT

β-CYFLUTHRIN, CYFLUTHRIN

January 30, 2018

Introduction

The Department of Pesticide Regulation (DPR) has initiated a comprehensive risk and exposure assessment of the active ingredient cyfluthrin and its isomeric enriched form, β-cyfluthrin. DPR has concerns about acute and chronic exposures to these pesticides and has identified potential adverse health effects in studies sufficient to initiate the risk assessment process. The first step in this process is to develop a Problem Formulation Document that provides a scope for the risk assessment, potential exposure scenarios, and future mitigation activities that may be proposed. DPR expects the scope of the risk assessment for these compounds to be broad. DPR plans on evaluating risks from acute, subchronic, and chronic exposures to workers, residents and bystanders.

Background

Risk assessment plays a critical role in DPR's evaluation of the potential human health hazards associated with pesticide exposure. The breadth and depth of the risk assessment depends on the data available and the level of concern DPR has for adverse effects of the pesticide. The toxicological effects are identified by a review of studies DPR requires from the registrants and peer-reviewed literature. The exposure assessment may be a simple assessment based on readily available data and conservative assumptions (screening-level assessment) resulting in point estimates for exposure assessment. If DPR believes a more refined assessment is necessary, then DPR may rely on data specific to the pesticide and the exposure scenario as well as complex models to generate a probabilistic exposure assessment. To support DPR's decision making, staff may assess potential dietary (food and drinking water), workplace, residence, and ambient air exposures.

During the Problem Formulation/Scoping phase, risk managers and risk assessors meet and discuss the scope of the risk assessment for a specific pesticide. Information and data relevant to the pesticide is reviewed and evaluated to determine the scope of the risk assessment. The information and data that may be evaluated during the process includes toxicology, pesticide use reports, pesticide sales, illness reports, monitoring data, primary uses of the pesticide, exposure scenarios identified on the labels, potential exposure pathways, adverse effects reports, relevant United States Environmental Protection Agency (U.S. EPA) risk assessments, important sources of uncertainty and variability in the data, and potential mitigation options.

The internal problem formulation/scoping discussions resulted in this Problem Formulation Document and a diagram of exposure pathways. These documents will be presented to the

Pesticide Registration and Evaluation Committee (PREC) for the committee's comments, as well as posted on DPR's website for public comment. The public comment period is 60 days after posting the documents. All written comments submitted to DPR will be considered in the preparation of the Risk Characterization Document (RCD).

Summary

1. Reasons for entering the risk assessment process

The primary reasons, DPR is entering β-cyfluthrin and cyfluthrin into the risk assessment process are:

a. DPR has concerns regarding toxicity in animal studies:
   - developmental effects, and
   - reproductive effects

b. As required by Food and Agricultural Code section 12825.5, registrants of β-cyfluthrin and cyfluthrin products notify DPR of adverse effects. DPR staff reviewed the potential adverse effects submitted from 2008 – 2016. There were five human deaths and 12 "moderate" reported cases (804 total human cases). The rest of the cases were classified as "minor" or "minimal." Although these incidents are typically self-reported by the public and are not confirmed to be attributed to actual β-cyfluthrin or cyfluthrin use or exposure, they indicate a potential for human exposure and suggest that further investigation of these compounds is warranted.

c. Based on DPR's Pesticide Illness Surveillance Program (PISP) database, there were a total of 101 cyfluthrin illness cases in 78 episodes reported from 2005-2014. Of these, 10 cases involved occupational bystander exposures and 91cases involved residential and bystander exposures. For beta-cyfluthrin, a total of 100 illness cases in 84 episodes were reported from 2005-2014. Of these, 9 cases involved occupational exposures and 91 cases involved residential and bystander exposures.

2. Primary uses in California

The primary use of β-cyfluthrin and cyfluthrin in California include:

a. Treatment of broad range of agricultural crops and commodities for insect pests. The three year (2013, 2014, and 2015) average reported agricultural use for β-cyfluthrin is 8,112 pounds and for cyfluthrin is 7,585 pounds.

b. Treatment of commercial and residential structures for roaches, ants, and other insect pests. The three year (2013, 2014, and 2015) average reported structural use for β-cyfluthrin is 41,712 pounds and for cyfluthrin are 23,041.

3. Potential toxicological effects

The effects of cyfluthrin treatment in animal studies included, but were not limited to, the following:

a. Neurotoxicity from acute, subchronic, and chronic exposures (e.g. sensory irritation, tremors, behavioral changes, altered gait, respiratory apnea, etc.).
b. Developmental effects from prenatal exposures (e.g. malformations and tremors).

4. Exposure scenarios to be considered in the exposure assessment

Cyfluthrin and β-cyfluthrin have products that are used in agriculture and/or residential settings. Staff will review the labels of active products containing cyfluthrin and β-cyfluthrin. Based on the label reviews and three guidance documents (Beauvais *et al.*, 2007; U.S. EPA, 2012; U.S, EPA, 2017), staff will identify the exposure scenarios for agricultural and residential applications for evaluation in the Exposure Assessment Document.

5. Potential exposure pathways diagram (conceptual model)

Figure 1 shows a diagram of potential exposure pathways (i.e., conceptual model) of human exposure to cyfluthrin and β-cyfluthrin containing products. Based on the agricultural and non-agricultural uses identified on the 67 product labels, different sources of pesticide release are possible, i.e., spray drift, direct application (outdoor and indoor), treated raw agricultural commodities, runoff, treated indoor environment, treated turf and crops. Near field computer models and (or) monitoring data coupled with human exposure assessment models will be used for characterizing the amount of pesticides released into the exposure media (e.g., air, soil, food, and drinking water) and eventually received by the receptors of interest (e.g., pesticide handlers and residential bystanders including women of childbearing age and children). The computer models useful in this assessment include Agricultural spray DRIFT (AgDRIFT) (Teske *et al.*, 2002), AGricultural DISPersal near-wake Lagrangian model (AGDISP) (Teske and Curbishley, 2011), exposure assessment model for reentry workers (U.S. EPA, 2017), Dietary Exposure Assessment Module (DEEM^{TM}) (Kidwell *et al.*, 2000), swimmer exposure assessment model (SWIMODEL) (U.S. EPA, 2016), various water exposure assessment models employed by the U.S. EPA (U.S. EPA, 1998) and indoor exposure models as specified in the U.S. EPA Standard Operating Procedures for Residential Pesticide Exposure Assessment (U.S. EPA, 2012). The monitoring data for use in assessing the exposure will be derived from both internal and external sources (Eberhart and Hixson, 1985; Eberhart, 1986; Loeffler, 1986; Stout *et al.*, 1995; Klonne *et al.*, 2000; Keenan *et al.*, 2010; Zhang, 2010; REJV, 2014). If applicable, pesticide use report (PUR) data in concert with information based on geographical information system (GIS) technology will be employed for characterizing the use pattern of the pesticides under agricultural settings. Also, information on track-in dust particles derived from outdoor

environment and pesticide laden dust generated indoor *in situ* will be identified (Julien *et al.*, 2008) and characterized (Roberts *et al.*, 1992).

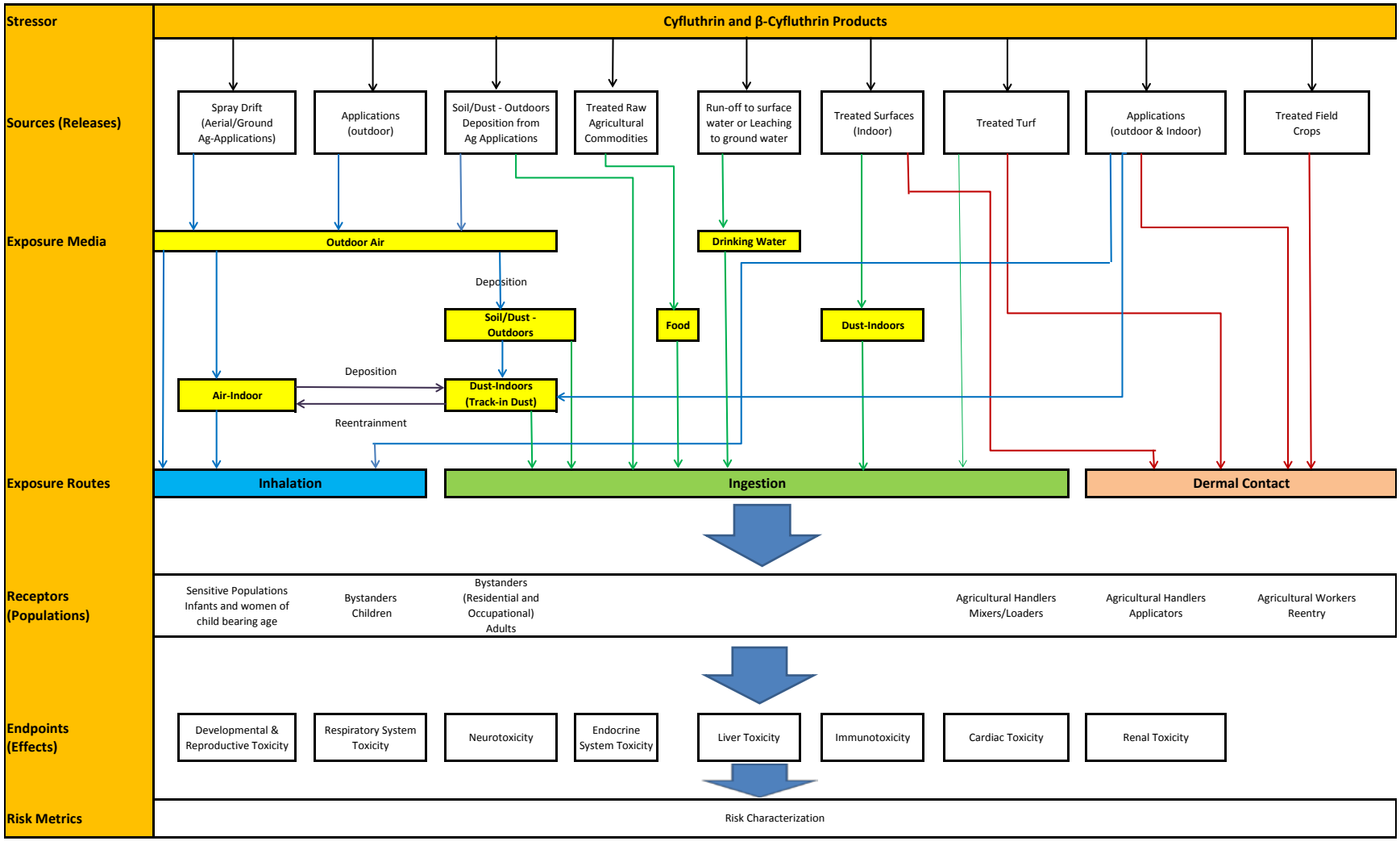

Figure 1. Potential exposure pathways of cyfluthrin and β-cyfluthrin containing products in humans.

6. Potential mitigation measures to be considered for evaluation in the risk assessment

The risk assessment will consider the ability of reduced application rates, reduced number of applications, buffer zones, and personal protective equipment to mitigate risks identified in the RCD.

7. Data gaps

No data gaps have been identified in the toxicologic database for β-cyfluthrin and cyfluthrin at this time. This problem formulation considered all pertinent data for establishing relevant sources, media, and routes of human exposure to cyfluthrin (i.e., exposure scenarios). The existing data are sufficient for identifying important exposure scenarios presented in Figure 1 (i.e., no data gap). However, additional data may be needed to conduct in-depth or refined analysis of the aforementioned exposure scenarios.

8. Analysis Plan

For the Toxicology Profile and Hazard Identification, DPR's Human Health Assessment Branch (HHA) plans to identify the main toxicological effects and the points of departure (PoD) according to the relevant route of exposure from the following databases:

- Toxicological studies submitted to DPR by the registrant or published in the literature;
- Human Incident Data based on: DPR's Pesticide Illness Surveillance Program (PISP), Sentinel Event Notification System for Occupational Risks (SENSOR)-Pesticides program, and case reports with cyfluthrin self-poisoning, Adverse Human Health Effects Reports;
- U.S. EPA Toxicity Forecaster (ToxCast) high-throughput screening assays (HTS, including zebrafish) for indications of pathway disruptions that could lead to toxic outcomes; and
- Existing human health risk assessments by other regulatory agencies including U.S. EPA.

For risk characterization, HHA will use the relevant PoDs and measured or estimated exposures to estimate non-cancer Margins of Exposure (MOEs) and/or cancer risk. These risk estimates will be compared to selected target MOEs.

HHA will inform the risk manager of the confidence it has in the risk estimates by discussing overall uncertainty and variability in the risk assessment.

Following review by the Office of Environmental Health Hazard Assessment (OEHHA) and U.S. EPA, DPR will respond to reviewers and generate a finalized risk assessment document.

9. Timeline for completion of the Risk Characterization Document

The Human Health Assessment Branch plans to complete the draft RCD by 2019.

10. References:

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Comments

This document will be posted on DPR's Web site on the Human Health Risk Assessment and Mitigation page for cyfluthrin and β-cyfluthrin (http://www.cdpr.ca.gov/docs/whs/active_ingredient/cyfluthrin.htm) for public viewing after being presented to the PREC. The comment period is open for 60 days. Written comments may be sent to:

Risk Assessment – (Cyfluthrin and β-Cyfluthrin)
Attn: Risk Assessment Coordinator
Pesticide Registration Branch
Department of Pesticide Regulation
1001 I Street, P.O. Box 4015
Sacramento, CA 95812-4015

Comments will be reviewed and where appropriate, technical suggestions will be incorporated into the text of the draft RCD.