UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: August 8, 2019

SUBJECT: **Tefluthrin:** Updated Human Health Draft Risk Assessment in Support of Registration Review.

PC Code: 128912
Decision No.: 553648
Petition No.: NA
Risk Assessment Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D453462
Registration No.: NA
Regulatory Action: Registration Review
Case No.: 7409
CAS No.: 79538-32-2
40 CFR: NA

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This document is an update to the 2016 Human Health Draft Risk Assessment (DRA) in Support of Registration Review for tefluthrin.

Executive Summary

Tefluthrin ((2,3,5,6-tetrafluoro-4-methylphenyl)methyl (1R,3R)-rel-3-[(1Z)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethylcyclopropanecarboxylate) is a synthetic pyrethroid insecticide. Tefluthrin is a member of the pyrethroid class of chemicals. Tefluthrin can be used in a variety

of occupational settings. It is used primarily in the control of soil insect pests on corn plants and the treatment of corn and sugar beet seed in commercial seed treatment facilities.

Since the previous draft risk assessment (DRA) (*Tefluthrin. Draft Human Health Risk Assessment for Registration Review,* S. Schlosser, D434435, 6/29/2016), new information has been submitted which allows the database uncertainty factor to be reduced from 3X to 1X for children less than 6 years old. This information is summarized in the hazard section below.

There have been no changes to the risk assessment endpoints or points of departure, exposure assessments (dietary, residential or occupational), aggregate, or cumulative assessments. However, an updated dietary assessment was conducted for the general population, including infants and children because the previous acute population adjusted dose (aPAD) for children < 6 years old has changed with the removal of the 3X FQPA safety factor. Currently an acute population adjusted dose (aPAD) of 0.005 mg/kg/day is selected for the general population, including infants and children and is used in the dietary assessment. The resulting acute dietary exposure to tefluthrin does not exceed the Agency's level of concern (<100% of the aPAD). No risks of concern were identified in the previous DRA for dietary or occupational exposure, and since the database uncertainty factor is now removed, risk estimates are further reduced for children. There were no public comments related to human health requiring input from HED.

Data Deficiencies

Submittal of 2 grams of tefluthrin acid product analytical standards to the EPA Nation Pesticide Standards Repository is required. For mailing information see Appendix C.

Hazard Assessment

The hazard assessment for tefluthrin can be found in the DRA (*Tefluthrin. Draft Human Health Risk Assessment for Registration Review*, S. Schlosser, D434435, 6/29/2016); the reader is referred to that document for detailed information regarding hazard identification and endpoint selection.

The hazard database for tefluthrin is complete. Data are now available allowing reduction of the database uncertainty factor for children < 6 years old from 3X to 1X. This revision is summarized in Appendix A in an updated Summary of Toxicological Doses and Endpoints for Tefluthrin for Use in Human Health Risk Assessments.

FFDCA section 408 requires the Agency to apply an additional 10X safety factor to account for the potential pre- and post-natal toxicity and completeness of the data with respect to infants and children unless, based on reliable data, EPA can conclude that another safety factor will be "safe." The Agency considers the FQPA safety factor as having two components, with 3X assigned to pharmacokinetic (PK) and 3X to pharmacodynamic (PD) differences. Previously, EPA's Office of Pesticide Programs (OPP) retained a 3X FQPA Safety Factor (1X for PD and 3X for PK differences) for children < 6 years old based on concerns for PK differences between adults and children (E. Scollon, DP381210, 2011). OPP has re-evaluated the need for an FQPA Safety Factor for human health risk assessments for pyrethroid pesticides based on a review of

the available guideline and literature studies as well as data from the Council for the Advancement of Pyrethroid Human Risk Assessment (CAPHRA) program. Because no new information of suitable quality was available on the age-related PD properties of the pyrethroids, the PD contribution to the FQPA safety factor remains at 1X. Regarding PK, recent data including human physiologically based pharmacokinetic (PBPK) models as well as *in vivo* and *in vitro* data on protein binding, enzyme ontogeny, and metabolic clearance, support the conclusion that the PK contribution to the FQPA safety factor can be reduced to 1X for all populations[1]. Therefore, the Agency concludes that the default 10X FQPA safety factor can be reduced to 1X for all populations for the pyrethroid pesticides.

Dietary Assessment

An updated dietary assessment was conducted for the general population, including infants and children. The previous acute population adjusted dose (aPAD) for children < 6 years old has changed with the removal of the 3X FQPA safety factor. Currently an aPAD of 0.005 mg/kg/day is selected for the general population, including infants and children and is used in the dietary assessment. The unrefined dietary assessment included one-half of the combined limit of quantitation (LOQ) for the parent at 0.005 ppm and the metabolite PP890 at 0.025 ppm for a total of 0.03 ppm residue values, 100% crop treated, the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID 7.81) default processing factor for corn syrup at 1.5 ppm. In addition, the previously estimated highest residues in drinking water, using the surface water concentration calculator (SWCC) model for surface water sources (1.18 ppb from Iowa (IA corn) scenario was used as the estimated residue in drinking water. Estimated drinking water concentrations (EDWCs) were incorporated directly into the dietary assessment. For the residue input files, see Appendix B.

The estimated dietary (food and water) risks associated with acute dietary exposure to tefluthrin do not exceed the Agency's level of concern (<100% of the aPAD) at the 95th exposure percentile for the U.S. population and all population subgroups. The acute dietary estimated exposure for the general U.S. population is 4.5% of the aPAD. For the most highly exposed population subgroup, all infants <1 year old, the estimated exposure was 12% of the aPAD. A chronic dietary endpoint is not required because repeated exposure to tefluthrin does not result in a lower point of departure. Therefore, a chronic dietary exposure assessment was not required. Table 1 summarizes the dietary risk and exposures from food and drinking water sources.

Table 1. Summary of Dietary (Food and Drinking Water) Exposure and Risk for Tefluthrin

Population Subgroup	aPAD (mkd)*	Acute 95th Percentile	
		Exposure (mkd)	% aPAD
General U.S. Population		0.000222	4.5
All Infants (<1 year old)		**0.000596**	**12**
Children 1-2 yrs. old		0.000418	8.4

[1] USEPA Office of Pesticide Programs' Re-Evaluation of the FQPA Safety Factor for Pyrethroids: Updated Literature and CAPHRA Program Data Review (2019).

Table 1. Summary of Dietary (Food and Drinking Water) Exposure and Risk for Tefluthrin			
Population Subgroup	aPAD (mkd)*	Acute 95th Percentile	
		Exposure (mkd)	% aPAD
Children 3-5 yrs. old	0.005	0.000380	7.6
Children 6-12 yrs. old		0.000306	6.1
Youth 13-19 yrs. old		0.000219	4.4
Adults 20-49 yrs. old		0.000189	3.8
Adults 50-99 yrs. old		0.000129	2.6
Females 13-49 yrs. old		0.000180	3.6

* (mKd) = mg/kg/day.
The highest exposed population subgroup **Bolded**

Residential and Aggregate Assessment

There are no proposed or registered residential uses of tefluthrin at this time. Therefore, a residential exposure assessment was not conducted at this time.

Spray Drift

Tefluthrin uses are not likely to result in spray drift. Tefluthrin end-use products are formulated as a liquid and granular formulations for application to corn and as a microencapsulated formulation for treating corn and sugar beet seeds. It is unlikely for tefluthrin to result in indirect residential spray drift exposure since tefluthrin is soil directed to covered bands or "in furrow" well before the crop matures. In addition, the treatment of commercial seeds are performed indoors and are also not likely to result in spray drift. Therefore, a quantitative spray drift exposure assessment was not conducted for the registered uses of tefluthrin.

Occupational Exposure and Risk

Occupational non-cancer inhalation and dermal exposures and risks were estimated for tefluthrin handlers in seed treatment facilities and agricultural settings. All the inhalation scenarios resulted in margins of exposure (MOEs) greater than the Agency's level of concern (LOC) of 30 for adults at baseline exposure (no respirator), and therefore, are not of concern. All the dermal scenarios resulted in MOEs greater than the Agency's LOC of 100 for adults at baseline exposure and therefore, are not of concern. Based on the use profile of tefluthrin, there is no potential for post-application exposures. For details, see (*Tefluthrin: Draft of Human Health Risk Assessment for Registration Review*, Chris Schlosser, D434435, 6/29/2016).

There is low potential for occupational post-application exposure is expected for workers since tefluthrin is soil directed to covered bands or "in-furrow" well before crop matures. In addition, harvesting of corn is primarily mechanical in nature which further reduced potential for dermal contact. The timing of the application relative to harvest activities can greatly reduce the potential for post-application exposure. Therefore, an occupational post-application exposure assessment was not conducted.

The potential for post-application exposures following the planting of tefluthrin-treated seeds is

unlikely because sustained levels of contact with treated seed after it has been placed in the soil or other planting media would not be expected because no routine cultural practice required for the production of agricultural commodities involves such an activity as defined in the no/low contact criteria in the Worker Protection Standard (WPS). Therefore, no quantitative post application assessment is required for exposure to treated seeds that have already been planted.

Appendix A. Updated Endpoints and Uncertainty Factors for Tefluthrin

Table A.1: Summary of Toxicological Doses and Endpoints for Tefluthrin*				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/FQPA Safety Factors**	**PAD, Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (General Population, including Infants and Children)	NOAEL = 0.5 mg/kg/day	UF_A= 10X UF_H=10X FQPA= 1X	aRfD = 0.005 mg/kg/day aPAD = 0.005 mg/kg/day	Chronic Dietary – Dog **MRID** 40141308 LOAEL = 2.0 mg/kg/day based on increased incidence of tremors in the dog (both sexes)
Chronic Dietary	A chronic dietary endpoint is not required because repeated exposure to tefluthrin does not result in a lower point of departure. Therefore, the acute endpoint is protective of chronic exposure scenarios.			
Dermal Short-Term (1-30 days)	NOAEL = 0.5 mg/kg/day (Microencapsulated formulations) Dermal absorption factor: Microencapsulated formulations= 0.79% Granular & Liquid formulations = 5.0%	UF_A =10x UF_H =10x	Occupational LOC for MOE = 100	Chronic Dietary – Dog **MRID** 40141308 LOAEL = 2.0 mg/kg/day based on increased incidence of tremors in the dog (both sexes)
Inhalation Short-Term (1-30 days)	NOAEL = 7.7 mg/m^3 **Occupational** HEC= 0.54 mg/kg; 11 mg/m^3	UF_A = 3X UF_H = 10X	Occupational LOC for MOE = 30	Acute Inhalation toxicity study- Rat **MRID** 40141302 LOAEL = 14.9 mg/m^3 based on CNS effects (decreased activity, reduced foot withdrawal reflex, and reduced righting reflex)
Cancer (oral, dermal, inhalation)	Tefluthrin is classified as "not likely to be a human carcinogen"			

*Point of Departure (POD) = A data point or an estimated point derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animals to humans (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = Margin of Exposure. LOC = level of concern. HEC = human equivalent concentration. HED = human equivalent dose.

Table A.2. Summary of HEC/HED values for Tefluthrin.

Population	Scenario	Tox Duration Adjustment		HEC		HED (mg/kg-day)
		hr/day	day/wk	mg/L	mg/m3	13.8 L/min
Occupational	Handler	8	5	0.013	12.763	1.208

HEC =human-equivalent concentration; HED =human-equivalent dose.
HEC =rat NOAEL*(daily duration adjustment) *weekly daily duration adjustment *RDDR*
HED = HEC*relative activity factor*human-specific conversion factor*daily duration

Appendix B: Acute Residue Input File for Food + Drinking Water

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US EPA                                                        Ver. 3.18, 03-08-d
DEEM-FCID Acute analysis for TEFLUTHRIN
Residue file name: F:\DEEM\Tefluthrin\Tefluthrin Acute food +water.r08
Analysis Date 07-29-2019             Residue file dated: 07-29-2019/16:24:06
Reference dose: aRfD = 0.005 mg/kg bw/day  NOEL = 0.5 mg/kg bw/day
--------------------------------------------------------------------------------
  EPA      Crop                                    Def Res     Adj.Factors   Comment
  Code      Grp  Food Name                          (ppm)       #1    #2
---------- ---- ------------------------------  ----------  ------ ------  -------
1500120000 15   Corn, field, flour                 0.030000   1.000  1.000
1500120001 15   Corn, field, flour-babyfood        0.030000   1.000  1.000
1500121000 15   Corn, field, meal                  0.030000   1.000  1.000
1500121001 15   Corn, field, meal-babyfood         0.030000   1.000  1.000
1500122000 15   Corn, field, bran                  0.030000   1.000  1.000
1500123000 15   Corn, field, starch                0.030000   1.000  1.000
1500123001 15   Corn, field, starch-babyfood       0.030000   1.000  1.000
1500124000 15   Corn, field, syrup                 0.030000   1.500  1.000
1500124001 15   Corn, field, syrup-babyfood        0.030000   1.500  1.000
1500125000 15   Corn, field, oil                   0.030000   1.000  1.000
1500125001 15   Corn, field, oil-babyfood          0.030000   1.000  1.000
1500126000 15   Corn, pop                          0.030000   1.000  1.000
1500127000 15   Corn, sweet                        0.030000   1.000  1.000
1500127001 15   Corn, sweet-babyfood               0.030000   1.000  1.000
8601000000 86A  Water, direct, all sources         0.001180   1.000  1.000
8602000000 86B  Water, indirect, all sources       0.001180   1.000  1.000
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Appendix B.1.: Acute Exposure Estimates for Food + Drinking Water

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US EPA                                                          Ver. 3.18, 03-08-d
DEEM-FCID ACUTE Analysis for TEFLUTHRIN                    NHANES 2003-2008 2-Day
Residue file: Tefluthrin Acute food +water.r08        Adjustment factor #2 used.
Analysis Date: 07-29-2019/16:41:19    Residue file dated: 07-29-2019/16:24:06
NOEL (Acute) =   0.500000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: ""
================================================================================

Summary calculations--per capita:

---   95th Percentile----   ---   99th Percentile----     ---99.9th Percentile----
 Exposure  % aRfD     MOE    Exposure  % aRfD     MOE    Exposure  % aRfD     MOE
---------- ------- -------- ---------- ------- -------- ---------- ------- --------
Total US Population:
  0.000222    4.45    2248    0.000380    7.60    1316    0.000712   14.24     702
All Infants:
  0.000596   11.92     839    0.000899   17.97     556    0.001092   21.83     458
Children 1-2:
  0.000418    8.35    1197    0.000707   14.13     707    0.001027   20.54     486
Children 3-5:
  0.000380    7.60    1315    0.000607   12.15     823    0.001008   20.16     495
Children 6-12:
  0.000306    6.12    1635    0.000463    9.25    1080    0.000653   13.05     766
Youth 13-19:
  0.000219    4.38    2282    0.000326    6.53    1532    0.000690   13.80     724
Adults 20-49:
  0.000189    3.79    2638    0.000284    5.68    1760    0.000450    9.01    1110
Adults 50-99:
  0.000129    2.57    3884    0.000194    3.88    2580    0.000304    6.08    1645
Female 13-49:
  0.000180    3.60    2779    0.000258    5.15    1940    0.000395    7.89    1267
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Appendix C Submittal of Analytical Standards

Analytical standards of tefluthrin is available (expires 03/31/2021) at the National Pesticide Standards Repository. However, analytical standards for metabolite PP 890 is not available. The registrant should send 2 grams of tefluthrin acid product analytical standard to the repository. (Email communication with G. Verdin, T. Cole 08/08/2019).

As reminder to the petitioner, supplies of analytical standards must be replenished as requested by the repository. The reference standards should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of Theresa Cole at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

(Note that the mail will be returned if the extended zip code is not used.)