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Subject: Triazine Cumulative Risk Assessment for the Proposed Use of Propazine on Grain Sorghum. DP Barcode 336673.

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Executive Summary

The definition of cumulative risk, developed as a result of the passage of FQPA, requires OPP to conduct a risk assessment for a group of pesticides with a common mechanism of toxicity that is multi-pathway, multi-route, and multichemical in scope. Based on the proposed use of propazine on grain sorghum and the likelihood of co-occurrence of residues of atrazine, simazine, and propazine as a result of this proposed new use, the Health Effects Division (HED) conducted a cumulative risk assessment in regions where high atrazine and propazine use on sorghum coincides with vulnerable drinking water sources. Simazine was excluded from this assessment because of its limited use in sorghum-growing areas. Drinking water was identified as the main exposure pathway affected by the proposed new use. This assessment is based on the surface water model, PRZM (Pesticide Root Zone Model) and EXAMS (Exposure Analysis Modeling System). Modeling was completed using both the Texas (TX) and Kansas (KS) sorghum scenarios for propazine use on sorghum and atrazine use on sorghum and corn. The results of the surface water model (PRZM/EXAMS) were used in Calandex™. Typically, model runs are reported as deterministic, or point estimates, for a variety of exposure durations. However, for this cumulative assessment daily distributions of surface water concentrations combined with consumption survey and body weight information are required as inputs to Calandex™.

Risk estimates are presented in this assessment as Margins of Exposure (MOEs) for populations potentially exposed to atrazine and propazine as a result of the new grain sorghum use. These populations represent both the most vulnerable and sensitive groups relative to the endpoint and toxic effects of interest, i.e., endocrine, developmental, and reproductive effects. All risk estimates with the exception of infants (<1 yr) are well above a MOE of 300. For infants, MOEs were estimated to be 217 for the TX scenario, and 284 for the KS scenario. A MOE of 300 or greater is not of concern.

The risk estimates provided for drinking water exposures in this assessment are based on concentrations of atrazine, propazine, and their common chlorinated degradates in raw (unfinished) surface water that may serve as a source of drinking water. These concentration estimates provided by PRZM/EXAMS for the TX and KS scenarios are based on maximum use rates for atrazine and propazine on sorghum and corn, and sorghum, respectively. The KS scenario assumed very conservative estimates of percent of sorghum crop treated for both atrazine and propazine. The TX scenario used refined estimates of percent of sorghum crop treated for atrazine and propazine. All existing atrazine labels require setback distances around intermittent/perennial streams and lakes/reservoirs. The presence of a well-vegetated setback between the site of atrazine application and receiving water bodies could result in reduction in loading. Therefore, the drinking water exposure estimates presented in this assessment may over-estimate exposure to residues of atrazine and propazine in finished drinking water.

Introduction

Gowan has recently requested a Section 3 use of propazine on sorghum grown for grain. HED recently analysed exposures to atrazine, simazine, and propazine via food, drinking water, and/or residential activities in regions where co-occurrence is most likely for currently registered uses (DP 317976, *Cumulative Risk from Triazine Pesticides March 2006,* 3/28/06). The March 2006 assessment indicated that cumulative exposure to residues of atrazine, simazine, and propazine in food is negligible, cumulative exposures to atrazine and simazine in drinking water is likely, and cumulative exposures to atrazine and simazine residues on lawns and golf courses is possible. Consequently, in March 2006, the following four scenarios were assessed:

1) exposure to atrazine, simazine, and the chlorinated degradates in drinking water in the Midwest (using monitoring data);
2) exposure to atrazine, simazine, and the chlorinated degradates in drinking water in California (using modeled concentration estimates for atrazine and simazine);
3) exposure to atrazine, simazine and the chlorinated degradates in drinking water in Florida (using modeled concentration estimates for atrazine and simazine);
4) exposure to atrazine, simazine, and the chlorinated degradates in drinking water and on home lawns and golf courses in Florida (using modeled concentration estimates for drinking water and estimates of exposure from residential activities);

Propazine was excluded from the March 2006 triazine cumulative risk assessment because current registrations for propazine (indoor green-house uses) do not affect food, drinking water, or homeowner exposures. This cumulative risk assessment incorporates propazine on the basis of the proposed grain sorghum use.

Hazard

The following triazine pesticides have been identified by EPA as a group sharing a common mechanism of toxicity: atrazine, simazine, propazine, and their chlorinated degradates: desethyl-s-atrazine, desisopropyl-s-atrazine, and diaminochlorotriazine (the triazines).

To estimate risk from exposure to the triazines, a No-Observed-Adverse-Effect-Level (NOAEL) of 1.8 mg/kg/day associated with effects on the estrus cycle of female rats at 3.65 mg/kg/day (the Lowest-Observed-Adverse-Effect-Level or LOAEL) was selected. This endpoint is considered relevant for all age groups as it is a biomarker for neuroendocrine effects seen in young and adult animals. This toxic endpoint is consistent with the common mechanism of toxicity identified for the triazines (USEPA 2000) and represents the most sensitive endpoint in the toxicity database for the triazines that is relevant to neuroendocrine effects.

This quantitative hazard estimate, modified by the application of relevant uncertainty factor(s), was compared with exposure estimates to estimate risk. In addition to the traditional uncertainty factors applied to each risk assessment (10X for intraspecies variation and 10X for interspecies variability), a FQPA safety factor of 3X for hazard-based residual uncertainty related to the health consequences of exposure to the triazines on the developing young was applied to the cumulative risk assessment. No additional FQPA safety factor for exposure-based uncertainties is warranted because conservative models were used to estimate concentrations of atrazine, propazine, and their common chlorinated degradates in drinking water. A summary of the toxic endpoint and safety factors used in this assessment is presented in Table 1.

Table 1: Summary of Toxicological Doses and Endpoints Used in the Cumulative Risk Assessment for the New Use of Propazine on Sorghum

Exposure Scenario	Dose used in Risk Assessment, UF	FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
90-Day Drinking Water Exposure	NOAEL = 1.8 mg/kg/day UF = 300	10X for interspecies variation 10X for intraspecies variability 3X SF for residual Hazard- based concerns.	**6-month LH surge study in rat w/ Atrazine** LOAEL = 3.65 mg/kg/day based on estrous cycle alterations and LH surge suppression

UF = uncertainty factor, FQPA SF = FQPA safety factor

Use Pattern

The use patterns associated with atrazine, propazine, and simazine are as follows:

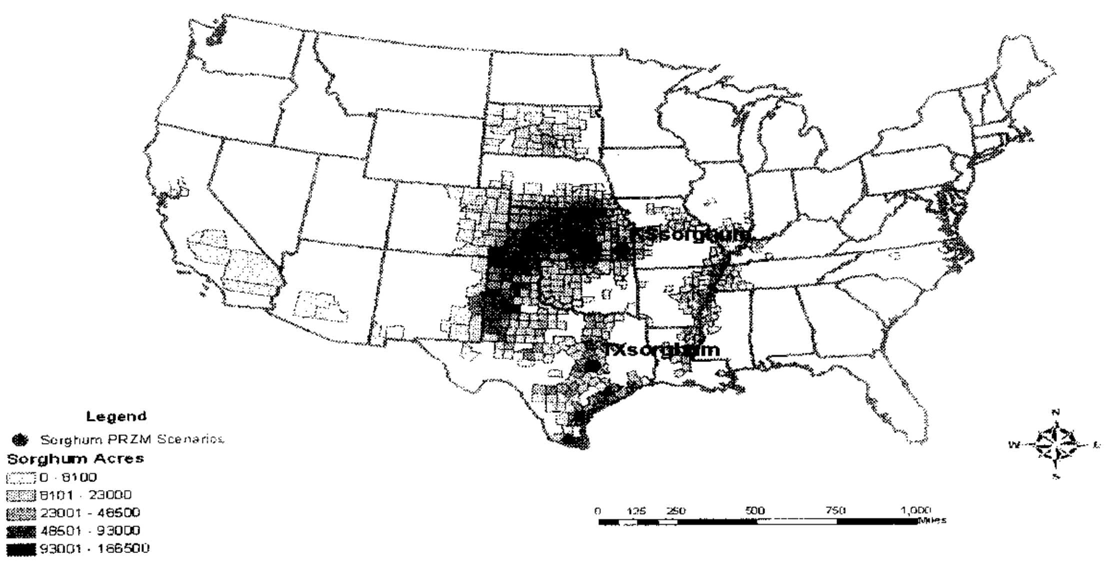
Atrazine: is a triazine herbicide registered for the control of broadleaf weeds and some grassy weeds. Atrazine is used on corn (field and sweet), sorghum, sugarcane, wheat (application to wheat stubble on fallow land following harvest), guava, macadamia nuts, hay, pasture, summer fallow, forestry or woodlands, conifers, woody ornamentals, Christmas trees, sod, and residential and recreational turf (parks, golf courses). Given the specific nature of the turf uses, much of atrazine's use on lawns is confined to Florida and the Southeast.

Simazine: is a systemic herbicide, and is usually applied to soil and absorbed through leaves and roots. Simazine acts by inhibiting photosynthesis within the targeted plant. Simazine is used in growing a variety of food and feed crops, primarily corn in the Midwest, fruits and nuts in California, and citrus (oranges and grapefruit) in Florida. Simazine is also used on home lawns, golf courses, and turfgrass grown commercially for sod, as well as in forestry. Simazine is not registered for use on sorghum.

Propazine: is also a systemic herbicide, currently is registered in the U.S. for indoor greenhouse use only, and has an import tolerance established for residues on imported sorghum. A new use on sorghum grown for grain in the US has been proposed and is the focus of this cumulative risk assessment.

Grain sorghum is grown primarily in five states in the US: Colorado (CO), Oklahoma (OK), Texas (TX), Kansas (KS), and New Mexico (NM). Acres grown to grain sorghum based on an average from 2003 o 2005 (USDA/NASS) for each state are 236,667 in CO, 280,000 in OK, 2,486,667 in TX, 3,166,667 in KS, and 133,333 in NM (DP330513, 11/08/06, M. Kaul). Texas and Kansas grow 90% of the grain sorghum crop in the US, and represent the major sorghum-growing regions in the US.

Sorghum PRZM Scenarios Relative to Sorghum Acreage



Exposure Pathways

HED has determined that the proposed use has the potential to impact drinking water sources. As previously determined in the March 2006 triazine cumulative risk assessment, exposures to the triazines in food are negligible for existing uses, and will be negligible (zero) as a result of the proposed propazine use on grain sorghum (DP323272, 12/13/05, J. Morales and W. Donovan, dietary risk assessment memo and DP 323271, 12/13/05, J. Morales, J. Liccione, and S. Weiss, HED risk assessment memo). There are no current or proposed residential uses of propazine. Since the March 2006 risk assessment covered residential exposures resulting from uses of atrazine and simazine, this cumulative risk assessment focuses on exposures to the triazines in drinking water as a result of their registered uses and the proposed use of propazine on grain sorghum. Drinking water is the dominant, single pathway of exposure likely to be impacted by the proposed new use of propazine on grain sorghum.

Drinking water is locally derived and concentrations of pesticides in source water fluctuate over time and location for a variety of reasons. Pesticide residues in water fluctuate daily, seasonally, and yearly as a result of the timing of the pesticide application. Concentrations are also affected by the method of application, the location and characteristics of the sites where a pesticide is used, the climate, and the type and degree of pest pressure.

To assess drinking water exposure to the triazines as a result of the proposed grain sorghum use, Health Effect Division (HED), the Environmental Fate and Effects Division (EFED), the Biological and Economic Analysis Division (BEAD), and the Registration Division (RD) considered usage data from the grain sorghum states interested in using propazine. As stated previously, TX and KS grow 90% of the grain sorghum crop; therefore, separate PRZM/EXAMS scenarios reflecting rainfall patterns and growing conditions relevant to grain sorghum in each of these two states were selected to estimate surface water residues of atrazine, propazine, and the three chlorinated degradates for this cumulative risk assessment. TX and KS were determined to encompass areas where atrazine and propazine could both be used in watersheds cropped to grain sorghum and corn containing vulnerable drinking water sources. The sorghum PRZM scenarios have been used as surrogates for corn to account for the use of atrazine on corn in these areas. Exposures to residues of atrazine and propazine in drinking water from the remaining parts of the country are expected to be substantially lower than from TX and KS.

Simazine was excluded from this assessment because it is not expected to impact drinking water exposures significantly relative to atrazine and propazine since it has limited use on all crops in the principal sorghum-growing states of Kansas (< 1% percent cropped treated), Colorado, Oklahoma, Texas, and New Mexico (Kaul and Kiely, 2005). An exception to this is simazine use on citrus and sugarcane in Texas, however, these uses are in Southern Texas which is far removed from the main sorghum growing regions in Northern Texas and thus simazine has not been included in this assessment. Exposure to simazine in drinking water as a result of its major uses on corn in the Midwest, sugarcane in Florida, and fruits and nuts in California and Florida was assessed in the March 2006 triazine cumulative risk assessment.

Exposure Estimates

EFED estimated the potential daily concentrations of atrazine, propazine, and the three chlorinated degradates in surface water sources using the simulation model PRZM/EXAMS. The modeling accounts for potential co-occurrence of atrazine and propazine by modeling all uses in a region/area, it can also adjust for crop area and acres treated. The model provides a daily time series of surface water concentrations of atrazine and propazine residues over multiple years (using 30 years of recorded weather data) to account for year-to-year variations in weather and to separate peak concentrations that are not likely to occur together in time. For each regional assessment, TX and KS, the following scenarios were modeled: propazine on sorghum, atrazine on sorghum, and atrazine on corn. Maximum application rates were assumed for the model runs, and EFED applied a Cumulative Adjustment Factor (CAF) to each run. The details of the adjustment factors and fate parameters used in EFED's modeling runs are contained in EFED's memorandum: DP336742 & DP329876, M. Corbin, 4/13/07.

Based on available usage information from 1987 to 1989 (the last three years atrazine and propazine were both registered for use in the US on grain sorghum), BEAD projected the highest percent of the US sorghum acreage potentially treated with propazine to be 18% for the state of TX. Based on the available usage information collected on atrazine when propazine was registered under the Section 18 program (1993 to 1995), on average 54% of the crop in TX is treated with atrazine (DP335065, J. Alsadek and N. Zinn, 3/9/07). These values reflect refinements to the estimates used in the original drinking water assessment (DP34595) dated December 2006. These revised values were provided by EFED on February 13, 2007. These refinements were used in the 4/13/07 PRZM/EXAMS assessment for TX.

Very conservative assumptions regarding the percentage of the grain sorghum crop treated with atrazine and propazine were used in the exposure assessment for KS. For the KS scenario, it was assumed that 70% of the crop was treated with atrazine and 29% of the crop was treated with propazine resulting in an assumption of 99% of the sorghum crop treated with triazine (memo from T. Kiely to D. Sherman, 1/11/05, "Projected Percent of Crop Treated Estimates for Propazine on Sorghum", No DP Barcode).

Risk Estimates

To estimate cumulative risk from exposure to triazine residues as a result of the proposed use of propazine on grain sorghum, 90-day average exposures to the sum of atrazine, propazine, and the three common chlorinated degradates in drinking water were calculated by the Calendex™ aggregate model and compared to a toxic endpoint of 1.8 mg/kg/day generating a distribution of MOEs for various population groups. MOEs were estimated for four populations: infants (< 1 year old), children (1 to 2 years old), females (13 to 49 years old), and adults (20 to 49 years old). A MOE of 300 or greater is not of concern. This is the most appropriate combination of toxicity endpoint and period of exposure when concentrations of triazine (atrazine and propazine) residues in water are their highest.

To generate a 90 day rolling average distribution of exposure for the subpopulation of interest a drinking water value taken from the estimated distribution of water residues for January 1 to March 31 is selected and paired with the water consumption reported in the CSFII consumption record. These values are used to calculate exposure from drinking water for that date. All of the exposures are converted to route-specific MOEs to define the range of risk estimates for the hypothetical individual from January 1 to March 31. The process is repeated for each consumption record for the age group in the CSFII twenty times to build a distribution of risks (MOEs) for January 1 to March 31. This process is repeated for January 2 to April 1st, January 3 to April 2 and so forth across the same year.

The distribution of daily exposures and resulting MOEs are developed such that the exposures from atrazine and propazine in drinking water are calculated simultaneously for each hypothetical individual in the subpopulation. HED used Calandex™ software to develop the distributions and resulting MOEs. Calandex™ permits incorporation of time-course information with regard to exposure through drinking water, but does not permit specific allowance for regional variability. As described in the previous section, HED and EFED addressed this issue by focusing on and developing separate assessments for regions where vulnerable drinking water sources may exist in areas where both atrazine and propazine are likely to be used, i.e., TX and KS.

The 365 daily exposure distributions are arrayed together in order to provide a profile of possible exposures by each route and in total as MOEs. This distribution of risk is expressed as a cumulative distribution function of MOEs versus percentile of exposure. Percentile of exposure refers to that portion of the population that has less than or equal exposure. For example, 99.9 % of the population has an exposure level that is equal to or less than the 99.9th percentile.

The results of this assessment are presented in Table 2. These risk estimates present the potential MOE for the population exposed to atrazine and propazine. These populations represent both the most vulnerable and sensitive groups relative to the endpoint and toxic effects of interest, i.e., endocrine, developmental, and reproductive effects. The scenarios included maximum use rates of atrazine and propazine for both TX and KS, conservative projections of percent crop-treated for Kansas, and refined estimates for TX. All risk estimates with the exception of infants (<1 yr) are well above a MOE of 300.

Table2. Atrazine and Simazine Cumulative Risk assessment: 90- Day Rolling Average in Drinking Water Assessment Using Modeling Data from Texas and Kansas (maximum)

		MOE	MOE	MOE
CWS	Population	95th %	99th %	99.9th %
Texas*	Infant<1	821	409	217
	Children 1-2yrs	>300	>300	>300
	Female 13-49 yrs	>300	>300	>300
	Adult 20-49 yrs	>300	>300	>300
Kansas**	Infant<1	>300	>300	284

Table2. Atrazine and Simazine Cumulative Risk assessment: 90- Day Rolling Average in Drinking Water Assessment Using Modeling Data from Texas and Kansas (maximum)				
	Children 1-2yrs	>300	>300	>300
	Female 13-49 yrs	>300	>300	>300
	Adult 20-49 yrs	>300	>300	>300

* PCT is 54% atrazine and 18% propazine
**PCT-is 70% atrazine and 29% Propazine

Characterization of the Risk Assessment

The risk estimates provided for drinking water exposures in this assessment are based on a conservative simulation model for raw (unfinished) surface water that may serve as a source of drinking water for Texas and Kansas. Atrazine use on corn reflected in these assessments is a major contributor to the risk estimates. Maximum use rates for both atrazine and propazine were used in the assessments. The KS scenario assumed very conservative estimates of percent of crop treated for both atrazine and propazine. All existing atrazine labels require setback distances around intermittent/perennial streams and lakes/reservoirs. It is expected that the presence of a well-vegetated setback between the site of atrazine application and receiving water bodies could result in reduction in loading. Therefore, the drinking water exposure estimates presented in this assessment may over-estimate exposure in finished drinking water.

The following refinements have been included in these assessments:

1) The surface water concentrations of atrazine and propazine produced by the PRZM/EXAMS model have been refined by a cumulative adjustment factor (CAF) to account for portions of the simulated watershed that are not treated with atrazine and/or propazine.
2) The chlorinated degradates: des-ethyl atrazine, isopropyl atrazine, and diaminochlorotriazine have been estimated and included in these assessments.
3) The TX scenario included refined estimates of percent of crop treated for atrazine and propazine.

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