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March 19, 2010

Gregg Regimbal,  
Minnesota Department of Agriculture  
Pesticide and Fertilizer Management Division  
625 Robert Street North  
St. Paul, MN 55-155-2538

**SUBJECT: Atrazine Special Registration Review: Syngenta Crop Protection Comments**

Dear Mr. Regimbal:

Syngenta Crop Protection, Inc., a registrant of atrazine containing products appreciates this opportunity to submit comments on the Minnesota Department of Agriculture's "Summary of the Special Registration Review of the Herbicide Atrazine" which was published on January 19, 2010. We also wish to thank the Minnesota Department of Agriculture, the Minnesota Pollution Control Agency, and the Minnesota Department of Health for their thorough review of this important agricultural tool. For 50 years, sound science has governed the U.S. regulation of atrazine, one of the most studied herbicides in history. Minnesota farmers, and growers in 60 countries around the world, use atrazine to produce safe, abundant and affordable crops. The Minnesota Special Registration Review has once again confirmed the science supporting the registration of atrazine and its importance to agriculture.

In response to recommendations by the Legislative Auditor for the State of Minnesota, the Minnesota Department of Agriculture (MDA) partnered with the Minnesota Department of Health (MDH) and the Minnesota Pollution Control Agency (MPCA) to review a select number of pesticides to consider appropriate additional state specific restrictions, limitations on use as a condition of registration or registration without state-specific restrictions. Atrazine was selected by the MDA as the first pesticide to go through this special registration review process.

The MDA prepared a scoping document to review atrazine use, impacts and registration in Minnesota. This scoping document identified three major actions:

- a) Review the Risks of Atrazine on Human Health and the Environment
- b) Review the Costs and Benefits of Atrazine Use on the Agricultural Economy in Minnesota
- c) Review Minnesota-Specific Registration and Non-Regulatory Actions

In a partnership with the MDA, MDH and MPCA, conducted assessments on: 1) Human Health, 2) Environmental, 3) Cost and Benefit, 4) Monitoring and 5) Label. These findings were presented in

“Atrazine Technical Assessments” published January 2010. Based on the atrazine technical assessments, MDA concluded:

- a) MDH did not find unacceptable human health risks resulting from currently registered uses of atrazine.
- b) Current Minnesota Human Health Atrazine Water Quality Standards are protective of human health.
- c) Current Minnesota Aquatic Life Water Quality Standards are protective of aquatic life.
- d) Over 16 years (1993 to 2008) atrazine was not detected in drinking water at concentrations that exceeded human health water quality standards in either surface or groundwater at public or private drinking water supplies
- e) Groundwater monitoring programs focused on highly sensitive aquifers, including sand and gravel outwash plains, karst areas, private wells and Community Water Systems and included data from MDA, MDH, USGS – NAWQA, Dakota County, NGO-Land Stewardship, MDH Flooded Wells (73) in Southeast Minnesota, and a 2009 MDA Special Project monitoring 92 private wells in Southeast Minnesota
- f) Over 16 years (1993 to 2008) atrazine was not detected in surface water at concentrations that exceeded Aquatic Life Water Quality Standards
- g) Surface water monitoring included grab, composite and time-weighted sampling in 9 regions, springs in the Southeast karst area and state wide lakes and included data from MDA, MDH, USGS-NAWQA and MDA lakes monitoring.

In context with these findings MDA, MPCA and MDH recommend the following actions:

- a) Continue monitoring for Atrazine and metabolites in geologic sensitive and high-use areas
- b) Future monitoring programs should include DACT and combined total chloro-triazine
- c) Increase education and outreach efforts to private well owners
- d) Continue to facilitate discussion between MDH and EPA OPP on key toxicology data and assessment for atrazine
- e) Continued vigilance and use of BMPs for atrazine
- f) MDA pesticide management activities continue to encompass protection of ambient water including small lakes, small streams and other surface waters that may be vulnerable
- g) MDA recommends current MDA atrazine BMPs be evaluated for revisions to address any identified in this review (no changes to BMPs were recommended)
- h) Non-regulatory changes in the atrazine label form and content (environmental hazard section moved up, MN definition of sensitive waters included, and printing in black and white)
- i) Continued enforcement of the atrazine label.

Your agency’s review of atrazine monitoring in ground and surface water showed that current label requirements for atrazine containing products are protective of human health and the environment and there is no scientific justification for any additional registration changes or product specific regulation in the state of Minnesota beyond those currently in place. This is reflected in the MDA, MPCA and MDH findings and recommended actions (above). We offer the following comments for your consideration.

## Human Health Assessment Comments

### Minnesota Assessment:

“The MDH is continuing to assess acute, short-term, subchronic, chronic, and cancer endpoints for atrazine and its chlorinated metabolites, DEA, DIA, and DACT. In some of the toxicological information available for DACT, the primary metabolite in mammals, critical effects are observed at doses lower than the same effects seen for atrazine. Based on this information, the health-based assessment for DACT indicates a potentially higher level of toxicity than for atrazine for some health endpoints. MDH is continuing to research the potential magnitude of this difference in potency. Based on currently available information and the magnitude of uncertainty factors that may be applied, it is unlikely that a new MDH Health Risk Limit (HRL) value for atrazine (parent) will be lower than the current drinking water HRL of 3 parts per billion (ppb). However, new, potentially lower health-based guidance values may be derived for DACT. Because DEA and DIA are rapidly metabolized to DACT, guidance values derived for DACT may be applicable to DEA and DIA. The conclusions stated in this summary reflect MDH’s current understanding of the available toxicity information for atrazine and its chlorinated metabolites.”

### Syngenta Response

A separate analysis for DACT is not warranted based on the available data. The US EPA reviewed this compound in depth during the atrazine re-registration, and concluded that atrazine and the chlorometabolites, including DACT, are equipotent (EPA, 2006, page 14). The World Health Organization has also made the same conclusion, stating that “The chloro-*s*-triazine metabolites DEA, DIA and DACT share the same mode of action as atrazine and have a similar toxicological profile and hence the Meeting decided to establish a group ADI and ARfD.” (WHO 2007b, p.48)

#### 1) **The *In Vivo* Toxicity of Atrazine Cannot Be Assessed Independent of Toxicity of DACT**

Atrazine rapidly undergoes phase I metabolism to DIA (G-28279), DEA (G-30033) and DACT (G-28273) with more DACT being formed in rodents than in humans. In a human study shortly after administration, atrazine levels in plasma falls below the limit of detection (WHO, 2007a). Therefore toxicity studies conducted on atrazine in animal models reflect the toxicity of atrazine and the metabolites.

#### 2) **The Toxicity of Atrazine *In Vivo* is Comparable to the Toxicity of DACT**

Side-by-side comparisons of the toxicity profile of atrazine to DACT in standard toxicity studies indicate that atrazine and DACT are equipotent (Table 1; Breckenridge et al., 2008).

#### 3) **EPA Has Concluded that Atrazine and its Chlorometabolites are Equipotent**

In EPA’s cumulative risk assessment of the chlorotriazines (EPA, 2006) they assumed that parent atrazine and its chlorometabolites are equipotent.

**Table 1: Comparison of the Toxicity of Atrazine to Diaminochlorotriazine**

Study	Endpoint	Atrazine	Diaminochlorotriazine
Acute Oral Toxicity (Range observed in 3 studies) Breckenridge (2008)	LD50 Male	1405-3520 mg/kg	3690-11300 mg/kg
	LD50 Female	2487-3000 mg/kg	2360-5230 mg/kg
Dermal Irritation (Breckenridge, 2008)		Non-irritating	Non-irritating
Eye Irritation Breckenridge, 2008)		Non-irritating	Irritant (R-36)
Pubertal female (Laws 2000; Laws,2003)	NOAEL	12.5 mg/kg/day	12.5 mg/kg/day(atrazine equimolar dose)
	LOAEL	50 mg/kg/day (delayed vaginal opening)	50 mg/kg/day (delayed vaginal opening)
Pubertal-male (Stoker, 2000; Stoker, 2002)	NOAEL	6.25 mg/kg/day	6.25mg/kg/day (atrazine equimolar dose)
	LOAEL	12.5 mg/kg/day (delayed preputial separation)	12.5 mg/kg/day (delayed preputial separation)
Developmental toxicity in rat (Infurna,1984; Giknis, 1989)	NOAEL	10/25 mg/kg/day (fetal and maternal)	2.5 mg/kg/day (fetal and maternal )
	LOAEL	75/100 mg/kg/day (incomplete ossification of bones)	25 mg/kg/day (incomplete ossification of bones)
90-day rat study (Bachmann, 1994; Pettersen, 1991)	NOAEL	3.3 mg/kg/day	6.7 mg/kg/day <sup>1</sup>
	LOAEL	34.0 mg/kg/day – reduction in body weight gain	16.7 mg/kg/day – reduction in body weight gain <sup>1</sup>
1-year dog study ( O'Connor,1987; Thompson, 1990)	NOAEL	3.75 mg/kg/day	3.3 mg/kg/day
	LOAEL	34 mg/kg/day (cardiac effects)	29 mg/kg/day (cardiac effects)

<sup>1</sup>WHO (2007a, pg 79) concluded that the LOAEL for effects on the estrus cycle for DACT in this study was 19.7 mg/kg/day and the NOAEL was 7.6 mg/kg/day. There is not a comparable 90-day estrous cycle study available for atrazine.

## Environmental Assessment

### Minnesota Assessment:

“However, an extensive evaluation of the literature to assess toxicity endpoints was not completed for this registration review because this area is still under extensive review by the EPA”. Also stated “The EPA’s Endocrine Disruptor Screening Program is poised to provide data needed to more accurately assess a broader spectrum of endpoints relative to ecological species health”.

### Syngenta Comment:

The EPA White Paper cited in the MPCA Environmental Assessment (U.S. EPA, 2007) concluded “that atrazine does not adversely affect amphibian gonadal development” (EPA 2007). A panel of independent expert scientists convened by the USEPA agreed that “reproductive fitness (sex ratio, intersex condition)

were unaffected” and “there is currently no available proof for the hypothesis regarding the purported action of atrazine on the induction of aromatase” (FIFRA SAP 2007).

Furthermore, subsequent to the SAP in 2007 three additional publications support this finding. Oka et al. (2008) exposed *X. laevis* larvae to atrazine and while a difference in sex ratios was reported at 10 and 100  $\mu\text{g/L}$ , the authors concluded that “higher female ratios in atrazine exposure groups in the present study were not caused by estrogenic action of atrazine.” LaFiandra et al. (2008) exposed North American treefrogs (*Hyla versicolor*) to 20 and 200  $\mu\text{g/L}$  atrazine and reported no effects on sex ratio or gonadal development. Likewise, Storrs and Semlitsch (2008) exposed three North American species (*Bufo americanus*, *Hyla versicolor*, and *Rana sphenocephala*) to atrazine (1, 3, or 30  $\mu\text{g/L}$ ) and reported no effects on metamorphosis or ovarian development.

The issue of atrazine’s potential to affect amphibian gonadal development has been exhaustively examined, and as stated in the MPCA Environmental Assessment, EPA is not recommending any additional testing on this issue.

Relative to the Endocrine Disruptor Screening Program, atrazine is one of 58 active ingredients being considered in the initial screens. However, in the case of atrazine an unprecedented amount of existing endocrine related testing has been performed and Syngenta believes this information satisfies and in fact exceeds the Tier 1 screens.

Finally, the Rohr and McCoy (2009) publication cited by MPCA, reports to be a “qualitative” meta-analysis across a large number of studies and biological endpoints. This study however, suffers from a number of design flaws which make its interpretation very limited. A properly conducted meta-analysis should draw “quantitative” rather than “qualitative” conclusions as was done in the Rohr and McCoy (2009) document. The “qualitative meta-analysis” used by the authors was simply a summation of the number of reported positive or negative responses. In their qualitative meta-analysis, the authors did not account for or incorporate the effects of differences in species, differences in magnitude of the effects, differences in exposure protocols, differences in experimental environments, differences in endpoints, etc.

## **Monitoring Assessment**

### Minnesota Assessment

“Concentrations of atrazine and its chlorinated degradates are sometimes combined when assessing health risks associated with drinking water consumption.”

### **Syngenta Response:**

The Minnesota HRL for atrazine between 2000 and 2006 was 20 ppb. In 2007 the HRL was modified by order of the MN State Legislature to the EPA Maximum Contaminant Level (MCL) for atrazine of 3 ppb. The U.S. EPA MCL was established for atrazine (parent only). The maximum atrazine concentration detected in wells in the MDA regional groundwater network from 2000 to 2006 was 0.52 ppb. Since 2007 the MDA has monitored for atrazine and metabolites in groundwater and found a maximum atrazine + metabolites concentration of 2.52 ppb. In 2003 the US EPA established Drinking Water Levels of Comparison (DWLOCs) for Total Chloro Triazines (TCT) for atrazine + metabolites (Table 2).

**Table 2**  
**Summary of Lowest Drinking Water Levels of Comparison (DWLOCs) for Atrazine and its Chlorinated Metabolites from EPA-OPP Interim Registration Eligibility Decision (IREED), January 31, 2003**

Population Subgroup	Acute (One Day) Exposure	Intermediate (Seasonal) Chronic (Annual) Exposure (ppb)	
		90-day	Annual
General Population	not available	--	68
Infants < 1 year old	not available	12.5/37.5 <sup>a</sup>	--
Children 1 to 6	not available	--	23
Children 7 to 12	not available	--	53
Females 13 to 50	298	--	60
Males 13 to 19	not available	--	68
Males 20 and over	not available	--	68
Seniors	not available	--	68

<sup>a</sup> Raw water at CWS intake structure.

Note: The 12.5 ppb TCT 90-day average is a screening trigger based on reliable, less frequent raw water monitoring data. CWS that exceed this screening trigger are incorporated into the weekly and biweekly (AMP) program. The 90-day raw water 37.5 ppb TCT performance standard applies to CWS in the atrazine monitoring program (AMP).

### Minnesota Monitoring Assessment – Buffers

The MDA BMPs currently recommend protective practices around surface tile inlets in any field with a surface tile inlet, and such BMPs should continue to be promoted and evaluated. If proven to be effective but not widely adopted, and unreasonable adverse effects on the environment are evident (e.g. through surface water impairment declarations, chronic standard exceedances or other concerns), surface tile inlet mitigation measures could form the basis of additional BMP review or a regulatory requirement supported by a Minnesota supplemental label.

### Syngenta Response - Buffers

Atrazine concentrations in surface water have not exceeded aquatic life or human health standards in Minnesota for the 16 years atrazine has been monitored. Research by Fawcett has shown no significant impact of surface instances and outflow atrazine concentrations (Fawcett, R.S., “Impact of Surface Intakes on Atrazine Concentrations in Outflow from Tile-Outlet Terraces and Subsurface Drainage Tile Systems”, technical report, November 5, 2004.). The current atrazine label and voluntary stewardship practices around tiled intakes have been shown to be sufficient to protect water quality.

This review and that of the USEPA-OPP demonstrate that current federal and state water quality standards are conservative and more than sufficient to protect human health and the environment. This review provides MDA and its interagency partners with validation of the importance of the continued safe use of atrazine. Utilizing the current label requirements and the current voluntary Best Management Practices have been proven effective in Minnesota.

### **MPCA Label Recommendations:**

On page 6 of MPCA Technical Environmental Review, the MPCA recommends several non-regulatory changes in atrazine label form and content.

Syngenta agrees with the MDA that label formatting should continue to be managed through MDA's involvement with U.S. EPA through the State-FIFRA Issues Research and Evaluation Group and that these changes be evaluated to ensure consistency across all product labels.

Currently MDA educates producers about sensitive areas and provides recommended BMPs through the promotion of Generic and Product Specific BMPs. Atrazine is a Restricted Use pesticide, ensuring that applicators undergo extensive education and training and receive continuing education through pesticide applicator licensing and certification training programs. The success of these atrazine BMP's and associated applicator training and education programs have been proven successful resulting in compliance with water quality standards and declining trends in detected concentrations. Therefore, label education and outreach should continue to be delivered through these programs and publications.

### **Conclusions**

Atrazine continues to be an extremely important tool to corn producer in Minnesota. In addition, to significantly improving crop yields it remains a vital tool in minimum and no-till cropping systems. These systems help protect Minnesota's farms from excessive erosion and Minnesota water resources from sedimentation concerns. Furthermore, atrazine has become an extremely important tool for managing weed resistance to both selective and nonselective herbicides such as glyphosate. Weed resistance management has become a significant issue throughout Minnesota and atrazine has continued to demonstrate its importance to effective resistance management programs.

The MDA's Special Registration Review of the Herbicide Atrazine clearly demonstrates continued importance and safety of atrazine as an irreplaceable tool for Minnesota producers. The report cites University of Minnesota weed scientists who agree that there is no effective replacement for atrazine especially in preemergent weed control. Furthermore, the success of the MDA's Pesticide Management efforts and the implementation of Generic and Pesticide Specific BMPs for atrazine and other active ingredients, as part of the Minnesota Pesticide Management Plan (PMP), have been extensive and impressive. These efforts have resulted in detected concentrations of atrazine which are very low relative to water quality standards in both surface water and groundwater. Furthermore, trend analyses have demonstrated that concentrations are declining or stable at very low levels. The MDA, Minnesota farmers, Retailers and Registrants should all be commended for their efforts to protect Minnesota water resources.

Current voluntary BMP education and outreach efforts are working and should remain targeted toward the most vulnerable areas of the state. The Minnesota PMP calls for continued monitoring and annual review of monitoring data. Evaluation of these atrazine data clearly and convincingly demonstrates the effectiveness of these voluntary efforts. There is clearly no need or justification for any further restrictions or conditions of registration for products containing atrazine.

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Syngenta would like to thank the MDA for this opportunity to comment. If there are questions about our comments please do not hesitate to call.

Sincerely,

David Flakne  
State Government Relations  
Syngenta Crop Protection

CC: Gene Hugoson, Commissioner, MDA  
Greg Buzicky, MDA  
MN Ag Coalition

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