



N. Beth Carroll, Ph.D  
Sr. Stewardship Manager  
P.O. Box 18300  
Greensboro NC 27419-8300

Telephone: (336) 632-7178  
Email: beth.carroll@syngenta.com

April 15, 2005

Agency for Toxic Substances and Disease Registry  
Division of Toxicology  
Attn: Hana Pohl, M. D., Ph.D.  
1600 Clifton Road, N.E.  
Mail Stop F-32  
Atlanta, GA 30333

Subject: Comments on the DRAFT INTERACTION PROFILE FOR:  
ATRAZINE, DEETHYLATRAZINE, DIAZINON, NITRATE, AND  
SIMAZINE [*Federal Register* Notice 69(245): 76768-76769]

Dear Dr. Pohl:

With this correspondence Syngenta Crop Protection (Syngenta) is providing comments on the Agency for Toxic Substances and Disease Registry's (ATSDR) Draft Interaction Profile for: Atrazine, Deethylatrazine, Diazinon, Nitrate, and Simazine (Draft Interaction Profile). Syngenta is, under separate cover, also providing a science chapter entitled "Critical Review of the ATSDR's Proposed Interaction Between the Chlorotriazines and Nitrate or Diazinon." This science chapter is being sent via mail as a CD.

Scientifically Syngenta finds no justification for the creation or publication of this Draft Interaction Profile. First ATSDR cites a mandate from the Comprehensive Environmental, Response, Compensation, and Liability Act (CERCLA) to assess whether adequate information on health effects is available for *priority hazardous substances*.

Syngenta has reviewed the latest list (2003) of *priority hazardous substances* as well as earlier lists and find that neither atrazine, deethylatrazine, nor simazine have been listed as priority substances for ATSDR. Therefore the decision to assess these chemicals in a mixture interaction is inappropriate.

The interaction profile proposed for nitrate plus the chlorotriazines is not supported by data. The formation of N-nitrosoatrazine in the environment is highly unlikely and does not occur at neutral pH's found in soil and water. Furthermore, the short photolytic half life of N-nitrosoatrazine in water precludes any reaching target

organisms, even if it were to form. No N-nitrosoatrazine has been confirmed as present in environmental samples over a 50 years of triazine use.

The formation of N-nitrosoatrazine in the stomach, again while theoretically possible, has not been demonstrated, even at high doses of nitrate and atrazine. Finally, when nitrosoatrazine or nitrososimazine were administered for a lifetime to rats and mice that exceeded maximum tolerated doses, no excess incidence of tumors were observed. Therefore ASTDR proposed interaction profile between atrazine and nitrate based upon carcinogenic potential is unwarranted.

In addition in a study conducted by NIEHS, mixtures of atrazine, simazine and nitrate at 100-fold higher levels than environmental concentrations did not cause any reproductive (mice), general or developmental toxicity (rats) (Heindel, et al. 1994).

The interaction profile proposed by ASTDR for diazinon and atrazine based upon enhanced acute toxicity in selected aquatic invertebrates is likewise unwarranted based on the fact that environmental concentrations or estimated human doses of atrazine or total chlorotriazine is substantially below those concentrations need to induced P450 enzymes capable of modulating diazinon acute toxicity. Furthermore, it is not clear why ASTDR chose these two chemicals to showcase interaction out of the myriad of combinatorial effects that could be considered between xenobiotics that co-occur, especially considering the fact that there is empirical evidence that all most environmental concentrations of atrazine and diazinon are below their respective standards.

Based upon the above facts, Syngenta requests that ASTDR withdraw the proposed interaction profile for the chlorotriazine plus nitrate and the chlorotriazines plus diazinon.

ATSDR cites the Food Quality Protection Act (FQPA) as requiring consultation with the Secretary of Health and Human Service (HHS) (which includes ATSDR) in implementing some of the provisions of FQPA. As far as this assertion is concerned, the requirements for consultation with the Secretary of HHS are quite specific in FIFRA/FFDCA as amended by FQPA, generally specified for vector controlling substances. Additionally, EPA under FQPA specifically addresses assessment of chemicals that have a common mechanism of toxicity. While atrazine, simazine and deethylatrazine have been deemed as having a common mechanism of toxicity by EPA, this does not hold true for the other substances described in the Draft Interaction Profile. Further, to Syngenta's knowledge, the testing of pesticide and fertilizer interactions is not a part of any validated federal toxicological testing protocol, nor any mandate to ATSDR. It appears therefore that the decision by ATSDR to develop this Draft Interaction Profile absent any request from the EPA Administrator is questionable.

Although the ATSDR Draft Profile correctly cites The International Agency for Research on Cancer's (IARC 1999a) atrazine classification as *not classifiable as to its*

*carcinogenicity to humans* (Group 3) based on inadequate evidence in humans and sufficient evidence in experimental animals, Syngenta wishes to point out that the IARC went on to evaluate atrazine (and simazine) with the statement: “Therefore there is strong evidence that the mechanism by which atrazine increases the incidence of mammary gland tumours in Sprague-Dawley Rats is not relevant to humans.” In addition, the EPA Office of Pesticide Programs (2002) classified atrazine and its chlorinated metabolites as *not likely to be carcinogenic to humans*.

The Draft Interaction Profile states in the first sentence of the “Summary” that “Atrazine, deethylatrazine, simazine, diazinon, and nitrate were chosen as the subject mixture for this interaction profile because they frequently occur together in rural well water.” The citation for this conclusion is not apparent in the summary but later is shown to be a study by Squillace et al. 2002. In review of the study however it is shown that neither atrazine, deethylatrazine, nor simazine were found at levels greater than their established standards. Additionally, ATSDR states that “diazinon was the most frequently detected organophosphate insecticide”, when in fact, in the report cited, it was the only organophosphate insecticide detected, and it was found in a total of one well.

Therefore it is extremely puzzling to Syngenta why these compounds were picked over VOCs, for example, which, as stated by the authors, were detected more frequently than pesticides. ATSDR seems to try to justify its choice of this mixture by ignoring that VOCs were detected more frequently than pesticides and by simply stating that it picked the most frequently occurring *four-chemical* mixture (emphasis added). Based on Squillace et al. 2002, VOCs should have been of much higher priority to ATSDR and therefore this is an extremely questionable choice of compounds for an interaction assessment. Syngenta’s science chapter provides additional information to scientifically show that the environmental concentrations of the triazines would not result in the formation of N-nitrosoatrazine or increase the toxicity of diazinon.

ATSDR states on Page iii: “A weight-of-evidence approach is commonly used in documents to evaluate the influence of interactions in the overall toxicity of the mixture. The weight-of-evidence evaluations are qualitative in nature, although ATSDR recognizes that observations of toxicological interactions depend greatly on exposure doses and that some interactions appear to have thresholds. Several statements made in the document also support the fact that this proposed Draft Interaction Profile is unwarranted.

Syngenta also notes that ATSDR has cited the EPA IRIS database with regard to atrazine and simazine. Syngenta refers the ATSDR to Federal Register Notice Integrated Risk Information System (IRIS); Announcement of 2004 Program; Request for Information (Vol. 69, No. 26 / Monday, February 9, 2004) which states for atrazine, simazine and diazinon (among others) that the Agency is “deleting from the IRIS agenda, a group of pesticides that will not be assessed through the IRIS process given that the Office of Pesticide Programs (OPP) has a large assessment program

Syngenta  
Page 4  
April 15, 2005

evaluating these chemicals. This step is being taken to more efficiently utilize Agency resources.”

ATSDR should take advantage of the EPA OPP’s extensive ongoing review of the triazines which will culminate in a cumulative risk assessment of the group of triazine-containing chemicals. These include atrazine, simazine, desethyl-s-atrazine (DEA), desisopropyl-s-atrazine (DIA), and diaminochlorotriazine (DACT). EPA OPP will complete its assessment on the chlorotriazines in 2006, and therefore it is a waste of federal resource for ATSDR to start a new assessment. In addition, the data do not support the need for a profile that includes diazinon and nitrate.

Reflected in all the facts stated here it is apparent that the there are no data or models for ATSDR to base its Draft Interaction Profile for Atrazine, Deethylatrazine, Diazinon, Nitrate, and Simazine. This Draft Interaction Profile does not withstand the test of scientific integrity nor data quality and therefore should be withdrawn from the ATSDR’s current draft interaction profiles.

Sincerely,

N. Beth Carroll, Ph.D.  
Sr. Stewardship Manager  
Syngenta Crop Protection

cc: Burleson Smith, Special Assistant Pest Management Policy, USDA  
Jon Scholl, Counselor to the Administrator for Agricultural Policy  
U.S Environmental Protection Agency  
Jere White, Executive Director Kansas Corn and Grain Sorghum Association