

SUMMARY FROM SYNGENTA'S SCIENCE OVERVIEW SUBMITTED TO EPA DOCKET

Syngenta's assessment concludes that atrazine hazard and exposure via drinking water have been well characterized. The current regulatory standards are protective of human health and result in large margins of exposure (MOEs).

Pulsatile LH is the Most Relevant Human Endpoint

- The pulsatile LH mechanism in rodents and human is similar, but the LH surge control mechanism is different. Therefore, the most relevant human endpoint is pulsatile LH.
- For studies on the LH surge in rodents, atrazine effects have been observed only after bolus/gavage administration or when atrazine was administered to reproductively aged female Sprague Dawley (SD) rats. Neither scenario is relevant to humans.
- The suppression of the LH surge is a conservative endpoint.

Proposed Point of Departure (POD) Selected by EPA is Highly Conservative

The proposed POD of 2.56 mg/kg/day based on the effect on the LH surge of a 4-day bolus dose atrazine administered to Long-Evans (LE) rat is a conservative surrogate for the human relevant endpoint (pulsatile LH) because:

- The NOEL for a functional indicator of effect on pulsatile LH release is 6.25 mg/kg/day.
- The NOEL for distributed dosing on the LH surge is greater than 50 mg/kg/day.
- The LE rat, which has a highly variable estrus cycle, may not be the best animal model upon which to base the POD; more data exist for SD and Wistar rats.

High Level of Confidence in Assessment

EPA's proposed endpoint selection (LH surge attenuation), POD (2.56 mg/kg/day), and dose duration (4 days) are highly conservative.

Extensive New Studies on Atrazine Establish Greater Confidence in MOEs because:

- Distributed dosing NOELs are at least 5X higher than bolus dosing NOELs,
- Developing animals are less sensitive than adults,
- Kinetic studies show pharmacokinetic scaling should be used for interspecies extrapolation,
- Four rat strains have been evaluated in the LH surge model
- The most sensitive strain has been selected by EPA.

Atrazine Exposure Is Well Characterized

- Most of the US population are minimally exposed, and SDWA data can be used to identify CWSs for high frequency monitoring.
- The extensive atrazine frequent monitoring database has wide temporal coverage across areas vulnerable to higher atrazine runoff.
- This database was used to characterize potential exposure to atrazine.

Margins of Exposure (MOEs):

- MOEs calculated for those CWSs with the highest total chlorotriazine residue concentrations do not exceed a level of concern, even when conservative factors are included in the analysis.
- Using the existing 7-day monitoring data along with a conservative bias factor shows that MOEs for short term exposure are acceptable.