

Chlorsulfuron

Proposition 65 Delisting

January 21, 2014

Summary

- Chlorsulfuron Prop 65 Listed
 - Developmental and Female Reproductive Toxicant
- Authoritative Body Listing
 - EPA TRI
- EPA Changed Conclusion in December 2013
 - No longer listed due to Developmental and Reproductive Effects
 - Listed only due to Toxicity to Aquatic Plants
- Satisfies Prop 65 Delisting Criteria
 - 27CCR 25306(j)(2):
 - “The chemical is no longer identified as causing cancer or reproductive toxicity by the authoritative body.”
- Questions on Process
 - Administrative Delisting or Delisting via DART-IC?

Timeline (leading up to Prop 65 listing)

- 1980 – Rabbit developmental toxicity study
 - Increase in incidence of resorptions reported
- 1981 – Reproductive toxicity study (3 gen combined)
 - Decrease in fertility index reported for 3rd gen
- 1982 – EPA registration
- 1990 – EPA “One-Liners” database includes two sentence summaries of 1980 and 1981 studies, cursory review
- 1991 – Replacement developmental toxicity studies
 - Rabbit and Rat
- 1993 – EPA review for TRI process
 - Used “One-Liners” as sole source – secondary source
 - Did not notice new 1991 developmental toxicity studies
- 1994 – TRI listed based on 1993 review
- 1999 – Listed under Proposition 65 based on TRI classification

Timeline (after Prop 65 listing)

- 2002 - EPA evaluation of 1991 rabbit develop. tox. study
 - No effects on resorptions
- 2002 - EPA completes several summaries – for RED
 - Developmental toxicity not a specific concern
 - 1980 rabbit study not referenced anymore
 - New rat reproductive toxicity study required, 1981 not acceptable
- 2005 - EPA completes RED
 - Reiterates 2002 conclusions
- 2005 - Replacement reproductive toxicity study completed
- 2007 - EPA evaluation of new reproductive toxicity study
 - No effects on fertility
- 2009 - DuPont petitions OEHHA to delist under Prop 65
- 2010 - OEHHA removes male reproductive effects as endpoint
- 2012 - DuPont petitions EPA to remove TRI classification
- 2012 – DuPont re-petitions OEHHA to delist under Prop 65
- 2013 – December – EPA completes response to 2012 petition

EPA Criteria for Chlorsulfuron's Listing in TRI in 1994

- 1980 rabbit developmental toxicity study reported an increased incidence of resorptions
- 1981 reproduction study in rats reported decreased fertility
- “In a rabbit developmental study, an increased incidence of fetal resorptions was observed at the LOEL of 75 mg/kg/day. The NOEL was 25 mg/kg/day. In a 3-generation rat reproduction study, a decrease in fertility index was observed at 125 mg/kg/day (LOEL). The NOEL was 25 mg/kg/day. EPA believes that there is sufficient evidence for listing chlorsulfuron on EPCRA section 313 pursuant to EPCRA section 313(d)(2)(B) based on the available developmental and reproductive toxicity data for this chemical.”

(Fed. Reg. Jan 12 1994)

EPA's Reevaluation of Chlorsulfuron for TRI Program

- December 9, 2013
- Formal conclusion
- Federal Register 78 : 73787-73793

EPA TRI Listing Criteria: EPCRA § 313(d)(2)

- A. The chemical is known to cause or can reasonably be anticipated to cause significant adverse acute human health effects at concentration levels that are reasonably likely to exist beyond facility site boundaries as a result of continuous, or frequently occurring, releases.
- B. The chemical is known to cause or can reasonably be anticipated to cause in humans:
 - Cancer or teratogenic effects, or
 - Serious or irreversible
 - reproductive dysfunction,
 - neurological disorders,
 - heritable genetic mutations, or
 - other chronic health effects.

EPA TRI Listing Criteria: EPCRA § 313(d)(2)

- C. The chemical is known to cause or can reasonably be anticipated to cause, because of:
- its toxicity,
 - its toxicity and persistence in the environment, or
 - its toxicity and tendency to bioaccumulate in the environment,
- a significant adverse effect on the environment of sufficient seriousness, in the judgment of the Administrator, to warrant reporting under this section.

EPA TRI Listing Criteria: EPCRA § 313(d)(2)

- 313(d)(2)
 - (A) – “Acute human health effects criterion”
 - (B) – “Chronic human health effects criterion”
 - (C) – “Environmental effects criterion”

EPA's Reevaluation of Chlorsulfuron for TRI Program

- Acute Human Health Effects Criterion (313(d)(2)(A))
- Chronic Human Health Effects Criterion (313(d)(2)(B))
- “Based on EPA’s review of the available data, there is no compelling evidence of the acute toxicity, carcinogenicity, reproductive or developmental toxicity, mutagenicity, or other serious chronic toxicity of chlorsulfuron. While treatment-related body weight changes were observed in some studies, the evidence for these changes is not sufficient to conclude that chlorsulfuron is expected to cause serious or irreversible systemic toxicity. Therefore, chlorsulfuron is not reasonably anticipated to cause acute or chronic toxicity in humans.”

EPA's Reevaluation of Chlorsulfuron for TRI Program

- Environmental Effects Criterion (313(d)(2)(C))
- “—chlorsulfuron is highly toxic to some species of aquatic plants.”
- “Therefore, EPA has concluded that chlorsulfuron meets the EPCRA section 313(d)(2)(i) listing criteria based on the available environmental toxicity data.”

Conclusion

- Prop 65 Delisting Criteria Satisfied
 - 27CCR 25306(j)(2):
 - “The chemical is no longer identified as causing cancer or reproductive toxicity by the authoritative body.”
- Process?
 - Administrative Delisting or Delisting via DART-IC?

Critical studies*

- **1980. Teratology Study in Rabbits. Hoberman et al. (HLO 534-80)**
 - 2011. Supplement 1, Revision 1. Reassessment of resorptions in view of replacement study (Alvarez 1991)
- 1991. Developmental Toxicity Study in Rabbits. Alvarez (HLR-306-90)
 - 2008. Supplement 2. Historical control assessment of sternebrae findings
 - 2012. Supplement 3. Statistical reassessment relevant to pup weights
- 1991. Developmental Toxicity Study in Rats. Alvarez (HLR-734-90)
- **1981. Reproductive Toxicity (3-Gen) & Chronic Feeding Study in Rats. Wood et al. (HLR 557-81)**
 - 2012. Supplement 3, Revision 2. Statistical assessment of fertility index and review of historical control data
- 2005. Reproductive Toxicity (2-Gen) Study. Mylchreest (DuPont-13475)

*Studies that led to TRI listing in ***bold italics***