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OFFICE OF  
PREVENTION, PESTICIDE  
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MEMORANDUM

**SUBJECT:** Review of Rebuttle to Data Evaluation Record on Early Life Stage Toxicity Test of Fentin Hydroxide (TPTH) using Sheepshead Minnows

**FROM:** Thomas M. Steeger, PhD, Senior Biologist  
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*Ed Fite 10/10/02*

**THROUGH:** Betsy Behl, Chief  
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**TO:** Wilhelmena Livingston, PM Team Reviewer  
Robert MaNally, Product Manager  
Special Review and Re-registration Division (7505C)

The Environmental Fate and Effects Division (EFED) has reviewed Landis International's and Springborn-Smithers Laboratories' response to EFED's data evaluation record on the early life stage toxicity test (Guideline 72-4; MRID 452760-01) of fentin hydroxide (TPTH) using sheepshead minnows (*Cyprinodon variegatus*). EFED originally classified the study as supplemental and as not having fulfilled guideline testing requirements since it failed to establish a no-observed effect concentration (NOEC) (**Attachment A**). In their rebuttle (dated August 22, 2002), the registrant maintains that the dose response was not monotonic and, therefore, it was inappropriate to analyze the data using William's test. William's test requires that the response variables follow a steady decline relative to increasing concentrations in test material. Springborn-Smithers is correct that the study's response variables (larval length and weight) do not follow a monotonic decline curve. Rather, at the lowest treatment level there is an initial decline in larval wet weight, length and dry weight, followed by an increase in response and then a steady decline. The William's test is capable of correcting for minor deviations from a monotonic decline curve through the use of isotonized means; however, there are no clear guidelines for distinguishing the extent to which this correction can be applied to the data.

EFED re-analyzed the data using an analysis of variance (ANOVA) procedure of SAS (Statistical Analysis System, Release 7.0, Cary, North Carolina) and a Dunnett's multiple means comparison test. The electronic data were provided by Dr. Ron Biever, Springborn-Smithers (see



**Attachment B).** The analysis (see **Attachment C**) indicate that larval weights at fentin hydroxide concentrations of 0.31, 2.5 and 5.0  $\mu\text{g/L}$  are significantly different than controls. For both larval length and dry weight the same pattern of response is clear, *i.e.*, initial decline followed by a recovery and then smooth decline; however, only larval weight is significantly lower than controls in the 0.3  $\mu\text{g/L}$  treatment. Based on discussions with other senior biologists in the Division, EFED is unclear whether this initial decrease in response represents a “low dose” effect or whether it is an artifact of variability. Therefore, EFED believes that the study should be repeated to better establish the NOEC and whether a “low-dose effect” is present.