

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

CASWELL FILE

4/23/86

APR 23 1986

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCE

MEMORANDUM

SUBJECT: Guidance regarding the dose levels to be used for the chronic studies being required in the linuron DCI: I.D. 035506; Record number 169837

TO: Ingrid Sunzenauer, PM #78  
Special Review Branch (TS-767C)  
and  
Robert Taylor, PM #25  
Registration Division (TS-767C)

FROM: James N. Rowe, Ph.D.  
Section V, Toxicology Branch  
Hazard Evaluation Division(HED) (TS-769C)

*James N. Rowe*  
4/16/86

THRU: William L. Burnam  
Deputy Chief  
Toxicology Branch/HED (TS-769C)  
and  
Theodore M. Farber, Ph.D.  
Chief, Toxicology Branch/HED (TS-769C)

*W. L. Burnam*  
4.18.86

BACKGROUND:

Data gaps for blood dyscrasias have been identified in a two-year chronic dog study (no NOEL determined for abnormal blood pigment believed to be sulfhemoglobin/LDT of 25 ppm; Hodge H.C. et al., 1963, MRID #00018374). In addition, no NOEL was determined in a two-year chronic rat feeding study where hematological effects at the LDT (50 ppm) were observed (increased mean corpuscular hemoglobin suggesting possible reticulocytosis; Kaplan A.M. et al., 1980, MRID # 00029680; Everett R.M. et al., 1980, MRID # 000269679). Guidance regarding the dose levels to be used in the chronic studies has been requested by the Special Review Branch.

RECOMMENDATION:

It is not the policy of the Toxicology Branch to give industry specific instruction on the dose levels to be used in a chronic study (this information can be best determined by the study director through the use of the range-finding studies and subchronic-phase of the tests). However the following suggestions should be considered:

In order for the chronic dog and rat studies to properly assess the lower end of the dose response curve in regard to blood dyscrasias, it is recommended that in both species the same strain and the same laboratory (if possible) be utilized to demonstrate the effects previously observed. The dose levels utilized should demonstrate an effect level (LEL) and a no-effect level (NOEL) at a dose(s) below the previously lowest effect levels that were noted in the two studies (dog= LDT of 25 ppm; rat= LDT of 50 ppm).