

State of California  
M e m o r a n d u m

**HSM-98009**

[Rescinded on Oct. 4, 2001, with approval  
from C. Andrews]

Gary Patterson, Chief  
Medical Toxicology Branch

Date: March 10, 1998

Place:

From: Department of Pesticide Regulation - 1020 N Street, Room 200  
Sacramento, California 95814-5624

Subject: DEFINITION OF EXPOSURE CONSTITUTING CHRONIC AND  
SUBCHRONIC

There is a need to define the frequency and duration of exposure which we call subchronic or chronic. Appropriate risk assessment requires that human exposures approximate the exposure time or time to effect in toxicology studies. Establishing a functional definition of these exposure terms will benefit exposure assessment personnel and the regulated public.

Ideally, toxicology studies on pesticides causing adverse effects in laboratory animals should have the same time frame as the human exposures used in the risk assessment process. In practice, non-dietary human exposures rarely occur daily for more than a few consecutive days. In contrast, laboratory animals are dosed with the pesticides every day in most regimens, with the exception of inhalation studies and some other special toxicology studies. Laboratory animals studies are typically conducted with terminal sacrifices. It is at these times that most reported adverse effects are observed. Cage side observations of signs and other effects are sometimes not included in final reports, so time to effect is frequently determined by when the study is terminated. A common default assumption in risk assessment is that one day of test animal exposure is equivalent to one day of human exposure.

Because of the intermittent nature of many human exposures during seasonal or annual usage of pesticides, it is necessary to amortize, or average, human exposures over nonexposure intervals during these periods. This amortization is an implicit use of Haber's Law, which says that the effect produced by a given product of exposure time and dosage will be the same over a limited range of times and dosages producing the same time weighted average exposure (Atherley, 1985).

Gary Patterson  
March 10, 1998  
Page 2

However, the length of time between exposures cannot be so long that there is no residual toxicant from one dose before the next dose is received. Nor, can there be complete recovery from the effect produced by one dose before the next dose is given.

Most pesticides or their toxic metabolites have biological half-lives in humans of less than 24-hours (Feldmann and Maibach, 1974), which means that less than 12 percent of the parent compound would remain in the body at the time of a second exposure 72-hours later. For this reason, we feel that averaging intermittent exposures over a period with more than three days between exposures would be inappropriate. In those specific, rare instances in which the half-life is very long, the re-exposure interval would be greater than three days for amortization purposes. In general, if there are less than 30 exposure days in a 90-day period (seasonal), or less than 120-days/year (chronic), it would not be appropriate to calculate subchronic, or chronic exposures, respectively. The exposure days in either period should not be consecutive, but rather spread out over the quarter or year.

John S. Sanders, Ph.D., Chief  
Worker Health and Safety Branch  
(916) 445-4222

cc: John Ross  
Keith Pfeifer

References:

Atherley, G. (1985). Critical Review of Time-Weighted Average as an Index of Exposure and Dose, and of Its Key Elements. *Am Ind Hyg Assoc. J.* 46 481-487.

Feldmann, R. and Maibach, H. (1974). Percutaneous Penetration of Some Pesticides and Herbicides in Man. *Toxicol. Appl. Pharmacol.* 28, 126-132.