

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline Number	Study Type	Results
870.7600	Dermal Penetration - Rats	<p>The report states that at 24 hours postdose, 5.11% of the dose was absorbed (application-site skin + carcass + urine + feces) in this second trial. However, it is noted that there was poor recovery (68% of the total dose) from one of the rats (C32545) sacrificed at 24 hours in the second trial; disregarding the findings from this one animal then the mean value of the dose that was absorbed was 5.88%, and this can be taken as a reasonable estimate of the dermal absorption at this dose level.</p> <p>This dermal absorption study is classified as acceptable. However, because only one dose was used, this study, by itself, does not satisfy the guideline requirement for a dermal penetration study in the rat for technical bifenthrin (FMC 54800). However, it can be used, in conjunction with other dermal penetration studies, as supporting data for the purposes of registration and/or reregistration of products containing or consisting of bifenthrin.</p>

B. Toxicological Endpoints

The dose at which no adverse effects are observed (the NOAEL) from the toxicology study identified as appropriate for use in risk assessment is used to estimate the toxicological level of concern (LOC). However, the lowest dose at which adverse effects of concern are identified (the LOAEL) is sometimes used for risk assessment if no NOAEL was achieved in the toxicology study selected. An uncertainty factor (UF) is applied to reflect uncertainties inherent in the extrapolation from laboratory animal data to humans and in the variations in sensitivity among members of the human population as well as other unknowns. An UF of 100 is routinely used, 10X to account for interspecies differences and 10X for intraspecies differences. In this case, EPA has determined that an additional 10X data base uncertainty factor (UF_{DB}) is needed to account for the lack of a developmental neurotoxicity (DNT) study when assessing acute (single dose) exposure scenarios. EPA has further determined that for repeated dose exposure scenarios (i.e., chronic dietary; short- and intermediate-term incidental oral; and short-, intermediate-, and long-term dermal and inhalation scenarios) a

3X UF_{DB} is adequate to account for the lack of the DNT study. The factors which EPA considered in making these determinations are discussed in detail below in Unit III.D.3.

For dietary risk assessment (other than cancer) the Agency uses the UF to calculate an acute or chronic reference dose (acute RfD or chronic RfD) where the RfD is equal to the NOAEL divided by the appropriate UF (RfD = NOAEL/UF). Where an additional safety factor (SF) is retained due to concerns unique to the FQPA, this additional factor is applied to the RfD by dividing the RfD by such additional factor. The acute or chronic Population Adjusted Dose (aPAD or cPAD) is a modification of the RfD to accommodate this type of FQPA SF.

For non-dietary risk assessments (other than cancer) the UF is used to determine the LOC. For example, when 100 is the appropriate UF (10X to account for interspecies differences and 10X for intraspecies differences) the LOC is 100. In this case, since 300 is the appropriate UF for repeated dose exposure scenarios (10X to account for interspecies differences; 10X for intraspecies differences and 3X for data base uncertainty) the LOC is 300. To

estimate risk, a ratio of the NOAEL to exposures (margin of exposure (MOE) = NOAEL/exposure) is calculated and compared to the LOC.

The linear default risk methodology (Q*) is the primary method currently used by the Agency to quantify carcinogenic risk. The Q* approach assumes that any amount of exposure will lead to some degree of cancer risk. A Q* is calculated and used to estimate risk which represents a probability of occurrence of additional cancer cases (e.g., risk is expressed as 1 x 10⁻⁶ or one in a million). Under certain specific circumstances, MOE calculations will be used for the carcinogenic risk assessment. In this non-linear approach, a "point of departure" is identified below which carcinogenic effects are not expected. The point of departure is typically a NOAEL based on an endpoint related to cancer effects though it may be a different value derived from the dose response curve. To estimate risk, a ratio of the point of departure to exposure (MOE_{cancer} = point of departure/exposures) is calculated. A summary of the toxicological endpoints for bifenthrin used for human risk assessment is shown in Table 2 of this unit:

TABLE 2.—SUMMARY OF TOXICOLOGICAL DOSE AND ENDPOINTS FOR BIFENTHRIN FOR USE IN HUMAN RISK ASSESSMENT

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General population including infants and children)	NOAEL = 32.8 mg ai/kg UF = 1,000 Acute RfD = 0.033 mg/kg/day	FQPA SF = 1X aPAD = acute RfD ÷ FQPA SF = 0.033 mg/kg/day	Acute Neurotoxicity Study in Rats LOAEL = 70.3 mg/kg/day based on observations of mortality (females only), clinical and functional operational battery (FOB) findings and differences in motor activity.
Chronic Dietary (All populations)	NOAEL = 1.3 mg/kg/day UF = 300 Chronic RfD = 0.004 mg/kg/day	FQPA SF = 1X cPAD = chronic RfD ÷ FQPA SF = 0.004 mg/kg/day	1-Year Oral Study in Dogs LOAEL = 2.7 mg/kg/day based on observations of increased incidence of tremors in both sexes.