

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

Guideline No.	Study Type	Results
870.4300	Chronic Feeding Toxicity/Carcinogenicity-Rat	NOAEL = 50 ppm (2.4 mg/kg/day in males, 3.0 mg/kg/day in females) LOAEL = 100 ppm (4.9 mg/kg/day in males, 6.2 mg/kg/day in females) (small, soft testes, decreased testicular weights, and testicular atrophy in males; decreased body weight gain in females)
870.5100	Bacterial Reverse Mutation Test (Ames Assay)	Negative
870.5375	<i>In Vitro</i> Chromosomal Aberration in Chinese Hamster Ovary (CHO) Cells	Negative
870.5450	Rodent Dominant Lethal Assay - Rat	Negative
870.5575	D4 Mitotic Gene Conversion Assay	Negative
	P1 Forward Gene Mutation Assay	Negative
870.7485	Metabolism - Rat	The majority of the administered dose of phenyl- or pyrimidinyl- $^{14}\text{C}$ -Cl 217,300 was recovered in the feces (85–98%). Recovery in the urine was minimal (1- to 2% of the administered dose). There were no sex or dose-related differences in urinary or fecal elimination.
870.7600	Dermal Penetration - Rat	Sprague-Dawley rats were dermally dosed with a gel formulation containing 2% a.i. (Maxforce Gel®). Total dose absorbed after 10 hours was 0.414%
870.7600	Dermal Penetration - Rat	Sprague-Dawley rats were dermally dosed with a gel formulation containing 2.16% a.i. (Siege®). Total dose absorbed after 10 hours was 0.97%

### 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 intra species differences.

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 ( $\text{RfD} = \text{NOAEL} / \text{UF}$ ). Where an additional safety factors (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. To estimate risk, a ratio of the NOAEL to exposures (margin of exposure (MOE) =  $\text{NOAEL} / \text{exposure}$ ) 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  $1 \times 10^{-6}$  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 ( $\text{MOE}_{\text{cancer}} = \text{point of departure} / \text{exposures}$ ) is calculated. A summary of the toxicological endpoints for hydramethylnon used for human risk assessment is shown in the following Table 2: