

“special FQPA safety factor;” and the “default FQPA safety factor.” By the term “traditional uncertainty factor,” EPA is referring to those additional uncertainty factors used prior to FQPA passage to account for database deficiencies. These traditional uncertainty factors have been incorporated by the FQPA into the additional safety factor for the protection of infants and children. The term “special FQPA safety factor” refers to those safety factors that are deemed necessary for the protection of infants and children primarily as a result of the FQPA. The “default FQPA safety factor” is the additional 10X safety factor that is mandated by the statute unless it is decided that there are reliable data to choose a different additional factor (potentially a traditional uncertainty factor or a special FQPA safety factor).

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 an UF of 100 to account for interspecies and intraspecies differences and any traditional uncertainty factors deemed appropriate ($RfD = NOAEL/UF$). Where a special FQPA safety factor or the default FQPA safety factor is used, 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 safety factor.

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) = $NOAEL/exposure$) 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). An example of how such a probability risk is expressed would be to describe the risk as one in one hundred thousand (1×10^{-5}), one in a million (1×10^{-6}), or one in ten million (1×10^{-7}). 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 ($MOE_{cancer} = \text{point of departure}/\text{exposures}$) is calculated.

A summary of the toxicological endpoints for fluroxypyr used for human risk assessment is shown in Table 2 of this unit:

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

| Exposure Scenario | Dose Used in Risk Assessment, Interspecies and Intraspecies and any Traditional UF | Special FQPA SF and Level of Concern for Risk Assessment | Study and Toxicological Effects |
|--|--|---|---|
| Acute Dietary(All populations) | NOAEL = NA UF = NA Acute RfD = NA | FQPA SF = NA aPAD = acute RfD/ FQPA SF = NA | No appropriate endpoint to quantify single dose exposure. |
| Chronic Dietary(All populations) | NOAEL= 100 mg/kg/day UF = 100 Chronic RfD =1 mg/kg/day | FQPA SF = 1x cPAD =chronic RfD/ FQPA SF = 1 mg/kg/day | Chronic/Onco-Rat LOAEL = 100 mg/kg/day based on kidney effects. |
| Short-TermIncidental Oral (1-30 days) | NOAEL= 100 mg/kg/day | Residential LOC for MOE = 100 Occupational = NA | Chronic/Onco-Rat LOAEL = 100 mg/kg/day based on kidney effects. |
| Intermediate-TermIncidental Oral (1- 6 months) | NOAEL= 100 mg/kg/day | Residential LOC for MOE = 100 Occupational = NA | Chronic/Onco-Rat LOAEL = 100 mg/kg/day based on kidney effects. |
| Dermal(All durations) | Dermal (or oral) study NOAEL=NA | Residential LOC for MOE = NA Occupational LOC for MOE = NA | Quantification not required since 21-Day dermal rabbit NOAEL = 1,000 mg/kg/day and there is no developmental toxicity concern. |
| Inhalation(All durations) | Inhalation (or oral) study NOAEL= 100 mg/kg/day (inhalation absorption rate = 100%) | Residential LOC for MOE = 100 Occupational LOC for MOE = 100 | Chronic/Onco-Rat LOAEL = 100 mg/kg/day based on kidney effects. |
| Cancer (oral, dermal, inhalation) | Classification: “not likely” human carcinogen | | |

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable