

# Considerations for Intraspecies Uncertainty Factor in Occupational Risk Assessment

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# Application of intraspecies UF in occupational risk assessments

- Intraspecies uncertainty factor used to account for human variability
- Consensus that variability is expected in any human population, including workers
  - Worker population typically assumed to be more homogeneous
- Intraspecies UFs applied for workers ranged from 1 to 10
  - 3 has been commonly applied
  - 5 is default value in European Union (EU) REACH guidance (May, 2008)

# Factors influencing magnitude of intraspecies UF for workers

- Type of toxicity
  - General agreement that developmental toxicant be evaluated as for general population
- Study population used as basis for exposure limit
  - Human vs. animal study
  - Small vs. large worker study
  - Relevance of worker population
- Chemical-specific information on sensitivity, variability can increase or decrease factor
- Potential for bystander exposure

# Examples of intraspecies UFs applied for workers

- OSHA:
  - Intraspecies UF = 10, developmental toxicant
  - OSHA (1993) noted that the “healthy worker effect” is not applicable to the developing fetus. There is no reason to assume that fetuses of female workers would be a homogeneous population, nor an intrinsically healthier population. OSHA further stated that “a fetus has two parents who contribute to its genetic identity, and there is no reason to assume that the father of a fetus of a working mother is also a ‘healthy worker’.”

# Worker intraspecies UFs, cont.

- US EPA, Significant New Alternatives Policy program
  - Intraspecies UF = 3 reproductive toxicant
  - UF intended to protect for potential unobserved reproductive medical conditions (*e g* decreased sperm motility, aberrant sperm formation) that are known to exist among otherwise healthy males of working age.

# Worker intraspecies UFs, cont.

- US EPA, Reregistration Eligibility Decision

- Intraspecies UF = 10, various toxic effects
- In response to comments recommending reduction of the UF to 3 for workers:

“Laboratory rodents are homogenous, but humans are not. Even among ‘healthy’ adults, there is considerable variation in chemical susceptibility. ‘Healthy’ adults vary considerably in height and weight. A high percentage of the population has some degree of asthma. Los Angeles residents have a 10% reduction in lung function due to smog. It is not unusual for employees to work when they are sick. A female worker may not know she is pregnant. A worker may be unaware of an underlying condition (e.g. kidney or liver damage, neurologic damage, compromised immune system, etc.) Exposure to alcohol, tobacco, and industrial chemicals can profoundly affect health. An adult who smokes or drinks may be more sensitive to a pesticide than a child. Unless all fumigators are Olympic athletes, there is no basis for reducing the intraspecies UF.”

# Worker intraspecies UFs, cont.

- Health Canada Pest Management Regulatory Agency
  - Intraspecies UF = 10
  - Consider additional factor of 10 to protect pregnant/nursing workers when appropriate
  - “general support for applying the same standard of protection to workers that is applied to the general population, i.e. should consider the completeness of the database with respect to the toxicity to infants and children and pre- and postnatal toxicity concerns in occupational risk assessment, where appropriate”

# Worker intraspecies UFs, cont.

- Netherlands, Health-Based Occupational Exposure Limits (OELs)
  - Intraspecies UF = 3
  - “The offspring of the worker must be regarded as a member of the general population. This means that a higher factor must be employed for the intraspecies variation in case embryotoxic or teratogenic effects are starting points of extrapolation.”

# Worker intraspecies UFs, cont.

- Netherlands Health-Based OEL
  - Intraspecies UF = 1, irritant
  - “The committee considered an intraspecies factor not necessary because the population under study consisted of 100 persons.”

# Worker intraspecies UFs, cont.

- European Centre for Ecotoxicology and Toxicology of Chemicals, Occupational Exposure Limits (OELs)
  - Intraspecies UF = 3
  - Similar to 90<sup>th</sup> percentile in analyses of pharmacokinetic parameters in human population; considered sufficiently protective for “more homogeneous” worker population

# Worker intraspecies UFs, cont.

- EU, Acceptable Operator Exposure Levels (AOELs), pesticides
  - Intraspecies UF = 10; protective for operators, workers and bystanders
  - “It is probable that genetics will determine interindividual variability to the same or a greater extent than age, gender or general health status, therefore the default inter-individual variability factor of 10 is applicable to all exposed groups.”
  - “The question of whether or not operators, being a ‘selected’ group, can be considered to be homogeneous and/or less susceptible in comparison with the general population is not resolved. Therefore, it is recommended that the precautionary approach followed at previous peer review meetings of applying a 10-fold factor continues, unless a convincing scientific case can be made to allow a deviation from the default factor. Even if an intraspecies factor of less than 10 could be justified for occupational operators and re-entry workers, it may not be applicable to non-occupational operators (home/garden users) and bystanders which may include infants, children, and unhealthy subjects.”

# Worker intraspecies UFs, cont.

- EU REACH, Derived No Effect Levels (DNELs)
  - Intraspecies UF = 5, systemic and local effects
  - Factor reduced from 10 for the general population to 5 for workers because “this sub population does not cover the very young, the very old, and the very ill.”