Uncertainty Distributions Assigned for POD and Uncertainty Factors

LOAEL to NOAEL

- **Purpose:** Adjusts from LOAEL to NOAEL on a study-specific basis, including uncertainty. Used only if POD is LOAEL. WHO/IPCS (2014) did not attempt to estimate this distribution from historical data because such data largely reflect dose spacing. It was therefore assumed that the reported UF_L reflected a best estimate of this factor. Since choices for this factor typically vary by 3-fold (e.g.,1, 3, or 10), the uncertainty was assigned this value.
- **Value:** Lognormal distribution, P50 = reported value for UF_L, P95/P50 = 3

NOAEL to BMD

- **Purpose:** Adjusts for uncertainty due to use of NOAEL instead of a BMD, based on historical data (i.e., what range of BMD might occur given particular NOAEL). Used only if POD is LOAEL or NOAEL.
- **Value:** Lognormal distribution (from WHO/IPCS 2014)
  - Continuous endpoint, non-developmental study: P50=1/3, P95/P50=4.7
  - Continuous endpoint, developmental study: P50=1/3, P95/P50=7.0
  - Quantal-deterministic endpoint: P50=2/9, P95/P50=5.0
  - Quantal-stochastic endpoint: P50=2/3, P95/P50=4.7

BMD

- **Purpose:** Accounts for uncertainty in the BMD. For quantal-deterministic endpoints, additional adjustment from BMD to ED50. Used only if POD is BMDL.
- **Value:** Lognormal distribution (from WHO/IPCS 2014)
  - If BMDU is reported, P50 = $(BMDL \times BMDU)^{0.5}$ and P95/P50 = $(BMDU/BMDL)^{0.5}$
  - If BMD, but not BMDU, is reported, P50=BMD, P95/P50=BMD/BMDL
  - If neither BMDU nor BMD not reported, P50=BMDL $\times$3.0, P95/P50=3.0
  - Quantal-deterministic endpoints, if ED50 not reported: BMD at the reported BMR is multiplied by an additional factor of 3.0; additional uncertainty through adding 1.5^2 to $(P95/P50)^2$

Subchronic to chronic

- **Purpose:** Accounts for uncertainty in using a less than chronic study (e.g., subchronic, subacute, etc.) instead of a chronic one. Used only if endpoint is from a less than chronic study
- **Value:** Lognormal distribution (from WHO/IPCS 2014), P50=2, P95/P50=4

Interspecies Body Weight (BW) scaling

- **Purpose:** Accounts for average interspecies differences due to allometry.
- **Value:** Lognormal distribution (from WHO/IPCS 2014)
  - P50=$(BW_{human}/BW_{animal})^{0.3}$, P95/P50=$(BW_{human}/BW_{animal})^{0.04}$
  - BW_{human} = 70 kg, BW_{animal} depends on species, from U.S. EPA (1988)

Interspecies toxicokinetics (TK) and toxicodynamics (TD)

- **Purpose:** Accounts for chemical-specific interspecies TK and TD differences after accounting for interspecies BW scaling.
- **Value:** Lognormal distribution (from WHO/IPCS 2014), P50=1, P95/P50=3.0

Human Variability at I%ile

- **Purpose:** Accounts for variability in sensitivity between the median human and the I%ile human.
- **Value:** Lognormal distribution (from WHO/IPCS 2014), for example, for I=1%, P50=9.7, P95/P50=4.3