

$$HI_{INT} = \sum_{i=1}^n (HQ_i * \sum_{j \neq i}^n f_{ij}) = \sum_{i=1}^n HQ_i$$

Scenarios 1 and 3 are not quite as simple. Because these scenarios are identical except for the direction of the interaction (and hence the WOE weighting factors), only scenario 1 will be examined in detail. If each of the chemicals in the mixture is present in equitoxic amounts, then all the Hazard Quotients are equal. Equation 4-15 yields an adjusted HI five times greater than the HI based on additivity. Note that in this simple case, both  $B_{ij} = 1$  and  $\theta_{ij} = 1$ . Assuming that M is set to 5 (the proposed scenario says each chemical is known to potentiate the other by a factor of 5), then Equation 4-15 reduces to:

$$HI_{INT} = \sum_{i=1}^n \left( HQ_i * \sum_{j \neq i}^n f_{ij} * 5 \right) = 5 * \sum_{i=1}^n HQ_i$$

Thus, if the HI based on additivity were 1, the HI considering interactions would be 5. The counterpart, scenario 3, would give an interaction-based HI of 0.2.

Suppose, however, that the mixture of chemicals 1, 2, and 3 was such that the hazard quotients of each chemical were 0.98, 0.01, and 0.01, respectively. For such a mixture, it would not seem reasonable to assume as great an interaction as in the equitoxic mixture because the relative amounts of chemicals 2 and 3 are much smaller than in the equitoxic mixture. For this 98:1:1 mixture of the three chemicals,  $\theta_{ij} < 1$  for pairs involving chemical 1, resulting in a decrease in the interaction-based HI. For the effect of chemical 2 on chemical 1, using Equation 4-17 gives:

$$\theta_{12} = (0.98 * 0.01)^5 / (0.99/2) = 0.2, \quad f_{12} = 0.01 / (1.00 - 0.98) = 0.5$$

Thus, the partial adjusted hazard quotient for just the effect of chemical 2 on chemical 1 is:

$$HQ_1 * f_{12} * M^{\theta_{12}} = 0.98 * 0.5 * 5^{0.2} = 0.676$$

By symmetry, the effect of chemical 3 on chemical 1 would also be 0.676. Thus, the adjusted hazard quotient for chemical 1 would be 1.35 [=0.676+0.676], a 38% increase over  $HQ_1$ .

By applying the same hazard quotients to the other terms in Equation 4-15, the adjusted hazard quotients for chemicals 2 and 3 can be determined. The adjusted hazard quotient for