Appendix B

Herbicide Mixture Analysis

Herbicide Mixture Analysis

The analysis of herbicide mixtures for site-specific projects would be performed according to the process described below. Under specified conditions, dose addition analysis is believed to provide a reasonable estimate of the cumulative toxicity of chemical mixtures. Standard #16 of the Proposed Action limits mixtures to three herbicides or fewer. When toxicity data is available for surfactants or other inert ingredients, that data should be included in the mixture analysis.

Dose addition is considered most appropriate for mixtures with components that affect the same endpoint by the same mode of action, and are believed to behave similarly with respect to uptake, metabolism, distribution, and elimination (Choudhury et al., 2000). The precise toxic mechanism(s) in fish are not clearly documented for the 10 herbicides contained in the proposed action, but effects to the kidney and liver are typical endpoints in terrestrial wildlife. In addition, it is known that the proposed herbicides have bioconcentration factors that fall within a range that does not indicate bioconcentration risk (all BCF <32), are relatively soluble, and their chemical structure indicates that they are likely to behave similarly in salmonids. Thus, it is believed that the assumption of similar uptake, metabolism, distribution, and elimination is adequately met in fish for dose-addition analysis at low concentrations.

Dose addition analysis is also a reasonable assumption when analyzing mixtures of chemicals with different or unknown toxicity mechanisms, when expected doses will be below known toxic levels (ATSDR, 2004). This is also supported by data from Feron et al. (1995), as cited in EPA (Choudhury et al., 2000), which showed interaction when mixture chemical components were present in concentrations at or near their respective LOAELs. No interaction was observed between chemical components when present at concentrations 1/10 or 1/3 or their respective LOAELs.

The dose addition analysis described in this document is believed to produce conservative estimates of mixture toxicity for several reasons. First, the assumption of dose addition in itself is conservative; the dose addition protocol assumes an additive response for all chemicals in the mixture, when in fact some chemicals may produce independent, non-additive responses. For example, the EPA description of dose addition analysis in Choudhury et al. (2000) states that separate dose addition analyses should be performed for each affected organ. The protocol described here utilizes one hazard index (HI) that includes all herbicides, regardless of toxicity site, potentially resulting in a higher HI value than if mixture components were analyzed in smaller groups by affected organ. In addition, by using a "level of concern" for the HI of 0.1, rather than the 1.0 specified by the EPA (Choudhury et al. 2000), an "uncertainty factor" of 10 is incorporated. This is in addition to the "uncertainty factors" (of 20 for endangered aquatics, and 10 for non-endangered) incorporated into calculation of the individual HQs.

The primary sources of uncertainty in utilizing dose addition analysis in the proposed manner are the lack of mixture analysis studies utilizing more than two chemicals, and the lack of information regarding toxicological mechanisms for the 10 proposed

herbicides in fish. The uncertainty risk, with respect to the lack of information on mixtures involving more than two chemicals, increases with the number of mixture components. Likewise, since little information is available on toxicity mechanisms in fish, uncertainty regarding toxicity mechanism interactions will increase with an increasing number of mixture components. In an effort to minimize these risks, the proposed action states the mixtures will contain no more than three active herbicide ingredients.

The hazard index method of assessing dose addition described below is relatively simple and straightforward. The approach is used or recommended by a number of agencies, including EPA, National Academy of Sciences, National Research Council, and Occupational Health and Safety Administration (ATSDR, 2004). The process essentially consists of calculating a hazard quotient (HQ) for each mixture component, and subsequently summing the HQs to create a HI. If the HI is < 0.1, then an acceptable level of mixture toxicity risk is assumed to be present. A HI would be calculated to assess potential effects to fish, aquatic invertebrates, algae, and aquatic macrophytes. Calculation of the HQ proceeds as described in the USFS contracted herbicide Risk Assessments prepared by Syracuse Environmental Research Associates (and discussed in detail in the effects analysis portion of this document) - the HQ is the ratio of the anticipated level of exposure to a level of exposure associated with a toxicity metric. The lowest available NOAEC (either measured or estimated) is the metric to be used in this analysis. Once the HQ for each component of the mixture has been calculated, then the HQs are summed to produce the HI. The HQ values for the standard exposure scenarios used in the SERA risk assessments are available in the project file. If the HI of the herbicide mixture is ≥ 0.1 for listed aquatic species, then further analysis of the exposure scenarios (calculation of the environmentally expected concentration portion of each HQ) should be conducted to ensure their accuracy. The SERA risk assessments (and other relevant literature sources) should be consulted to determine the degree to which fate and transport factors and site-specific design features may ameliorate herbicide delivery. If the HI remains ≥ 1.0, then the mixture is unacceptable to use under Standard #16.

Literature Cited

ATSDR (Agency for toxic substances and disease registry). 2004. Public Health Assessment Guidance Manual.

Choudhury, H. Cogliano, J., Hertzberg, R., Mukerjee, D., Rice, G., and Teuschler, L. 2000. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures. U.S. Environmental Protection Agency. Washington, DC 20460

Feron, VJ; Groten, JP; Jonker, D; Cassess, FR; van Bladeren, PJ. (1995) Toxicology of chemical mixtures: challenges for today and the future. Toxicology 105:415-427.