APPENDIX A

Summary of Available and Relevant Toxicity Data from Ecological Risk Assessment Literature Review for Bromacil

Appendix A

Summary of Available and Relevant Toxicity Data from Ecological Risk Assessment Literature Review for Bromacil

Introduction

A literature review and ecological data evaluation was conducted on nine herbicides that are currently being used or are proposed for use by the Bureau of Land Management (BLM) for vegetation management on 261 million acres of public lands in the Western U.S., including Alaska. The information gathered from this evaluation will be included along with other collected data to derive toxicity reference values for use in the ecological risk assessment (ERA; ENSR 2005). The ERA was conducted in conjunction with the Vegetation Treatments Programmatic Ecological Impact Statement (PEIS) for the BLM. Scientific papers were gathered during this process to provide data on acute and chronic toxicity of selected herbicides to the non-target species. The review process included consideration of U.S. Fish and Wildlife Service (USFWS) draft literature search guidance. The nine herbicides that were investigated during this evaluation were as follows:

- Diflufenzopyr
- Diquat
- Fluridone
- Imazapic
- Sulfometuron-methyl
- Bromacil
- Chlorsulfuron
- Diuron
- Tebuthiuron

This review process was carried out in three tiers: Tier I – Literature search and preliminary review to select individual manuscripts; Tier II – Screening to determine whether the manuscript is acceptable; and Tier III – Thorough review to obtain data for possible toxicity reference value (TRV) use. This report provides information for bromacil; the other chemicals are discussed in separate reports.

Literature Search Methodology

The literature review process was initiated by conducting a keyword search pertaining to each of the nine chemicals in selected databases. The keyword search for all databases, except for one (Chemical Abstracts/Scifinder Scholar), included the herbicide name but not the commercial name (i.e., some commercial names are common words). The search parameters for Chemical Abstracts consisted of the herbicide name and chemical abstracts service (CAS) registry number. The open literature search was conducted at Colorado State University, Fort Collins, CO. The search period for bromacil was from 1970 (the start of the database) to 2003. The following 12 databases were searched:

- AGRICOLA
- ASFA (Aquatic Sciences and Fisheries Abstracts)
- Biological Sciences
- BIOSIS / Biological Abstracts
- Chemical Abstracts / Scifinder Scholar
- Environmental Science and Pollution Management
- MedLine
- Safety Science and Risk

- Toxline
- Water Resources Abstracts
- Web of Science / Science Citation Index
- Zoological Records

All of the documents obtained in the open literature searches were then evaluated by a Senior Toxicologist to select manuscripts pertaining to the specific objectives of this project (Tier I). Relevant studies were those that were judged, to the extent possible while searching literature databases (i.e., relying on title and abstract, when available), to provide useful data for conducting the ERA. Relevant studies contained the following information at a minimum:

- Acute (mortality vs. survival) or chronic (largely growth or reproduction, although other sublethal data—if available—were also considered potentially relevant) toxicity data for the active ingredient.
- Verifiable numeric endpoint values (e.g., LC_{50}, NOEC) that could be used in the risk characterization process.
- Toxicity data for clinical test species (e.g., mice, rats) and species used for screening non-human impacts (all other mammals, birds, invertebrates, algae, plants).
- Field or mesocosm studies were also included, but only if effects from exposure to the single herbicide in question could be identified and separated from other stressors.

Literature that was excluded as part of this initial literature gathering process included:

- analytical chemistry studies;
- methods papers without specific toxicity data;
- modeling studies that contained no empirically-derived data; and
- reviews or reports that were not primary toxicity data sources (except as a source for obtaining primary literature).

These search criteria enhanced the ability to screen scientific papers for the type of toxicity information needed in the ERA. Hard copies of all manuscripts that met these criteria were then obtained for further evaluation. Once articles were obtained, they were incorporated into a comprehensive management database (EndNote®). There were 243 documents identified from this process and obtained for further consideration. The bibliography list of articles obtained for bromacil is included in this report (Appendix A.1).

Literature Review Methodology

A cursory review (Tier II) was performed on each manuscript after a hard copy was obtained. Exclusion and inclusion criteria to determine acceptability for further review were developed prior to the process in conjunction with the BLM. Manuscripts were excluded that dealt only with the following subjects:

- Human health effects
- Effects on microorganisms: (e.g., fungi, bacteria)
- Genotoxic effects (mutagenic, carcinogenic)
- Bioassays on cells of a whole organism (e.g., rat hepatocytes, rat liver S9)
- Effects on target plants (efficacy testing)
- Non-toxic effects (e.g., fate, transport, leaching, analytical methods)
- Mixtures including herbicides other than the nine being reviewed

In addition, manuscripts that solely included data on marine receptors were originally excluded; however, these data were later included because marine ecosystems could be adjacent to application areas on BLM lands.

Inclusion criteria and rating (on a scale of 1 [weak] to 5 [strong]) of issues that were to be emphasized (requiring a subsequent review step) were as follows:

1. Effects on nontarget receptors related to ERA protocol
2. Chronic, sub-lethal, or reproductive effects that may have adverse effects on populations
3. Effects form inerts, degradates, and metabolites
4. Studies with mixtures that include bromacil and any of the 8 other herbicides (i.e., not containing other herbicides)
5. Indirect effects to food supply or cover

Additional criteria that were used in reviewing papers (reviewers answered 'Yes' or 'No') are listed below:

- Were the corroborating studies described in sufficient detail (i.e., weight of evidence)?
- Did the study have a proper exposure dose, mechanism, and duration?
- Did the test include proper sample size, statistical analysis, and especially statistical endpoints (e.g., NOAEL, EC_{50}) or dose response curves?
- Were proper controls used and were they acceptable?
- Were the data published in a peer-reviewed journal?

Each of the 243 identified papers was scored on the selection criteria listed above, including documentation of the number of test organisms, statistical analysis, proper use, and performance of controls, and the study was classified as either "adequate" on "not adequate".

In Tier III, papers that were found to be acceptable for use were evaluated more thoroughly based on criteria developed with the BLM, and the following information is included as a second review form page for each manuscript (Appendix A.2):

- Author(s).
- Date of publication.
- Title of publication.
- Name of publication.
- Herbicide(s) used in the study.
- Receptor category: 20 g mammal, honey bee, 70 kg herbivore, small bird, large bird, non-target plants (monocot and dicot), warmwater fish, coldwater fish, aquatic invertebrate, aquatic plant, aquatic macrophyte). The specific life history stage was also recorded when available.
- Exposure conditions specifying the formulation, concentration, or amount of active ingredient and medium.
- Effect: Acute or sublethal effect end points of product formulations and breakdown products, and/or their component chemicals, such as: larval and embryonic developmental effects, endocrine disruption, reproductive impairment, changes in behavioral traits such as predator avoidance, feeding/appetite, lethargy or excitement, homing ability, swimming speed, or attraction to or repulsion from the chemicals.
- Toxicity endpoints (e.g., NOAEL, EC_{50}, LC_{50}, or dose response curve).
- Degradates, inerts, if available.
- Ecological conditions of study (e.g., mescosm, static/flow-through, water quality parameters).
- Comments (e.g., mixture effects: additive, synergistic, or antagonistic effect end points of multiple products, other observations).

The Tier II and III reviews for bromacil were conducted by only one senior toxicologist (this is consistent with the scope of work outlined for the review process). In some cases, a second (or third) review of data adequacy took

place when a separate senior toxicologist compiled the Tier III reviews and entered the pertinent information into a master spreadsheet documenting review findings for possible use in TRV derivation. The documents used in this TRV derivation are designated in **bold** in the bibliography (Appendix A.1), and the derivation of TRVs from all available sources is reported in the ERA (ENSR 2005).

Results

Ten papers were discovered in the review of the open literature for bromacil, and of these, seven were reviewed as part of Tier III and incorporated into the spreadsheet for TRV derivation for bromacil (Table 1; Appendix A.3).

TABLE 1

Summary of the Results of the Open Literature Review for Bromacil

Total number of papers obtained for bromacil	10
Total number of papers accepted for Tier II review	7
Total number of papers used in TRV derivation	7

The data collected during this review resulted in toxicity information for algae, macrophytes, aquatic invertebrates (cladoceran), fish (minnow), and small mammals (mouse and rat). Data were available on the chronic toxicity of bromacil to several species including life-cycle studies with a plant (Ratsch et al. 1986), fish (Call et al. 1987) and mouse (Bishop et al. 1997). There were no studies found that examined the toxic effects of degradation products of bromacil or that examined the toxicity of mixtures of bromacil and any of the other eight herbicides. There were two studies that examined the indirect effects of bromacil on food supply via changes in algal density (Schafer et al. 1994) and macrophyte biomass (Ratsch et al. 1986).

References

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APPENDIX A.1

BIBLIOGRAPHY LIST

APPENDIX A.2

TIER II AND III LITERATURE REVIEW FORMS

APPENDIX A.3

SPREADSHEET OF TOXICITY DATA FOR BROMACIL TRV