The Agency does not routinely include, in its risk assessments, an evaluation of mixtures of active ingredients, either those mixtures of multiple active ingredients in product formulations or those in the applicator’s tank. In the case of the product formulations of active ingredients (that is, a registered product containing more than one active ingredient), each active ingredient is subject to an individual risk assessment for regulatory decision regarding the active ingredient on a particular use site. If effects data are available for a formulated product containing more than one active ingredient, they may be used qualitatively or quantitatively.1, 2

Currently, the Agency’s guidance for assessing the potential risk of chemical mixtures is limited to human health applications (USEPA, 2000). However, the guidance includes principles for evaluating mixtures to assess potential interactive effects that are generally applicable. Consistent with EPA’s Overview Document (USEPA 2004), the Agency’s mixture guidance (USEPA 2000) discusses limitations in quantifying the risk of specified mixtures when there is differential degradation, transport and fate of chemical components following environmental release or application. The LD50 values are potentially useful only to the extent that a wild mammal would consume plants or animals immediately after these dietary items were directly sprayed by the product. Increasing time post application, the differential rates of degradation, transport, etc. for the active ingredients in the formulation only permit a qualitative discussion of potential acute risk (USEPA 2004).

As discussed in USEPA (2000) a quantitative component-based evaluation of mixture toxicity requires data of appropriate quality for each component of a mixture. In this mixture evaluation, LD50s with associated 95% confidence intervals are needed for the formulated product. The same quality of data is also required for each component of the mixture.

In the case of chlorpyrifos, only one product (EPA Reg. No. 8329-36) has a definitive product LD50 value with an associated confidence interval. Although there are no 95% confidence intervals for the two active ingredients in this product (chlorpyrifos and permethrin), an evaluation of the available data show that for EPA Reg. No. 8329-36, the product toxicity can be attributed solely to the toxicity of chlorpyrifos. When the product


LD50 (1836 mg/kg) and associated confidence interval (1476-2285 mg/kg) are adjusted for the percent chlorpyrifos (12%); the adjusted LD50 value for the product is (220 mg/kg) is not toxicologically distinct from the LD50 value for the chlorpyrifos technical (223 mg/kg).

Because the active ingredients are not expected to have similar mechanisms of action, metabolites, or toxicokinetic behavior, it is reasonable to conclude that an assumption of dose-addition would be inappropriate. Consequently, an assessment based on the toxicity of chlorpyrifos is the only reasonable approach that employs the available data to address the potential acute risks of the formulated products.
### Pesticide Products Formulated with Chlorpyrifos and Other Pesticide Active Ingredients

#### CHLORPYRIFOS PRODUCTS\(^3,4\)

<table>
<thead>
<tr>
<th>PRODUCT/TRADE NAME</th>
<th>EPA Reg.No.</th>
<th>% Chlorpyrifos</th>
<th>PRODUCT</th>
<th>ADJUSTED FOR ACTIVE INGREDIENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHITMIRE PT 1920 TOTAL RELEASE INSECTICIDE</td>
<td>000499-00405</td>
<td>8</td>
<td>630</td>
<td>No Data</td>
</tr>
<tr>
<td>ULV MOSQUITO MASTER 412</td>
<td>008329-00036</td>
<td>12</td>
<td>1836</td>
<td>1476-2285</td>
</tr>
<tr>
<td>ULV MOSQUITO MASTER 2+6</td>
<td>008329-00073</td>
<td>6</td>
<td>No Data</td>
<td>No Data</td>
</tr>
<tr>
<td>WARRIOR INSECTICIDE CATTLE EAR TAG</td>
<td>039039-00006</td>
<td>10</td>
<td>No Data</td>
<td>No Data</td>
</tr>
<tr>
<td>WOODLIFE F-4WT</td>
<td>060061-00100</td>
<td>0.1</td>
<td>&gt;5000</td>
<td>N/A</td>
</tr>
</tbody>
</table>

\(^3\) From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Registration and Health Effects Divisions.

\(^4\) Chlorpyrifos: Oral LD50= 223 mg/kg

N/A= Not Applicable
List of Citations on Chlorpyrifos Mixtures – studies rejected by ECOTOX due to multiple active ingredients in the test substance.

The citations in this appendix were considered for inclusion in ECOTOX but rejected due to multiple active ingredients. Citations include the ECOTOX Reference number, as well as chemical codes and rejection codes (MIXTURE denotes multiple active ingredients). The query was run in October, 1999 and revised March and June, 2000.


Chapin, J. W. and Thomas, J. S. Soil Insecticide and Fungicide Treatment Effects on Lesser Cornstalk
Notes: Chemical of Concern: CPY. Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: BMY,Captan,DMT,CPY Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CPY,TFT,TBO,ACR,ATZ,PDM,MTL,DMB,CZE Rejection Code: MIXTURE.


(NTIS/OTS0539375).
Chem Codes: Chemical of Concern: DMT,CPY Rejection Code: MIXTURE.


Chem Codes: Chemical of Concern: DMT,CPY,PIRM,DDVP,PFF Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: DZ,CPY,AZ,DS,CBL,MLN,EP Rejection Code: MIXTURE.

Rejection Code: MIXTURE.


Rejection Code: MIXTURE.

Rejection Code: MIXTURE.

Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: PDM,IPN,PEB,CPY,MLX,FMP Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CPY,PRN Rejection Code: MIXTURE.


Chem Codes: Chemical of Concern: CYP,CPY Rejection Code: MIXTURE.


Chem Codes: Chemical of Concern: OMT,BMY,Captan,CPY Rejection Code: MIXTURE.

Lodovici, Maura; Casalini, Chiara; Briani, Carla, and Dolara, Piero. Oxidative liver DNA damage in rats treated with pesticide mixtures. 117, (1): 55-60 CODEN: TXCYAC; ISSN: 0300-483X.
Notes: Chemical of Concern: CPY. Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: ATZ,CYP,MSMA,Hg,CPY Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: MLN,DCTP,ACP,ADC,CPY Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: TDC,CPY,FNV,CYF Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: GYP,CPY,DMT Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CPY Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: Captan,CPYM,THM Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CPY Rejection Code: CAS # UNAVAILABLE/MIXTURE.

Chem Codes: Chemical of Concern: DM,IPD,PIRM,VCZ,DMT,DZ,PHSL,FNT,CPY,CYH,TFZ,FRM Rejection Code: MIXTURE.

Pasquini, Rossana; Scassellati-Sforzolini, Giuseppina; Dolara, Piero; Pampanella, Lucia; Villarini, Milena; Caderni, Giovanna; Fazi, Marilena, and Fatigoni, Cristina. Assay of linuron and a pesticide mixture commonly found in the Italian diet, for promoting activity in rat liver carcinogenesis. 75, (3-4): 170-6 CODEN: PHTOEH; ISSN: 0901-9928.
Notes: Chemical of Concern: CPY. Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CBL,CPY,PMR,PPHD,MLN,ES,HCCH,TBA,MZB, ZIRAM,THM,TPM,ACP Rejection Code: MIXTURE.


Chem Codes: Chemical of Concern: TDF,Captan,CPY,AZ,DOD,CBL,FUZ Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: AZ,CPY Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: PIM,OMT,CPY,ADC,FUZ,CBD Rejection Code: MIXTURE/NO CONC.

Chem Codes: Chemical of Concern: MOM,ES,CPY,BFT Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CPY,HCCH Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: CPY Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: DZ,CPY,CBF Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: ES,CPY,Ziram,FRM,DOD,AZ,MZB Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: DMB,24DXY,CPY,MCPP1,BS Rejection Code: MIXTURE.

Chem Codes: Chemical of Concern: DM,CTN,DMT,CPY,CYH,CYP,FNV Rejection Code: MIXTURE.