



## **US Environmental Protection Agency Office of Pesticide Programs**

### **Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations & Supporting Retrospective Analysis**

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## Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations & Supporting Retrospective Analysis

### 1.0 Introduction

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) authorizes EPA to register pesticides and require supporting studies to meet statutory safety standards as stipulated under 40 Code of Federal Regulations (CFR) Part 158. There is flexibility, however, in implementing Part 158. Additional data can be required (§158.75), alternative approaches can be accepted, and studies can be waived (§158.45). The 2007 NAS report on Toxicity Testing in the 21<sup>st</sup> Century describes a new vision for toxicity testing. EPA's Office of Pesticide Programs has developed a Strategic Direction for New Pesticide Testing and Assessment Approaches (<https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/strategic-vision-adopting-21st-century-science>) which describes OPP's approach to implementing the NAS vision. One component of OPP's strategic vision describes the need for improved approaches to more traditional toxicity tests to minimize the number of animals used while expanding the amount of information obtained. OPP's document on *Guiding Principles for Data Requirements* notes the importance of only requiring data that inform regulatory decision making and avoid unnecessary use of time and resources, data generation costs, and animal testing(<https://www.epa.gov/pesticide-registration/guiding-principles-data-requirements> ). Waiving studies, when such data offer little or no additional scientific information or public health protection, is an important component of the guiding principles for data requirements. OPP staff can focus on the information most relevant to a particular assessment and still ensure there is sufficient information for regulatory decisions that are protective of public health and the environment.

In 2012, OPP published a "*Guidance for Waiving or Bridging of Mammalian Acute Toxicity Tests for Pesticides and Pesticide Products (Acute Oral, Acute Dermal, Acute Inhalation, Primary Eye, Primary Dermal, and Dermal Sensitization)*," which consolidated previously existing guidance on waivers for acute toxicity tests. That 2012 guidance document noted that generally, waivers are considered when data to support a particular endpoint are not relevant to the chemical. Specifically, data related to dermal acute toxicity for conventional, antimicrobial, and biochemical pesticides may be waived if any of the following criteria are met:

- The test material has been placed in Toxicity Category I for primary dermal irritation. Such products will be placed in dermal Toxicity Category I.<sup>1</sup> on the basis of potential dermal effects.
- The test material is corrosive to skin, or has a pH less than 2 or greater than 11.5. (40 CFR 158.500(e)(3); 40 CFR 158.2050(e)(2); 40 CFR 158. 2083(e)(2); 40 CFR 161.340(b)(2). Such products will be placed in dermal Toxicity Category I on the basis of potential dermal effects.
- The product design prevents dermal exposure. Products such as childproof insect baits and rodent bait boxes typically meet these criteria.

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<sup>1</sup> Acute toxicity categories are defined in Table 2.

The current document expands the potential for data waivers for acute dermal studies for formulated pesticide products. Several published studies (Creton et al, 2010; Seidle et al., 2011; Moore et al., 2013)<sup>2</sup> have investigated comparability between oral and dermal acute hazard classifications to assess whether tests for both routes are needed. Together, these studies suggest that dermal and oral acute studies generally classify chemicals into similar categories, but none suit the needs of OPP since they did not evaluate the EPA OPP categorization scheme and primarily evaluated single agents. OPP and the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) have conducted a retrospective analysis of oral and dermal acute lethality studies that fit the regulatory context relevant for OPP. This analysis focuses on formulated pesticide products and considers the EPA pesticide categorization scheme which uses acute study results (see 40 CFR 156.212 and 40 CFR 156.62). The OPP/NICEATM analysis is designed to evaluate the relative consistency of the findings of oral and dermal studies (Section 2.0). ***The agency has used this analysis to support a policy statement in Section 3.0 to waive all acute lethality dermal studies for formulated pesticide products.***

Ecological effects assessments often rely on acute studies for the technical active ingredient and are thus needed to ensure the safety to non-human mammals. As such, *this document focuses only on formulated pesticide product testing*. However, many more acute toxicity studies are submitted to OPP annually for formulated pesticide products than are acute studies on active ingredients. Thus, the potential animal and resource savings from waivers is derived more from formulated pesticide products than single chemical acute toxicity studies.

## **2.0 Retrospective Analysis**

The retrospective analysis conducted by OPP/NICEATM is provided below.

### **2.1 Dataset for Analysis**

The agency developed a dataset of rat acute oral and acute dermal LD<sub>50</sub> studies. The spreadsheet of data used in the analysis is provided in Dermal Data Spreadsheet for 592 Active Pesticide Ingredients.xlsx, and is available in the docket. Inclusion/exclusion criteria are described below.

#### **2.1.1. Selection of Studies**

Identification of Active Ingredients: The active ingredients include conventional pesticides, antimicrobials, and biopesticides across numerous chemical classes and Toxicity Categories. Fumigants and rodenticides were excluded because of their physical forms and the types of exposures that would

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<sup>2</sup> Creton et al. 2010. Acute toxicity testing of chemicals-Opportunities to avoid redundant testing and use alternative approaches. Crit Rev Toxicol 40: 50-83. Seidle et al. 2011. Examining the regulatory value of multi-route mammalian acute systemic toxicity studies. ALTEX 28:95-102. Moore et al. 2013. Can acute dermal systemic toxicity tests be replaced with oral tests? Regul Toxicol Pharmacol 66:30-7.

be anticipated for them. There are 316 active ingredients<sup>3</sup> in the dataset used in the current analysis (Appendix 1).

*Identification of Acute Oral & Dermal Studies:* Searches were conducted from the Office of Pesticide Programs Information Network (OPPIN) database in December 2013-January 2014, which included all available acute studies for formulated pesticide products available for the active ingredients listed in Appendix 1. Information collected from OPPIN included: Master Record Identification (MRID) number, product registration number, Pesticide Chemical (PC) code, CAS number, formulation name, formulation type, registration status, species (and sex), LD<sub>50</sub> value, EPA toxicity category, test acceptability, and study type. This search yielded thousands of studies across different taxa and different routes/toxicities. From this initial search, acute oral and dermal studies were identified. To achieve a dataset that was broadly representative, but manageable in size, the following considerations were used:

1. **Only rat studies were selected.** To reduce uncertainty associated with comparing results across species, non-rat species were eliminated.
2. **Focus on studies from last decade.** With changes to approved inerts and revisions to the acute oral guideline, when data on multiple formulation types were available for a particular active ingredient, the study selection focused on newer studies. This was balanced with the need to have broad representation of formulation type and Toxicity Category.
3. **Because toxicity (particularly absorption) can be influenced by the nature of the exposure, multiple formulation types were selected.** For each active ingredient in the dataset, generally, one oral-dermal study pair was selected for each formulation type available for that active ingredient.
4. **Impregnated materials & microencapsulated formulations were excluded.** These types of products were excluded because they tend to have a unique composition that can affect the rate of release from the product. This uniqueness does not lend itself to an analysis intended for groups of products to be used in a generic approach.
5. **Formulation intermediates were excluded.** Since there will be limited/no exposure to pesticide handlers & applicators to intermediates, these data are not relevant to the analysis.

*From the identified oral & dermal studies, “paired” studies were selected.* ‘Paired’ studies are those that were conducted on the same formulated pesticide product for oral and dermal lethality. This pairing was achieved by matching the registration number and formulated pesticide product name with consideration of PC code and CAS number. Data evaluation records (DERs) were collected for paired studies. From these DERs, the LD<sub>50</sub> and Toxicity Category were entered into the spreadsheet.

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<sup>3</sup> Note: Some active ingredients come in multiple forms such as salts or acids; each form is counted as a separate active ingredient for this document.

### **2.1.2. Characterization of the Dataset**

The dataset of rat acute oral and acute dermal LD<sub>50</sub> studies includes 592 formulated pesticide products, representing 316 active ingredients; all four Toxicity Categories; and 13 different formulated pesticide product types (Table 1). Among the 592 formulations, 272 of these formulations have a single active ingredient, 185 have two, 78 have three, and 58 have four or more.

| <b>Table 1. Formulated pesticide product types in the dataset</b> |               |
|---|---------------|
| <b>Formulation Type</b>   | <b>Number</b> |
| Dust  | 16            |
| Emulsifiable concentrate  | 143           |
| Flowable concentrate  | 64            |
| Granular  | 45            |
| Pellet/tablet   | 7             |
| Pressurized dust  | 1             |
| Pressurized liquid  | 20            |
| Ready to use solution   | 69            |
| Soluble concentrate   | 125           |
| Soluble concentrate/solid   | 8             |
| Water dispersible granule   | 64            |
| Water soluble package   | 14            |
| Wettable powder   | 13            |
| Not available (n/a)   | 4             |

### **1.1 Comparison of Toxicity Category between oral and dermal studies**

As shown in the blue boxes in Table 2 below, for 338 of the 592 formulations, the paired oral and dermal studies provide the same Toxicity Category (blue boxes). For 224 formulations, the oral study provides a lower (i.e., more potent) Category than the dermal study (light orange boxes).

For 30 formulations, the dermal study provides a lower (i.e., more potent) Category than the oral study (tan and purple boxes). Two formulations (tan box) have a Toxicity Category II for dermal and Toxicity Category III for oral (i.e., a more potent Category for dermal compared to oral) and 28 formulations in the dataset have a Toxicity Category III for dermal and a Toxicity Category IV for oral (purple box).

One of the most important uses of acute study data in the registration process for pesticides is in making personal protective equipment (PPE) decisions (such as a requirement to wear gloves when using the product). Therefore, for the 30 formulated pesticide products where the dermal study provides a lower Toxicity Category than the oral study, the agency further investigated additional information used for evaluating dermal worker PPE (see Section 2.3). The Toxicity Categories are also used for hazard labeling, first aid, and precautionary statements (<https://www.epa.gov/pesticide-registration/label-review-manual>).

| Table 2. Results of comparison analysis for oral & dermal formulation acute studies |                                  |                      |                         |                 |
|---|----------------------------------|----------------------|-------------------------|-----------------|
| Rat Dermal Hazard Category (mg/kg)  | Rat Oral Hazard Category (mg/kg) |                      |                         |                 |
|   | EPA I<br>≤50                     | EPA II<br>>50 – ≤500 | EPA III<br>>500 – ≤5000 | EPA IV<br>>5000 |
| EPA I<br>≤200   | 1                                | 0                    | 0                       | 0               |
| EPA II<br>>200 – ≤2000  | 0                                | 2                    | 2                       | 0               |
| EPA III<br>>2000 – ≤5000  | 0                                | 23                   | 133                     | 28              |
| EPA IV<br>>5000   | 0                                | 28                   | 173                     | 203             |
| Total   | 1                                | 53                   | 308                     | 231             |

### ***1.2 Detailed Evaluation of Studies with Lower Dermal Category Compared to Oral***

As noted above, for the 30 formulations (purple & tan boxes in Table 2) which showed a lower Toxicity Category from the dermal study compared to the oral, the agency further investigated what information was used for determining dermal PPE to determine if the dermal hazard study was critical to decisions on required protective equipment.

EPA's Label Review Manual<sup>4</sup> provides information on how acute toxicity information is used in pesticide labeling; Table 3 was extracted from Chapter 10 (Worker Protection Labeling).

<sup>4</sup> <https://www.epa.gov/pesticide-registration/label-review-manual>

| <b>Table 3. Toxicity Category by Route of Exposure of End-Use Product</b> |   |   |  |                                   |
|---|---|---|--|-----------------------------------|
| <b>Route of Exposure</b>  | <b>I<br/>DANGER</b>                                   | <b>II<br/>WARNING</b>                                   | <b>III<br/>CAUTION</b>                 | <b>IV<br/>CAUTION</b>             |
| Dermal Toxicity or Skin Irritation Potential <sup>1</sup>                 | Coveralls worn over long-sleeved shirt and long pants | Coveralls worn over short-sleeved shirt and short pants | Long-sleeved shirt and long pants      | Long-sleeved shirt and long pants |
|   | Socks   | Socks   | Socks                                  | Socks                             |
|   | Chemical-resistant footwear                           | Chemical-resistant footwear                             | Shoes                                  | Shoes                             |
|   | Chemical-resistant Gloves <sup>2</sup>                | Chemical-resistant Gloves <sup>2</sup>                  | Chemical-resistant Gloves <sup>2</sup> | No minimum <sup>4</sup>           |
| Inhalation Toxicity   | Respiratory protection device <sup>3</sup>            | Respiratory protection device <sup>3</sup>              | No minimum <sup>4</sup>                | No minimum <sup>4</sup>           |
| Eye Irritation Potential  | Protective eyewear <sup>5</sup>                       | Protective eyewear <sup>5</sup>                         | No minimum <sup>4</sup>                | No minimum <sup>4</sup>           |

<sup>1</sup> If dermal toxicity and skin irritation toxicity categories are different, PPE shall be determined by the more severe toxicity category of the two. If dermal toxicity or skin irritation is category I or II, refer to Section 2 below to determine if additional PPE is required beyond that specified in Table 1

<sup>2</sup> Refer to Section 3, Table 3 to determine the specific type of chemical-resistant glove.

<sup>3</sup> Refer to Section 4 to determine the specific type of respiratory protection.

<sup>4</sup> Although no minimum PPE is required for these toxicity categories and routes of exposure, the Agency may require PPE on a product-specific basis.

<sup>5</sup> "Protective eyewear" is to be used instead of "goggles" and/or "face shield" and/or "shielded safety glasses" and similar terms to describe eye protection, unless the assessment requires a specific type of eyewear for adequate protection.

Two of the 30 formulations are consumer products for which EPA does not require gloves or any other form of protective clothing (e.g., use of a coverall).

Three of the remaining 28 formulations (FINALE--glufosinate ammonium; SCALA--pyrimethanil; DREXEL SUFFA-8--sulfur) were tested at a limit dose of 4000 mg/kg in the dermal study with no mortalities. The limit dose to achieve Category IV is 5000 mg/kg. For these three formulations, the agency believes that a dermal dose of 4000 mg/kg is close in magnitude to 5000 mg/kg and believes the dermal Category III is an artifact of dose selection, not due to toxicity from dermal exposure below 5000 mg/kg.

As noted in Table 3, the dermal irritation study is also used in pesticide labeling. Of the remaining 25 formulated pesticide products, five of the products have a dermal irritation study that provides a Toxicity Category equal to or lower than the dermal acute Toxicity Category.

For the remaining 20 products, the agency considered the chemical-specific worker protection labeling requirements identified in regulatory assessment documents (Reregistration Eligibility Decision (RED), Registration Review Documents, etc.). In the pesticide labeling process, label reviews consider not only the product specific labeling defined in the acute toxicity review, but also the chemical-specific worker protection labeling defined by the RED/registration review document and the most current regulatory risk assessment document. As such, the acute toxicity review is not the only source of information for pesticide labeling. Table 3 provides the framework for defining personal protective equipment for acute dermal toxicity and dermal irritation studies; however, the framework in Table 3 is supplemented by the

human health risk assessment, which may identify potential concern for worker risk that requires more PPE than identified by the acute toxicity review.

Information on how pesticide handler<sup>5</sup> exposure assessment is conducted to assess worker dermal risk can be found at: <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data>. This exposure assessment approach specifically considers exposure scenarios for specific type(s) of application equipment, formulation type, job function, and level of PPE. Calculated exposure values are then compared to toxicology values (e.g., no-observed adverse effects levels, NOAELs) to assess potential worker risk. These toxicity values are derived from acute or repeat dosing studies in laboratory animals evaluating systemic toxicity, not lethality. Thus, these toxicity values are more robust and appropriate for assessing worker safety than are acute lethality studies. As such, the human health risk assessment provides the agency a means to specifically consider whether or not PPE are required to protect against human health effects.

Of the 20 remaining pesticide products identified with lower dermal toxicity categories than oral, 11 had active ingredients for which the human health risk assessment indicated PPE was required based on risk concerns. Risk assessments for the active ingredient in five formulations indicated no dermal risk at 'baseline' (baseline scenario means that the analysis is conducted assuming long sleeved shirt, pants and socks and shoes (i.e., *without* a consideration for use of gloves)), and risk assessments for the active ingredient in four formulations indicated no dermal hazard based on subchronic dermal toxicity studies—together suggesting that the glove requirement associated with the Toxicity Category III from the acute lethality study over labeled the PPE for these nine.

## ***2.0 Discussion: Implications of Retrospective Analysis on Utility of Acute Dermal Formulated pesticide product Studies***

The overall purpose of this analysis is to address the utility of the acute dermal toxicity study for formulations in pesticide labelling for end use products as described in 40 CFR 156.212<sup>6</sup>. To this end, this analysis includes a large number of formulations (592) and active ingredients (316) across numerous classes representing conventional pesticides, antimicrobials, and biopesticides.

For 57% of the 592 formulations, the results of both oral and dermal acute toxicity studies fall within the same Toxicity Category. For 38% of the formulations, the oral study falls within a lower (i.e., more protective) Toxicity Category. Thus, for 95% of the formulations in the analysis, if the dermal study had not been available and labelling had been based only on the Toxicity Category for the oral acute toxicity study, the PPE requirements on the labelling would have been equally protective or more protective. For the remaining 5%, as noted above, factors other than the dermal acute toxicity may influence PPE labeling requirements. In some cases, dermal irritation studies or risk management decisions based on

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<sup>5</sup> Individuals who are involved in, and potentially can experience exposure during, the pesticide application process in agricultural and non-agricultural settings.

<sup>6</sup> The agency is aware that with respect to pesticide labeling of end use products based on Toxicity Categories, other aspects such as the signal word (40CFR156.64) and precautionary statements (40CFR156.70) may be effects.



other factors (e.g., chemical-specific worker protection labeling defined by the RED/registration review document and the most current regulatory risk assessment, where the risk assessments utilize more robust approaches to worker protection) may result in label PPE requirements more protective than what would otherwise be required based on acute oral toxicity alone. When all these sources of information are considered together, the dermal acute toxicity study for formulations provides little to no added value in regulatory decision making.

### ***3.0 Waiver Guidance.***

The agency believes this retrospective analysis fully supports the conclusion that waivers may be granted for acute dermal toxicity studies for formulated pesticide products. Applicants should submit formal waiver requests as part of their registration application through existing processes<sup>7</sup>. Waiver requests should contain all relevant information to support the waiver (e.g., acute oral LD<sub>50</sub> and dermal irritation study data) and cite this guidance.

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<sup>7</sup> Online waiver guidance may be found at <https://www.epa.gov/pesticide-registration/bridging-or-waiving-data-requirements>

**Appendix 1. List of active ingredients in the retrospective analysis**

|   |
|---|
| 1-Decanaminium, N-decyl-N,N-dimethyl-, chloride   |
| 1-Methylheptyl ester  |
| 1,2-Benzisothiazolin  |
| 1,2-Benzisothiazolin-3-one  |
| 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-2-(Thiocyanomethylthio)benzothiazole |
| 2-Bromo-2-nitro-1,3-propanediol   |
| 2-Bromo-2-nitropropane-1,3-diol   |
| 2-Methyl-3(2H)-isothiazolone  |
| 2-Methyl-4-chlorophenoxyaceticacid  |
| 2-Methyl-4-isothiazolin-3-one   |
| 2-N-Octyl-4-isothiazolin-3-one  |
| 2-Pyridinecarboxylicacid  |
| 2-Pyridinesulfonamide   |
| 2,4-D   |
| 2,4-D, dimethylamine salt   |
| 2,4-Dichlorophenoxy   |
| 3-Iodo-2-propynylButylCarbamate   |
| 3-Iodo-2-propynylester  |
| 4,5-Dichloro-2-n-octyl-3(2H)-isothiazolone  |
| 5-Chloro-2-methyl-3(2H)-isothiazolone   |
| 5-Chloro-2-methyl-4-isothiazolin  |
| 5-Chloro-2-methyl-4-isothiazolin-3-one  |
| AA10717   |
| Abamectin   |
| Acephate  |
| Acequinocyl   |
| Acetamiprid   |
| Acetochlor  |
| Aldicarb  |
| Alkyl dimethyl benzyl ammonium chloride   |
| Alkyl* dimethyl benzyl ammonium chloride *(60%C14, 30%C16, 5%C18, 5%C12)                                      |
| Alkyl* dimethyl benzyl ammonium chloride *(67%C12, 25%C14, 7%C16, 1%C18)                                      |
| Ametoctradin  |
| Amicarbazone  |
| Aminochloropyridazinones  |
| Aminocyclopyrachlor   |
| Aminopyralid  |
| Amitraz   |

|                               |
|-------------------------------|
| Amitrole                      |
| Ammonium bromide              |
| Ammonium soaps of fatty acids |
| Atrazine                      |
| Azoxystrobin                  |
| Benzeneacetate                |
| Bifenazate                    |
| Bifenthrin                    |
| Bispyribac-sodium             |
| Boscalid                      |
| Bromadiolone                  |
| Bromoxynil                    |
| Bronopol                      |
| Buprofezin                    |
| Butoxy polypropylene glycol   |
| Captan                        |
| Carbamic acid                 |
| Carbamic acid, butyl-         |
| Carbendazim                   |
| Carboxin                      |
| Carfentrazone-ethyl           |
| Carobxin                      |
| Chlorantraniliprole           |
| Chlorfenapyr                  |
| Chlorimuron-ethyl             |
| Chlorine dioxide              |
| Chlorothalonil                |
| Chloroxylonol                 |
| Chlorpropham                  |
| Chlorpyrifos                  |
| Chlorpyrifos-methyl           |
| Chlorsulfuron                 |
| Cinnamaldehyde                |
| cis-9-tricosene               |
| Citric acid                   |
| Clopyralid                    |
| Clothianidin                  |
| Copper Carbonate              |
| Copper Pyrethrin              |
| Cupric oxide                  |
| Cuprous oxide                 |
| Cyclanilide                   |

|                                     |
|-------------------------------------|
| Cyfluthrin                          |
| Cyhalofop-butyl                     |
| Cymoxanil                           |
| Cypermethrin                        |
| Cyproconazole                       |
| Cyprodinil                          |
| Cyromazine                          |
| DDVP                                |
| Deltamethrin                        |
| Desmedipham                         |
| Di-potassium phosphite              |
| Dicamba                             |
| Dicamba, dimethylamine salt         |
| Dicamba acid                        |
| Dichlorophenylpyridazinones         |
| Didecyl dimethyl ammonium chloride  |
| Difenconazole                       |
| Diflubenzuron                       |
| Dimethenamid                        |
| Dimethoate                          |
| Dimethomorph                        |
| Dimethylamine                       |
| Dinotefuran                         |
| Diocetyl dimethyl ammonium chloride |
| Diphacinone                         |
| Diquat bromide                      |
| Diquat Dibromide                    |
| Dithiopyr                           |
| Diuron                              |
| Econea                              |
| Emamectin benzoate                  |
| Esfenvalerate                       |
| Ethaneperoxoic acid                 |
| Ethanol                             |
| Ethephon                            |
| Ethofumesate                        |
| Ethyl alcohol                       |
| Ethylhexyl ester                    |
| ETOC                                |
| Etofenprox                          |
| Etoazole                            |
| Famoxadone                          |
| Fenhexamid                          |

|                                 |
|---------------------------------|
| Fenpropathrin                   |
| Fenpropimorph                   |
| Fipronil                        |
| Flazasulfuron                   |
| Flonicamid                      |
| Florasulam                      |
| Fluazifop-p-butyl               |
| Flubendiamide                   |
| Fludioxonil                     |
| Flufenacet                      |
| Flumetsulam                     |
| Flumioxazin                     |
| Fluopicolide                    |
| Fluopyram                       |
| Fluoxastrobin                   |
| Fluroxypyr                      |
| Fluroxypyr 1-methylheptyl ester |
| Fluroxypyr-meptyl acetic acid   |
| Flurprimidol                    |
| Fluthiacet-methyl               |
| Flutriafol                      |
| Fluxapyroxad                    |
| Folpet                          |
| Forchlorfenuron                 |
| Fosthiazate                     |
| Gamma-cyhalothrin               |
| geraniol                        |
| Glufosinate                     |
| Glufosinate-ammonium            |
| Glutaraldehyde                  |
| Glycolic acid                   |
| Glyphosate                      |
| Glyphosate IPA                  |
| Halosulfuron-methyl             |
| Hydrogen peroxide               |
| Hydroprene                      |
| Imazalil                        |
| Imazamox                        |
| Imazethapyr                     |
| Imazosulfuron                   |
| Imidacloprid                    |
| Imiprothrin                     |
| Indaziflam                      |

|   |
|---|
| Indoxacarb  |
| Iodosulfuron-methyl-sodium  |
| IPBC  |
| Ipconazole  |
| Iprodione   |
| Isopropanol   |
| Isoxaben  |
| Isoxaflutole  |
| Kresoxim-methyl   |
| lambda-cyhalothrin  |
| Malathion   |
| Maleic hydrazide  |
| Mancozeb  |
| Mandipropamide  |
| MCPA  |
| MCPA (and salts and esters)   |
| MCPppacid   |
| Mecoprop  |
| Mecoprop-p  |
| Mecoprop-p acid   |
| Mefenoxam   |
| Mepiquat chloride   |
| Mesosulfuron-methyl   |
| Mesotrione  |
| Metaflumizone   |
| Metalaxyl   |
| Metalaxyl-M   |
| Metaldehyde   |
| Metconazole   |
| Methiocarb  |
| Methomyl  |
| Methoxyfenozide   |
| Methylene bis(thiocyanate)  |
| Methyleugenol   |
| Metiram   |
| METRAFENONE   |
| Metribuzin  |
| Metsulfuron   |
| MGK264  |
| Mono-potassium phosphite  |
| Myclobutanil  |
| N-[[[4,6-dimethoxy-2-pyrimidinyl]amino]carbonyl]-3-(2,2,2-trifluoroethoxy)-, monosodium salt, |

|   |
|---|
| monohydrate   |
| n-Alkyl dimethyl benzyl ammonium chloride   |
| N-Alkyl dimethyl ethylbenzyl ammonium chlorides                                   |
| N-Cyclopropyl-N-N'-(1,1-dimethylethyl)-6-(methylthio)- 1,3,5-triazine-2,4-diamine |
| N-Octyl bicycloheptene dicarboximide  |
| Napropamide   |
| Nicosulfuron  |
| NOIT  |
| Nonanoic acid   |
| Noviflumuron  |
| o-Phenylphenol  |
| Octhilinone   |
| Octyldecyldimethylammoniumchloride  |
| ortho-benzyl-para-chlorophenol  |
| Orthosulfamuron   |
| Paclobutrazol   |
| para-tertiary-amyphenol   |
| PBO   |
| Pelargonic acid   |
| Pendimethalin   |
| Penflufen   |
| Penoxsulam  |
| Pentachloronitrobenzene   |
| Penthiopyrad  |
| Permethrin  |
| Phenmedipham  |
| Phosmet   |
| Picloram  |
| Picoxystrobin   |
| Pinoxaden   |
| Piperonyl Butoxide  |
| Potassium phosphate, monobasic  |
| Potassium Salts of Fatty Acids  |
| Potassium silicate  |
| Prallethrin   |
| Prohexadione calcium  |
| Promethryn  |
| Propiconazole   |
| Propoxycarbazone-sodium   |
| Propyzamide   |
| Prothioconazole   |

|   |
|---|
| Pyraclostrobin                            |
| Pyraflufen-ethyl                          |
| Pyrasulfotole Technical                   |
| Pyrazon                                   |
| Pyrethrins                                |
| Pyridine                                  |
| Pyrimethanil                              |
| Pyriproxyfen                              |
| Pyroxasulfone                             |
| Pyroxsulam                                |
| Quinclorac                                |
| Quinoxifen                                |
| Rimsulfuron                               |
| S-bioallethrin                            |
| S-Methoprene                              |
| S-metochlor                               |
| Saflufenacil                              |
| Sedaxane                                  |
| Silver                                    |
| Silver nitrate                            |
| Simazine                                  |
| Sodium bromide                            |
| Sodium chloride                           |
| Sodium dichloro-s-triazinetrione          |
| Sodium percarbonate                       |
| Sodium salt of dicamba                    |
| Spinetoram                                |
| Spinosad                                  |
| Spirodiclofen                             |
| Spirotetramat                             |
| Stabilene                                 |
| sulfentrazone                             |
| Sulfosulfuron                             |
| Sulfur                                    |
| Tau-fluvalinate                           |
| Tebuconazole                              |
| Tembotrione                               |
| Tepraloxydim                              |
| Terbutylazine                             |
| Tetrachloroisophthalonitrile              |
| Tetrachlorvinphos                         |
| Tetraconazole                             |
| Tetrahydro-3,5-dimethyl-1,3,5-thiadiazine |

|                              |
|------------------------------|
| Thiabendazole                |
| Thiamethoxam                 |
| Thidiazuron                  |
| Thiencarbazone-methyl        |
| Thifensulfuron               |
| Thifensulfuron-methyl        |
| Thiophanate-methyl           |
| Thiram                       |
| Thymeoil                     |
| Tolfenpyrad                  |
| Topramezone                  |
| Tralopyril                   |
| Triasulfuron                 |
| Tribenuron Methyl            |
| Trichlorfon                  |
| Triclopyr                    |
| Trifloxystrobin              |
| Trifluralin                  |
| Trinexapac-ethyl             |
| Triticonazole                |
| Zeta-Cypermethrin            |
| Zinc pyriithione             |
| Zinc 2-pyridinethiol-1-oxide |
| Zoxamide                     |