NOTICE TO MANUFACTURERS, FORMULATORS, PRODUCERS AND REGISTRANTS OF PESTICIDE PRODUCTS

ATTENTION: Persons Responsible for Registration of Pesticide Products

SUBJECT: Guidance for Pesticide Registrants on Pesticide Resistance Management Labeling

The Office of Pesticide Programs (OPP) of the United States Environmental Protection Agency (EPA) announces purely voluntary pesticide resistance management labeling guidelines based on mode/target site of action for agricultural uses of herbicides, fungicides, bactericides, insecticides, and acaricides. This document provides acceptable schemes of classification of pesticides according to their mode/target site of action (Appendices I-III), a standard format for showing group identification symbols on the end-use product labels, and examples of resistance management labeling in the use directions. These guidelines are the result of a joint effort of the U.S. and Canada under the North American Free Trade Agreement (NAFTA).

I. Scope

The mode/target site of action symbols and pesticide resistance management labeling statements described in this Pesticide Registration (PR) notice are voluntary. This PR Notice is directed to Registrants of herbicide, fungicide, bactericide, insecticide, and acaricide products that are intended for general agricultural use, including both new products and old (existing) products and is not mandatory. EPA does not expect to require the use of this labeling in any individual licensing proceeding. However, EPA believes that this approach to resistance management is sound and would be highly beneficial to pesticide manufacturers and pesticide users. EPA is hopeful that Registrants will embrace this approach and work with EPA to implement it for all relevant products. EPA believes this approach is an important element of international harmonization.
II. Introduction

The United States Environmental Protection Agency (EPA) and the Pest Management Regulatory Agency of Canada (PMRA) are committed to long-term pest resistance management through pesticide resistance management and alternative pest management strategies. Under the auspices of the North American Free Trade Agreement (NAFTA), the U.S. and Canada have joined together to develop and publish guidelines for voluntary pesticide resistance management labeling for implementation in North America. The development of these guidelines is part of the activities of the Risk Reduction Subcommittee of the NAFTA Technical Working Group on Pesticides. A uniform approach across North America will help reduce the development of pest resistance and support joint registration decisions by providing consistency in resistance management labeling being considered for approval in any or all of the NAFTA countries.

Pesticide resistance is defined for the purposes of this document as an heritable and significant decrease in the sensitivity of a pest population to a pesticide that is shown to reduce the field performance of pesticides. Pests covered by this initiative include insects, mites, weeds, and fungi and bacteria which cause plant disease. The management of pesticide resistance development is an important part of sustainable pest management and this, in conjunction with alternative pest management strategies and Integrated Pest Management (IPM) programs, can make significant contributions to reducing risks to humans and the environment. In support of these goals, the purpose of this document is to provide guidance on resistance management labeling based on mode/target site of action to Registrants. A consequence of this PR notice will be to provide guidance to users about pesticide resistance management strategies based on mode/target site of action.

Pesticides are important pest management tools. Many pesticides have gradually lost their effectiveness due to the development of resistance by pests they once controlled. An important pesticide resistance management strategy is to avoid the repeated use of a particular pesticide, or pesticides that have a similar target site of action as the pest control mechanism in the same field. Mode/target site of action refers to the biochemical mechanism by which the pesticide acts on the pest and should not be interpreted to imply that these chemicals share a common mechanism for purposes of cumulative human health risk assessment under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Federal Food Drug and Cosmetics Act (FFDCA) as amended by the Food Quality and Protection Act of August 3, 1996. One pest control strategy is rotating pesticides and/or using tank mixtures or premixes with different mode/target sites of action. This will delay the onset of resistance,

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1 Common mechanism of toxicity for purposes of cumulative human health risk assessment under FFDCA is described in detail in EPA’s guidance document “Guidance for identifying pesticide chemicals and other substances that have a common mechanism of toxicity” located at http://www.epa.gov/fedrgstr/EPA-PEST/1999/February/Day-05/6055.pdf.
as well as slow the development and subsequent buildup of resistance, without resorting to increased rates and frequency of application, and ultimately, will prolong the useful life of many pesticides.

A resistance management strategy should also consider cross-resistance between pesticides with different modes/target sites of action. Pests may develop cross-resistance to pesticides based on mode/target site of action. This voluntary labeling initiative will provide pesticide users with easy access to important information regarding pesticide mode/target site of action, the cornerstone of most resistance management programs.

To ensure consistency in pesticide grouping and labeling, and to contribute to the management of the pesticide resistance problem, the following guidelines have been developed for agricultural uses of herbicides, fungicides, bactericides, insecticides, and acaricides. The following classification schemes are based on mode/target site of action.

III. Presentation and Format of Resistance Management Information on Pesticide Labels

The use of target site of action symbols and pesticide resistance management statements in this PR Notice is voluntary. Canada and Australia have adopted color schemes that are consistent across target site of action groupings. The Canadian system is voluntary and is analogous to the guidelines presented by EPA. The Australian system is mandatory. If the approach described here is used, the following format and presentation are recommended.

A. Mode/Target Site of Action Grouping and Identification Symbol

Herbicides, fungicides, bactericides, insecticides, and acaricides are separately grouped according to their mode/target site of action by various technical/research committees consisting of representatives of the pesticide industry, researchers, extension specialists and regulatory officials. The Agency based its mode/target site of action groupings on those previously defined by the following industry technical committees: Herbicide Resistance Action Committee (HRAC), Fungicide Resistance Action Committee (FRAC), and Insecticide Resistance Action Committee (IRAC). Information on each of these organizations, the mode/target site of action groups, and recommended resistance management strategies may be found at the following web site: [http://www.gcpf.org](http://www.gcpf.org). Additional guidance for herbicides was provided by the Weed Science Society of America (WSSA). The WSSA and HRAC have sponsored Dr. Ian Heap to set up a web site dedicated to ongoing surveys of herbicide resistance world-wide: [http://www.weedscience.com](http://www.weedscience.com). This web site includes information on identifying mode/target site of action for each herbicide using both the HRAC alphabetic classification system and the WSSA numerical classification system that is currently in use by Canada and will be used by EPA. The target site of action groups plus the identifier numbers for herbicides, fungicides/bactericides, and insecticides/acaricides are located in Appendix I, II and III, respectively.

If used, the target site of action identification symbol should be shown on all end-use product
labels (except products for homeowner/residential uses) in a standard format as outlined below, and should:

1. be located in the upper right quadrant of the front panel surrounded by a black (or suitable color) rectangle, but should not conflict with the required placement of any other front panel element;

2. be in black and on a white background (or other suitable contrasting colors) except the target site of action number(s) which should be white on a black background with a clear white gap (or other suitable contrasting colors) between the target site of action numbers; and

3. include the words “GROUP” and “HERBICIDE” (or “FUNGICIDE” or “INSECTICIDE”) in capital letters, and between these words the number(s) representing the target site of action group(s) of each active ingredient(s). Where a product has two or more active ingredients, and these are represented by two or more sites of action, then two or more appropriate target site of action identifier numbers should be used. For products containing an active ingredient that has multiple sites of action, the letter "M" should be used to represent the target site of action group. Alternatively, if sites of action are known, the label should specify each target site of action by the appropriate number.

Example 1: Product containing one active ingredient represented by one target site of action.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>1</th>
<th>HERBICIDE</th>
</tr>
</thead>
</table>

Example 2: Product containing two or more active ingredients represented by two or more target sites of action.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>HERBICIDES</th>
</tr>
</thead>
</table>

Example 3: Pre-mixture of a fungicide and an insecticide.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>1</th>
<th>FUNGICIDE</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP</td>
<td>2</td>
<td>INSECTICIDE</td>
</tr>
</tbody>
</table>
B. Resistance Management Statements

Use of the resistance management statements described below is voluntary. If used, these statements should be included in the general use directions for end-use products (except products for homeowner/residential uses) for the control of weeds, plant pathogens (diseases), insects and mites under the heading "Resistance Management Recommendations." The section “Resistance Management Recommendations” should be segregated under the “General” portion of the “Use Directions” and preferably boxed to distinguish these statements from mandatory statements on the pesticide label.

The examples of standard resistance management labeling statements listed below provide a general framework of actions that have been noted to be useful in mitigating pest resistance and should be used as appropriate. The development and use of specific resistance management strategies and labeling statements should be developed on the basis of scientific data on a product/class specific basis based on the pesticide product/class, crop, and pest(s) combination and the use history for the pesticide and crop/pest(s) combination. These strategies and labeling statements should be included in any product-specific literature. Efforts should be made to include all appropriate active ingredients and products. In addition to known pest resistance to (a) pesticide(s), appropriate resistance management labeling language should be provided for situations in which pest resistance has not occurred to a given pesticide product or to a given pesticide class, but is part of a good pesticide stewardship program to delay the onset of pest resistance.

1. Herbicides

The following general herbicide resistance management labeling statements may be applicable.

“(Name of product) is a Group (target site of action group number) herbicide. Any weed population may contain or develop plants naturally resistant to (name of product) and other Group (target site of action group number) herbicides. Weed species with acquired resistance to Group (target site of action group number) may eventually dominate the weed population if Group (target site of action group number) herbicides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by (name of product) or other Group (target site of action group number) herbicides.”

“To delay herbicide resistance consider:

- Avoiding the consecutive use of (name of product) or other target site of action Group (target site of action group number) herbicides that
have a similar target site of action, on the same weed species.

- Using tank-mixtures or premixes with herbicides from different target site of action Groups as long as the involved products are all registered for the same use, have different sites of action, and are both effective at the tank mix or prepack rate on the weed(s) of concern.

- Basing herbicide use on a comprehensive IPM program.

- Monitoring treated weed populations for loss of field efficacy.

- Contacting your local extension specialist, certified crop advisors, and/or manufacturer for herbicide resistance management and/or integrated weed management recommendations for specific crops and resistant weed biotypes.”

If available to company, consider including:
- “For further information or to report suspected resistance, you may contact (company representatives) at toll free number: ________ or at Internet site: ______________.”

**Note:** The above are general statements for products containing one or more active ingredients from the same target site of action group, e.g., tank mixes and premix products. For products containing two or more active ingredients from different target site of action groups, the following general statements may be applicable. For example:

“(Name of product) is both a Group (target site of action group number) and a Group (target site of action group number) herbicide. Any weed population may contain or develop plants naturally resistant to Group (target site of action group number) and/or Group (target site of action group number) herbicides. Weed species with acquired resistance to Group (target site of action group number) and/or Group (target site of action group number) herbicides may eventually dominate the weed population if Group (target site of action group number) and/or Group (target site of action group number) herbicides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by (name of product) or other Group (target site of action group number) and/or Group (target site of action group number) herbicides.” [Follow with resistance management
2. **Fungicides and Bactericides**

The following general fungicide/bactericide resistance management labeling statements may be applicable.

“(Name of product) contains a Group (target site of action group number) (fungicide/bactericide). Fungal isolates/bacterial strains with acquired resistance to Group (target site of action group number) may eventually dominate the fungal/bacterial population if Group (target site of action group number) fungicides/bactericides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by (name of product) or other Group (target site of action group number).”

“To delay fungicide/bactericide resistance consider:

- Avoiding the consecutive use of (name of product) or other target site of action Group (target site of action group number) fungicides/bactericides that have a similar target site of action, on the same pathogens.

- Using tank-mixtures or premixes with fungicide/bactericides from different target site of action Groups as long as the involved products are all registered for the same use and are both effective at the tank mix or prepack rate on the pathogen(s) of concern.

- Basing fungicide/bactericide use on a comprehensive IPM program.

- Monitoring treated fungal/bacterial populations for loss of field efficacy.

- Contacting your local extension specialist, certified crop advisors, and/or manufacturer for fungicide/bactericide resistance management and/or IPM recommendations for specific crops and resistant pathogens.”

If available to company, consider including:

- “For further information or to report suspected resistance, you may contact (company representatives) at toll free number: ________ or at Internet site: __________________.”
Note: The above are general statements for products containing one or more active ingredients from the same target site of action group, e.g., tank mixes and premix products. For products containing two or more active ingredients from different target site of action groups, the following general statements may be applicable. For example:

“(Name of product) contains both a Group (target site of action group number) and Group (target site of action group number) fungicide/bactericide. Fungal isolates/bacterial strains with acquired resistance to Group (target site of action group number) and/or Group (target site of action group number) may eventually dominate the fungal/bacterial population if Group (target site of action group number) and/or Group (target site of action group number) fungicides/bactericides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by (name of product) and/or Group (target site of action group number) and/or Group (target site of action group number) fungicides/bactericides.” [Follow with resistance management labeling statements.]

3. Insecticides and Acaricides

The following general insecticide/acaricide resistance management labeling statements may be applicable.

“(Name of product) contains a Group (target site of action group number) insecticide (or acaricide). Insect/mite biotypes with acquired resistance to Group (target site of action group number) may eventually dominate the insect/mite population if Group (target site of action group number) insecticides/acaricides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by (name of product) or other Group (target site of action group number).”

“To delay insecticide (or acaricide) resistance consider:

- Avoiding the consecutive use of (name of product) or other group (target site of action group number) insecticides/acaricides that have a similar target site of action, on the same insect/mite species.

- Using tank-mixtures or premixes with insecticides/acaricides from a
different target site of action Group as long as the involved products are all registered for the same use and have different sites of action.

- Basing insecticide/acaricide use on a comprehensive IPM program.
- Monitoring treated insect/mite populations for loss of field efficacy.
- Contacting your local extension specialist, certified crop advisors, and/or manufacturer for insecticide/acaricide resistance management and/or IPM recommendations for the specific site and resistant pest problems.”

If available to company, consider including:
- “For further information or to report suspected resistance, you may contact (company representatives) at toll free number: ________ or at Internet site: ______________.”

Note: The above are general statements for products containing one or more active ingredients from the same group, e.g., tank mixes and premix products. For products containing two or more active ingredients from different groups, the following general statements may be applicable. For example:

“(Name of product) contains both a Group (target site of action group number) and Group (target site of action group number) insecticides/acaricides. Insect/mite population(s) with acquired resistance to Group (target site of action group number) and/or Group (target site of action group number) may eventually dominate the insect/mite population if Group (target site of action group number) and/or Group (target site of action group number) insecticides/acaricides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by (name of product) or Group (target site of action group number) and/or Group (target site of action group number).” [Follow with resistance management labeling statements.]

4. **Pesticides of Unspecified Groups or Pesticides Without History of Resistance**

Some herbicides, fungicides, bactericides, insecticides, and acaricides have not been assigned to any particular target site of action group, or are not on the lists in this
document because of the lack of clear understanding of their target site of action or the absence of a history of resistance development for the product, e.g., nematicides. Also, in general, herbicides with an unknown target site of action and/or multiple sites of action historically have been less prone to the development of weed resistance.

Registrants are encouraged to establish the appropriate group identifications for their products in consultation with representatives of the pesticide industry, technical working groups such as the WSSA, IRAC, FRAC, HRAC, researchers, extension specialists, crop consultants, and regulatory officials. Appropriate resistance management statements for the product, i.e., herbicides, fungicides, bactericides, insecticides, and/or acaricides, should be developed similar to those described above.

IV. Addition or Changes to Target Site of Action Lists

The pesticide lists will be updated from time to time (approximately annually) to include product names and/or new/revised target site of action classification. This will be done in consultation with WSSA, IRAC, HRAC, and FRAC and other appropriate organizations. Updated lists will be posted on the Office of Pesticide Program’s home page. Hard copies will be made available from the Agency upon request.

V. Implementation

The implementation of this program is purely voluntary by the pesticide industry and is part of a NAFTA labeling harmonization effort on pesticide resistance management with Canada. Canada’s guidelines, Regulatory Directive DIR99-06, for voluntary pesticide resistance management labeling were finalized, October 6, 1999. Canada has set a target date of January 1, 2004 for implementation of its pesticide resistance management labeling guidelines. As part of the Agency’s harmonization efforts on pesticide resistance management labeling with Canada, Registrants are encouraged to add the resistance management grouping symbols and statements to product labels in a similar time frame. Registration and reregistration approval will not be contingent on inclusion of either the resistance management labeling statements or the mode/target site of action classification. However, in view of the importance of resistance management to a long-term pest management strategy, the EPA will evaluate the industry’s implementation of resistance management labeling. The process for how to change labels is described in Section VI.

Resistance management strategies are not requirements for the user, even if the product bears resistance management statements or the mode/target site of action classification. Failure to follow the recommended resistance management strategies on the labeling is not regarded by EPA as a misuse of the product.
VI. How to Change Labels

No registrant will be required to add resistance management statements or appropriate mode/target site of action classification to the product label. Because pesticide resistance management is important, though, EPA encourages Registrants to include both the resistance management statements and the mode/target site of action classification on the product label whenever submitting new or revised labeling to the Agency for registration or reregistration. In order to make it easy for Registrants to add resistance management statements and the target site of action classification to their product labels, and because so many products may be affected, EPA will permit the statements and the target site of action classification to be added by notification.

Registrants who wish to add the appropriate mode/target site of action classification and the resistance management statements may do so by notification to the Agency, provided that:

1. The statements as worded and the appropriate mode/target site of action classification as stated in this notice are used. The resistance management statements and mode/target site of action classification system in this notice have been developed in conjunction with international efforts including industry/academic technical working groups, and Registrants are urged to consider adopting it as written.

OR

2. Similarly worded statements are used. EPA recognizes that Registrants may wish to use wording of their own development or more specific resistance management strategies. Therefore, EPA will permit the addition of similarly worded statement also by notification. Wording may be varied to accommodate the needs of the individual products. However, the following information is considered important to user understanding, and EPA strongly encourages Registrants to include the following points in their statements (in addition to the mode/target site of action Group classification on the front panel):

   a. The product is classified in one or more listed mode/target site of action Groups;

   b. The target pest species may develop natural resistance to the pesticide product and resistant species may become dominant in any given field situation if the product is used repeatedly;

   c. If resistance develops, the product may lose effectiveness in controlling the pest species.

   d. Effective resistance management can delay resistance:

      Avoid repeated or sequential use of products in the same Group;
      Use tank mixes or premixes from a different Group;
Use an effective IPM program; 
Monitor [pest, weed, insect, etc.] populations for loss of efficacy; 
Contact your extension specialist, certified crop consultant, or manufacturer for the latest resistance management information; 
Contact the producer to report loss of efficacy.

EPA emphasizes that the recommended resistance management statements and mode/target site of action Group classification number are not mandatory for users, but provide information and guidance that will benefit users. Registrants are strongly encouraged to use the mode/target site of action classification system and to use a heading such as “Resistance Management Recommendations” and to clearly segregate the information from mandatory use instructions by presentation, such as by boxing the statements. This will ensure that users are fully informed about resistance management, while making clear that compliance is not required.

EPA will work with existing pesticide education efforts that will be used to implement the guidance of this PR notice such as the WSSA extension committee, State Pesticide Applicator Training Programs, federal and state extension programs, IRAC, HRAC, and FRAC to demonstrate how effective resistance management strategies benefit users, the agricultural community, and environmental groups. EPA intends to develop a Fact Sheet about effective resistance management strategies that will provide more extensive information about our efforts.

U.S. Postal Service Deliveries

The following official mailing address must be used for all correspondence or data submissions sent to OPP by mail:

Document Processing Desk (NOTIFICATION), (AMEND), or (APPL), as applicable
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460-0001

Personal/Courier Service Deliveries

The following address must be used for all correspondence or data submissions that are hand-carried or sent by courier service Monday through Friday, from 8:00 AM to 4:30 PM, excluding Federal holidays:

Document Processing Desk (NOTIFICATION), (AMEND), or (APPL), as applicable
Office of Pesticide Programs (7504C)
VII. Scope of Policy

This PR Notice provides guidance to EPA, to pesticide Registrants and applicants, and to the public. As a guidance document, this notice is not binding on either EPA or pesticide Registrants, and EPA may depart from the guidance provided in individual circumstances and without notice. For the matters covered by this particular PR Notice, EPA does not expect to require that any Registrant adopt the labeling set forth here as part of any individual licensing decision or action. However, if any Registrant seeks to use the language set forth here in the manner and circumstances described here, EPA does generally expect to find such language acceptable in any licensing proceeding. However, EPA believes that the approach to resistance management described in this PR Notice is sound and would be highly beneficial to pesticide manufacturers and pesticide users. EPA is hopeful that Registrants will embrace this approach and work with EPA to implement it for all relevant products. EPA believes this approach is an important element of international harmonization.

VIII. For Further Information

If you have general questions about this PR Notice, or about resistance management labeling, please contact:

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Microbial Pesticides Branch
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U.S. Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington D. C. 20460
Telephone: 703-605-0514.
FAX: 703-308-7026
e-mail: matten.sharlene@epa.gov
If you have specific product questions, contact the Labeling Team (703-308-9068/69), the appropriate Product Manager (Registration Division and Antimicrobial Division) or Regulatory Action Leader (Biopesticides and Pollution Prevention Division) for your product.

Marcia E. Mulkey, Director
Office of Pesticide Programs

Attachments:
Appendix I: Herbicide Groups Based on Target Site of Action
Appendix II: Fungicide/Bactericide Groups Based on Activity Group/Target Site of Action
Appendix III: Insecticide and Acaricide Groups Based on Target Site of Action
Date: 11/10/2005


Notice: The following appendices below, that were originally attached to this document have been removed from the document as they are now out of date.

- Appendix I: Herbicide Groups Based on Target Site of Action
- Appendix II: Fungicide/Bactericide Groups Based on Activity Group/Target Site of Action
- Appendix III: Insecticide and Acaricide Groups Based on Target Site of Action

These appendices above are being replaced with direct URLs to mode of action (MOA) lists maintained by the committees listed below. These Web sites are outside of EPA.gov.

- Fungicide Resistance Action Committee (FRAC): http://www.frac.info/frac/index.htm
- Insecticide Resistance Action Committee (IRAC): http://www.irac-online.org/resources/moa.asp