NOTICE TO MANUFACTURERS, PRODUCERS, FORMULATORS, AND REGISTRANTS
OF PESTICIDE PRODUCTS AND DEVICES; U.S. AND STATE DEPARTMENTS OF
AGRICULTURE; COMMODITY AND GROWER GROUPS, GROWERS, AND OTHER
INTERESTED PERSONS

ATTENTION: Persons Responsible for Initial and Continuing Registration of Pesticide Products


1. BRIEF OVERVIEW, PURPOSE AND APPLICABILITY

Pesticides can be used to control a variety of pests, such as insects, weeds, rodents, bacteria, fungi, etc. Over time many pesticides have gradually lost their effectiveness because pests have developed resistance – a significant decrease in sensitivity to a pesticide, which reduces the field performance of these pesticides. The Agency is concerned about resistance issues and believes that managing the development of pesticide-resistance, in conjunction with alternative pest-management strategies and Integrated Pest Management (IPM) programs, is an important part of sustainable pest management. To address the growing issue of resistance and preserve the useful life of pesticides, the Agency is beginning to embark on a more widespread effort and several activities that are aimed at combating and slowing the development of pesticide resistance.

One of these activities is the concurrent but separate release of PR Notice 2016-X, Guidance for Pesticide Registrants on Pesticide Resistance Management Labeling. PR Notice 2016-X, which revises and updates PRN 2001-5, applies to all conventional, agricultural pesticides (i.e., herbicides, fungicides, bactericides, insecticides and acaricides). The updates in PR Notice 2016-X focus on pesticides labels and are aimed at improving information about how pesticide users can minimize and manage pest resistance. PR Notice 2016-X updates PRN 2001-5 with...
users can minimize and manage pest resistance. PR Notice 2016-X updates PRN 2001-5 with the following three categories of changes: (a) provides additional guidance to registrants and a recommended format for resistance-management statements or information to place on labels; (b) includes references to external technical resources for guidance on resistance management; and (c) updates the instructions on how to submit changes to existing labels in order to enhance resistance-management language.

Another activity is the release of this PR Notice (2016-XX). PRN 2016-XX, which only applies to herbicides, communicates the Agency’s current thinking and approach to address herbicide-resistant weeds by providing guidance on labeling, education, training, and stewardship for herbicides undergoing registration review or registration (i.e., new herbicide actives, new uses proposed for use on herbicide-resistant crops, or other case-specific registration actions). It is part of a holistic, proactive approach to slow the development and spread of herbicide-resistant weeds, and prolong the useful lifespan of herbicides and related technology. The Agency is focusing on the more holistic guidance for herbicides first because they are the most widely used agricultural chemicals, no new herbicide mechanism of action has been developed in last 30 years, and herbicide-resistant weeds are rapidly increasing. In the future, the Agency plans to evaluate other types of pesticides (e.g. fungicides, bactericides, insecticides, and acaricides) to determine whether and what guidance may be appropriate for these types of pesticides.

The Agency’s herbicide-resistance management approach in this PR Notice (2016-XX) divides 28 herbicide Mechanisms of Actions (MOAs) into three categories of concern (low, moderate, high) based on the risk of developing herbicide-resistant weeds. This PRN also provides 11 elements that are focused on labeling, education, training, and stewardship strategies. Herbicides with the least concern for developing herbicide-resistant weeds will have the fewest resistance-management elements, and herbicides with the greatest concern will have the most elements. The guidance in this PR Notice is intended to provide herbicide users and registrants useful strategies that, when implemented, will slow herbicide resistance and prolong the useful life of herbicides. The beneficiaries of this PR Notice will be growers of crops that are, or may be, affected by herbicide-resistant weed and the registrants of herbicides.

This PR Notice is applicable to all herbicides regulated by the Agency.

2. **EFFECTIVE DATE**

Effective immediately once finalized.

3. **BACKGROUND**

   A. **HERBICIDE RESISTANCE**

   The development and spread of herbicide-resistant weeds in agriculture is a widespread problem that has the potential to fundamentally change production practices in U.S. agriculture. While herbicide-resistant weeds have been known since the 1950s, the number of species and their
geographical extent has been increasing rapidly in the last decade. As of March 2016, Heap\textsuperscript{1} reports that there are 249 weed species with confirmed herbicide resistance worldwide. There are 80 unique weed species with herbicide resistance in the U.S. Considering that some weed species have developed resistance to more than MOA independently, there are 155 weed species/MOA combinations with confirmed resistance.\textsuperscript{2} These 155 combinations have shown resistance to herbicides with 18 different MOAs. In the U.S., 48 states have reported the presence of herbicide-resistant weeds. And there are over 80 crops and sites (e.g. roadsides, pastures, and railways) with herbicide-resistant weeds. Often only the first few confirmed cases are reported to the International Survey of Herbicide-Resistant Weeds website\textsuperscript{3}, so the prevalence and geographical extent is underestimated.

Some populations of a weed species have confirmed resistance to multiple MOAs. In the U.S., eleven weed species have populations with confirmed resistance to two MOAs, three weed species have populations with confirmed resistance to three MOAs, and three weed species have populations with confirmed resistance to four MOAs. Some of the most troublesome and widespread weed species in U.S. agriculture include redroot pigweed, waterhemp, kochia, ragweed, wild oat, and Palmer amaranth. Cross resistance, where a weed is resistant to multiple MOAs, can be due to an alteration of the target enzyme or in a small number of cases due to enhanced detoxification. Enhanced detoxification can lead to herbicide failures the first time they are used without taking multiple generations to select for the resistance gene.

While the general resistance-management approach described in this PR Notice is applicable to all types of pesticides, the Agency is primarily focusing on herbicides at this time for several reasons. First, herbicides are the most widely used agricultural chemicals. Over 285 million acres were treated on nearly 800,000 farm operations in 2012\textsuperscript{4}. Second, unlike fungicides and insecticides, there have been no new herbicide MOAs developed in the last 30 years. Therefore, users do not have a new MOA to control herbicide-resistant weeds and it’s important to protect the long term efficacy of these chemistries. Third, the number of herbicide-resistant weeds and the affected acreage infested is rapidly increasing. Finally, growers are facing severe economic impacts from herbicide-resistant weeds with up to 100% crop loss in some cases.

For example, in 1998 glyphosate was applied to about 80 million acres (multiple applications are counted separately) and by 2014, the total acreage had increased to nearly 300 million acres. In 2010, glyphosate-resistant weeds infested up to 33 million acres and this number had almost doubled to over 61 million acres infested by 2012.\textsuperscript{5} The USDA reported that in 2010 growers

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\textsuperscript{1} Heap, I. 2016. \textit{op. cit.}


\textsuperscript{3} Heap, I. 2016. \textit{op. cit.}


\textsuperscript{5} Fraser, 2013. \textit{Glyphosate resistant weeds intensifying.} Accessioned online on July 23, 2015 at
with glyphosate-resistant weed problems received over $67 per acre less for corn and over $23 per acre less for soybeans due to increased costs to control weeds. In 2010 and 2011, growers in Georgia spent over $100 million to control glyphosate-resistant Palmer amaranth in cotton fields.

Herbicide resistance in a particular weed species develops over time because of selection pressure placed on the population from the repeated use of an herbicide. A few individuals with natural resistance to the herbicide survive an application of the herbicide. As these individuals reproduce and as each generation is exposed to the herbicide, the proportion of resistant individuals in the population increase and eventually the herbicide-resistant individuals dominate the population. The speed at which this genetic shift occurs depends on the intensity of the selection pressure. Variance in the intensity of selection pressure depends upon from the interaction of characteristics of the chemical, characteristic of the weed species, and characteristics of the crop production system.

Table 1 identifies some of characteristics of herbicide, weed species, and production practices that influence the intensity of selection for the development of herbicide resistance. This table is provided to show several factors that influence selection pressure. Many of these factors cannot be integrated into an herbicide-resistance management approach, because they are inherent to the herbicide, the target weed, and the production practices.

Table 1. Some of the chemical and weed characteristics, and agronomic practices influencing the intensity of selection pressure for herbicide resistance.

<table>
<thead>
<tr>
<th>Lower Selective Pressure</th>
<th>Higher Selective Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbicide MOA</td>
<td></td>
</tr>
<tr>
<td>Multiple-site Mechanism of Action</td>
<td>Single-site Mechanism of Action</td>
</tr>
<tr>
<td>No cross resistance</td>
<td>Cross resistance</td>
</tr>
<tr>
<td>Not persistent</td>
<td>Persistent</td>
</tr>
<tr>
<td>Multi-genic resistance</td>
<td>Monogenic Resistance</td>
</tr>
<tr>
<td>Metabolism difficult</td>
<td>Metabolism relatively easy</td>
</tr>
<tr>
<td>Target Weeds</td>
<td></td>
</tr>
<tr>
<td>Long life cycle</td>
<td>Short life cycle / many generations per year</td>
</tr>
<tr>
<td>Few progeny / limited dispersal</td>
<td>High fecundity / widespread dispersal</td>
</tr>
<tr>
<td>Low inherent genetic variability</td>
<td>High inherent genetic variability</td>
</tr>
<tr>
<td>Metabolic pathway lacking</td>
<td>Pathway for metabolism present</td>
</tr>
<tr>
<td>No cross resistance</td>
<td>Cross resistance already exists</td>
</tr>
<tr>
<td>Low fitness of resistant strains</td>
<td>High fitness of resistant strains</td>
</tr>
</tbody>
</table>

http://stratusresearch.com/blog/glyphosate-resistant-weeds-intensifying


## B. DEFINITIONS

The Agency uses the following definitions for weed resistance in this document: 9

**Confirmed resistance** – The Agency considers a weed biotype to demonstrate confirmed resistance when it meets all of the following criteria10:

- Fulfillment of the Weed Science Society of America (WSSA) definition of resistance and the survey's definition of an herbicide-resistant weed;
- Data confirmation using acceptable scientific protocols;
- The resistance must be heritable;
- Demonstration of practical field impact;
- Identification as a problem weed to species level, not the result of deliberate/artificial selection.

**Herbicide resistance** – The inherited ability of a plant to survive and reproduce following exposure to a dose of herbicide normally lethal to the wild type. Resistance may be naturally occurring or induced by such techniques as genetic engineering or selection of variants produced by tissue culture or mutagenesis.

**Herbicide tolerance** – The inherent ability of a species to survive and reproduce after herbicide treatment. This implies that there was no selection or genetic manipulation to make the plant tolerant; it is naturally tolerant.

**Lack of product performance** – Failure of a product to perform as expected. The lack of performance may result from many conditions such as weather, incorrect timing of application, equipment malfunction, in addition to likely herbicide resistance.

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10 Heap, 2016. *op. cit.*
Likely herbicide resistance – This term is synonymous to “possible resistance”\textsuperscript{11}. Indicators include:
- Failure to control a weed species normally controlled by the herbicide at the dose applied, especially if control is achieved on adjacent weeds;
- A spreading patch of non-controlled plants of a particular weed species; and
- Surviving plants mixed with controlled individuals of the same species.

Mechanism of Action – The biochemical mechanism within a plant that the herbicide detrimentally affects so that the plant succumbs to the herbicide. For example, the inhibition of an enzyme that is vital to plant growth or the inability of the plant to metabolize the herbicide before it has caused damage.\textsuperscript{12} Site of action is sometimes used instead of mechanism of action.

C. REGULATORY BASIS FOR HERBICIDE-RESISTANCE MANAGEMENT

1. Basis and Reporting of Likely Resistance

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provides for federal regulation of pesticide distribution, sale, and use. Section 3(a) of FIFRA requires that pesticides be registered to be sold or distributed in the U.S. To be granted a registration, the applicant must show, among other things, that using the pesticide according to specifications will not generally cause “unreasonable adverse effects on the environment.” FIFRA 2(bb) defines the term "unreasonable adverse effects on the environment" to mean: "(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under section 408 of the Federal Food, Drug, and Cosmetic Act." Herbicide-resistant weeds can reduce the efficacy of an herbicide application thus lowering the overall benefit to a grower which changes the overall balance between risk and benefit of that herbicide.

2. Reporting Under 6(a)(2)

FIFRA also provides the Agency with broad authority to establish or modify data needs for individual pesticide registration actions to achieve statutory and program objectives. Herbicide-resistant weeds (either confirmed or in the early stages of resistance) change the benefits of an herbicide and should be reported.

Section 6(a)(2) of FIFRA requires “if at any time after the registration of a pesticide the registrant has additional factual information regarding unreasonable adverse effects on the environment of the pesticide, the registrant shall submit such information to [EPA].” The Agency has implemented this requirement through regulations at 40 CFR Part 159. In particular,

\textsuperscript{11} Norsworthy et al., 2012. \textit{Ibid.} p. 39.

\textsuperscript{12} Vencill, et al., 2012. \textit{op. cit.}
40 CFR 159.188(c), states:

“(c) Development of pesticide resistance. Information must be submitted concerning substantiation of any incident of a pest having developed resistance to any pesticide (both public health and non-public health) that occurred under conditions of use, application rates and methods specified on the label if either of the following conditions is met:

(1) The survival of the suspected pesticide-resistant pest was significantly higher than that of a known susceptible pest when both the suspected resistant and susceptible pests were treated with the pesticide under controlled conditions.

(2) Biochemical tests or DNA sequencing indicate that the pest is resistant to the pesticide.”

The Agency is here reiterating the requirements for reporting resistance (confirmed and likely resistance as defined above) in accordance with FIFRA 6(a)(2) and 40 CFR Part 159. The identification of any likely resistant weed, defined by meeting the three criteria of likely resistance in Section 3.B., must be reported to the Agency under 6(a)(2).

The schedule for reporting resistance is, described in PR Notice 98-413 as follows:

Reports may be accumulated for three months, and submitted to the Agency by the end of the second month after the accumulation period. The first accumulation period will begin on 1 April of each year.

All information submitted to the Agency under 6(a)(2) is not entitled to confidential treatment, based on Class Determination 99-1, available at 64 FR 70019. Please note that required reporting under 6(a)(2) is separate from the reporting that may be required as part of the herbicide resistant moderate and high categories of concern.

3. Labeling

Another aspect of the registration process is EPA’s review of the pesticide’s labeling. In granting a registration, EPA must determine that the pesticide’s “labeling” complies with the requirements of FIFRA (FIFRA § 3(c)(5)(B)). In Section 2(p)(2)(A), FIFRA defines “labeling” to include all written, printed, or graphic matter accompanying the pesticide at any time. One of FIFRA’s requirements for labeling is that it not be false or misleading in any particular. (See definition of “misbranding” in FIFRA § 2(q)(1)). Should an herbicide label lack information described herein, it could be misleading to users of the pesticide and if so therefore could not be approved by the EPA. Further, for labels that had previously been approved before resistance became a concern, the development of resistance could cause the pesticide’s outdated labeling to be misleading making the product misbranded and unlawful for sale or distribution. See FIFRA §§ 2(q)(1) and 12(a)(1)(E). Flaws or inadequacies in the labeling could lead EPA to cancel the product under

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FIFRA § 6(b).

D. STAKEHOLDER INPUT

The Agency discussed the new herbicide resistance-management approach with stakeholders including registrants, grower groups, crop consultants, retailers, scientists, USDA, and the Weed Science Society of America, which helped inform its decision to provide these recommendations to registrants and other interested persons. The Agency first consulted USDA/APHIS (Animal and Plant Health Inspection Service) and USDA/OPMP (Office of Pest Management Policy) about herbicide-resistance management in July 2013 and presented the draft method to USDA/OPMP in October 2015.

In September 2014, the Weed Science Society of America sponsored an international meeting, the Herbicide Resistance Summit II, hosted by the National Research Council14. This meeting was organized to facilitate a more unified understanding of the herbicide-resistance issues across the country, understanding of differences of viewpoints, and approaches to solutions. The meeting was attended in person or via webinar by participants from approximately 100 locations across the United States, Australia, Canada and Germany, underscoring the significance and widespread nature of this problem and its impact on agricultural productivity. The EPA announced at this meeting that it would take a more proactive role in developing regulatory approaches for managing resistant weeds15. Shortly after this meeting, the Secretary of Agriculture announced USDA's herbicide-resistance actions that were developed in collaboration with EPA and are complementary to this strategy16.

In February 2016, the EPA described this herbicide-resistance management strategy at the Regulatory Aspects Section of the WSSA annual meeting, which was held jointly with the Southern Weed Science Society (SWSS). Discussions with various stakeholders at this meeting provided important insight into how herbicide resistance can be managed and most stakeholders were receptive to the overall approach.

Management of herbicide-resistant weeds, both in mitigating established herbicide-resistant weeds, and in slowing or preventing the development of new herbicide-resistant weeds is a complex problem without a simple solution. Coordinated efforts of growers, agricultural

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extension, academic researcher, scientific societies, pesticide registrants, and state and federal agencies are necessary to address this problem.

4. GUIDANCE

EPA’s Office of Pesticide Programs (OPP) is proposing measures for the registrants of herbicides to provide growers and users with detailed information and recommendations to slow the development and spread of herbicide-resistant weeds. This is part of a more holistic, proactive approach recommended by crop consultants, commodity organizations, professional/scientific societies, researchers, and the registrants themselves. OPP’s approach considers the inherent risk of weed resistance developing for a given herbicide as well as the target weeds and the agronomic practices of the registered crops. The approach divides 28 herbicide MOAs into three categories of concern (low, moderate, high) based on the risk of developing herbicide-resistant weeds (see Appendix I). The approach also provides 11 elements (Appendix II) that are focused on labeling, education, training, and stewardship strategies. Situations with the least concern for the development of herbicide-resistant weeds will have the fewest resistance-management elements and the situations with the highest concern will have additional resistance-management elements.

While developing the approach for herbicide-resistance management, the Agency considered a number of ways to identify those situations with the greatest risk of herbicide resistance. One factor was to select those MOAs with the most herbicide-resistant weeds (found in the U.S.) or an MOA that plays an important role in herbicide-resistance management (e.g. inhibitor of glutamine synthetase) (Appendix I). If new, resistant weed species are found, an MOA may move to higher level of concern. A second factor was whether herbicide-resistant crops (genetically modified or conventionally bred) have been implicated in the development and spread of herbicide-resistant weeds. Currently, the majority of commercialized herbicide-resistant crops use MOAs that have many herbicide-resistant weeds. A third factor would be to protect any new or novel MOA. OPP’s resistance-management approach for those herbicides in the highest category captures all of these factors. Two additional factors that were considered and not utilized were specific herbicide-resistant weeds and those crops or sites with the most herbicide-resistant weeds. After considering the potential effects that these two factors could have on registered crops, these factors were not included.

A. LOW CONCERN CATEGORY AND PROPOSED HERBICIDE-RESISTANCE ELEMENTS

The Agency considers currently-registered herbicides that belong to an MOA with no confirmed cases of herbicide-resistant weed in the U.S. to be of low concern of developing herbicide-resistant weeds in the future. The herbicide MOAs that fall into this category can be found in Appendix I-I. There can be several reasons for the lack of confirmed cases such as inherent characteristics of the chemical, limited use in crop-production systems, or use on crops not typically associated with herbicide-resistant weeds (e.g., short-season vegetable production).
Nevertheless, the Agency considers that even these low concern cases present some risk of
developing herbicide-resistant weeds. Therefore, the Agency is proposing to recommend that the
following resistance-management elements (also listed in Appendix II) be added to all herbicide
labels and labeling for the herbicide MOAs listed in Appendix I-1.

1. **The MOA using the WSSA Groupings (as described in PRN 2016-X).** This provides
critical information to growers and crop advisors when developing herbicide programs
and following best management practices for weed resistance. It allows the user to rotate
between effective MOA’s to reduce the buildup of resistant pests.

2. **The seasonal and annual maximum number of applications and amounts for each crop.**
This information is critical to allow the user to know how many applications and amounts
can be applied in order to develop an effective IPM plan for the season and the entire
year.

3. **Inclusion of Best Management Practices (BMPs) for herbicide-resistance management, as
appropriate, or general language from PRN 2016-X.** This element provides the users with
ready information about managing resistance and should be part of the registrant’s
education and stewardship program. Appendix III lists these BMPs for herbicide
resistance.

4. **Statement that scouting should be done both before and after a pesticide application (as
described in PRN 2016-X).** Reminding the user to scout can help insure that the proper
pesticide is applied based on the weed species and growth stage and determine if the
herbicide applied has provided effective control.

**B. MODERATE CONCERN CATEGORY AND PROPOSED HERBICIDE-
RESISTANCE ELEMENTS**

Currently, registered herbicides belonging to MOAs with a few confirmed cases of herbicide-
resistant weeds in the U.S. are considered by EPA to be of moderate concern of developing more
herbicide-resistant weeds in the future. The herbicide MOAs that fall into this category can be
found in Appendix I-2. In addition to the four elements described in Section 4.A above for the
Low Category of Concern, the Agency is proposing to recommend the following elements (also
listed in Appendix II) be added to the relevant herbicide labels:

5. **Label statement defining likely resistance.** This element provides critical information for
the user, and the registrant or their representative, to identify likely resistant weeds and
proactively take action before they become widespread in their fields.

6. **Label statement that the grower should report lack of performance to the registrant or
their representative.** EPA expects that the registrant or their representative will
investigate to determine if the situation meets the criteria of likely resistance. By
reporting and investigating these incidents, cases resulting from likely resistant weeds
may be distinguished from lack of performance from causes (e.g., equipment
malfunction, weather events, etc). This allows early action to be taken to control these
weeds before resistance becomes widespread in their fields. The prevention of the
development of herbicide-resistant weeds should be the first priority of a weed resistance
plan. However, when likely resistant weeds are identified, the highest priority is to achieve control of these weeds over any sampling to confirm herbicide resistance.

7. Separate label table of confirmed resistant weed species with the effective or recommended rates specifically for these weeds. This will allow the users to have a clear list of herbicide-resistant weeds that may be a problem in their fields and provides specific use instructions for their control. The Agency considers this to be an important part of education and stewardship.

8. Registrant reports new cases of likely and confirmed resistance to EPA and users yearly. This will allow all stakeholder access to information about likely and confirmed resistance in a timely manner so they are aware of and can proactively address the problem. The Agency expects yearly reporting of likely and confirmed resistance to be in compliance with 6(a)(2) requirements.

C. HIGH CONCERN CATEGORY AND PROPOSED HERBICIDE-RESISTANCE ELEMENTS

Currently registered herbicides belonging to MOAs with many confirmed cases of herbicide-resistant weed in the U.S. are of high concern of developing additional herbicide-resistant weeds in the future or for the existing herbicide-resistant weeds to spread. Also of high concern are: (1) any new herbicide with a new or novel mechanism of action, and (2) herbicide partner for conventionally bred or GM herbicide-resistant crops. The herbicide MOAs that fall into the high category of concern are listed in Appendix I-3.

In addition to the elements listed in Sections 4.A and 4.B above for the Low and Moderate Category of Concern, the Agency is proposing to recommend the following elements (also listed in Appendix II) for MOAs of high concern:

9. Educational and training materials for users. These materials may include resistance-management plans, remedial-action plans, and other educational and training materials on herbicide resistance and its management. In general, these plans should be easily modifiable to adapt to changing conditions and to account for local situations. The Agency recommends that registrants work with agricultural extension, crop consultants, individual crop associations, the Herbicide Resistance Action Committee, and the U.S. Department of Agriculture in developing these plans.

10. For formulated products containing multiple herbicides that are in different MOA groups, for each herbicide list the weeds controlled and their minimum recommended rate on the label. In general, the purpose of using multiple herbicides in a single product is to increase the spectrum of weeds controlled and not for herbicide-resistance management. Some products may contain one or more active ingredients at less than the optimal rate for control on a given weed species. Without clarification, the user may use a product with multiple herbicides and assume that multiple MOAs are being used for herbicide resistance. This element will allow the user to make informed decisions about the need
for additional control measures. The Agency considers this to an important part of education and stewardship.

11. **Additional case-specific requirements.** EPA and the registrants may identify additional measures that are deemed appropriate to reduce the risk of development and spread of herbicide-resistant weeds during registration review or registration actions. This could include such measures as mandatory crop rotation or time-limited registration among others. These elements may be on the label, the technical use agreement for the seed trait, or as a reporting requirement.

### D. RELATED INFORMATION

The Agency is also issuing a Pesticide Registration Notice, PRN-2016-X, providing guidance to pesticide registrants regarding labels and labelling for pesticide resistance. PRN-2016-X updates and supersedes the guidance provided in PR Notice 2001-5.

### 5. IMPLEMENTATION

OPP is beginning to implement herbicide-resistance measures for existing chemicals during registration review. In registration review, EPA plans to include herbicide-resistance elements in every herbicide proposed decisions and proposed interim decisions and in final decisions and interim decisions. For registration, OPP proposes to implement herbicide-resistance measures for new herbicide active ingredients and new uses of herbicides proposed for use on herbicide-resistant crops, and possibly other case-specific registration actions.

### 6. SCOPE

This PR Notice communicates the Agency’s approach to address herbicide-resistant weeds. While the requirements in FIFRA and agency regulations are binding on EPA and applicants, this Notice is not binding on EPA personnel, pesticide registrants and applicants, or the public. EPA may depart from the guidance where circumstances warrant and without prior notice. Likewise, pesticide applicants may assert that the guidance is not appropriate generally or not applicable to a specific pesticide or decision. Registrants and applicants may propose alternatives to the guidance provided in any application to the Agency.

### 7. PAPERWORK REDUCTION ACT NOTICE

Under the PRA, “burden” means the total time, effort or financial resources expended by persons to generate, maintain, retain or disclose or provide information to or for a Federal agency. The registrant/applicant may incur a burden from the following activities associated with this PR Notice:

1) reading and understanding this PR Notice,
2) incorporating information into labels or making revisions to pesticide product labels consistent with a pesticide’s pest resistance concern category and associated recommended resistance management elements,

3) reporting cases of likely and confirmed resistance, and

4) providing growers with a pesticide resistance management plan and remedial action plan.

The information collection activities associated with the activities described in this PR Notice are already approved by the Office of Management and Budget (OMB) under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 et seq., under several Information Collection Request (ICR) documents.

Reading and understanding this PR Notice is not expected to be a recurring burden for applicants. Similarly, revising product labels with resistance management elements and developing resistance management/remedial action plans are largely one-time activities for each herbicide. As indicated in Section 5, Implementation, these activities are expected to occur as part of the section 3 registration and reevaluation processes. Reporting cases of resistance (activity 3) may be a recurring burden.

The ICR document for the Pesticide Data Call-In Program has been assigned EPA ICR Number 2288.02 and is approved under OMB control number 2070-0174. This ICR captures the burden of activities 1, 2, and 4 above for registrants implementing herbicide resistance measures for registered herbicides at the time the chemical undergoes registration review. Typical activities include reading and understanding relevant PR Notices and submitting appropriate paperwork, including any label changes. The ICR is being amended by the Agency to include the burden for a registrant or consortium of registrants to develop a pesticide resistance management and remedial action plan as part of pesticide registration review. The average annual burden for the development of a plan is an estimated 42.5 hours. EPA estimates respondents will develop an average of 10 plans per year.

The ICR document for the Application for New and Amended Pesticide Registration has been assigned EPA ICR Number 0277.16 and is approved under OMB control number 2070-0060. This ICR captures the burden of activities 1, 2, and 4 above for registrants implementing herbicide resistance measures for new chemicals and uses at the time of registration. The annual average burden for the application process is estimated to be 194 hours for a conventional pesticide registration (see Type A action) to 646 hours for a conventional pesticide documenting reduced risk in comparison to existing alternatives (see Type C action)\(^{17}\). These actions also include over 45,000 hours associated with generating data to support the registrations. The burden associated with the application process includes reading and understanding germane PR Notices and gathering and creating information needed to support a registration, including the label and other labeling and supporting documents. Based on past applications, EPA estimates

\(^{17}\) Type B actions are new products or label amendments, which would not necessitate implementing herbicide resistance management measures.
there are 205 new a.i. and new use applications, of which 167 are for conventional pesticides; the remaining are for antimicrobial pesticides and biopesticides. Of the conventional pesticides, the historical distribution of pesticide types indicates slightly less than half are herbicides. Therefore, EPA estimates that there will be about 78 new herbicide a.i. and new uses. Because several new uses may be requested for a single a.i., EPA estimates fewer than 17 actions per year will involve implementing herbicide resistance measures and only about 10 actions, including four new a.i., will be of a high level of concern such that resistance management and remedial action plans will be part of the burden. Given the relatively few number of actions involving these plans, EPA is not revising the overall average burden associated with 205 new a.i. and new use applications.

The ICR document for Submission of Unreasonable Adverse Effects Information under Section 6(a)(2) has been assigned EPA ICR Number 1204.12 and is approved under OMB control number 2070-0039. This ICR captures the burden associated with activity 3, reporting cases of resistance. The average annual incident reporting burden for a registrant is an estimated 2.37 hours per submission. The paperwork burden consists of processing and reviewing the information about the incident and submitting the report to EPA. Investigation of the incident is not considered paperwork.

8. FOR FURTHER INFORMATION

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

Bill Chism,
Biological and Economic Analysis Division (7503P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460-0001
Telephone: 703-308-8136
E-mail: chism.bill@epa.gov

_____________________________                       Date: _______________________
Jack Housenger, Director
Office of Pesticide Programs
U. S. Environmental Protection Agency
APPENDIX I. Herbicide Mechanisms of Action (MOA) and the Agency’s Level of Concern for Herbicide Resistance

The following tables list the herbicide MOA for each level of concern for herbicide resistance. These tables are current as of March 2016. The Agency plans to make these tables available on the Agency’s website. These tables should be checked periodically to determine if there are changes to the groupings or level of concern categories. The Agency will use the WSSA groupings preferentially.

If new resistant weed species are found, an MOA may move to higher level of concern. There are 234 herbicides listed by the Weed Science Society of America in 28 different MOAs. These tables take the MOA groups as defined by the Weed Science Society of America and the number of resistant weed species in the U.S. from the International Survey of Herbicide-Resistant Weeds which uses the Herbicide Resistance Action Committee (HRAC) MOA Groups. Both the HRAC and the WSSA MOA classification systems are presented because individual herbicides are not grouped similarly between the two systems.

Table I-1. Herbicide Mechanisms of Action of Low Concern for Herbicide Resistance. As of March 2016, there are 32 herbicides in these MOAs without any herbicide-resistant weeds.

<table>
<thead>
<tr>
<th>MOA Classification by WSSA (HRAC)</th>
<th>Mechanism Of Action (MOA) of Low Concern</th>
<th>Resistant Species in U.S. (#)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 (I)</td>
<td>Inhibitor of 7, 8-dihydropteroate synthetase (DHP) (e.g. amitrole)</td>
<td>0</td>
</tr>
<tr>
<td>19 (P)</td>
<td>Inhibitors of indoleacetic acid transport (e.g. naptalam)</td>
<td>0</td>
</tr>
<tr>
<td>20 (L)</td>
<td>Inhibitor of cell wall synthesis site A (e.g. dichlobenil)</td>
<td>0</td>
</tr>
<tr>
<td>21 (L)</td>
<td>Inhibitor of cell wall synthesis site B (e.g. isoxaben)</td>
<td>0</td>
</tr>
<tr>
<td>23 (K2)</td>
<td>Inhibitors of mitosis (e.g. carbetamide)</td>
<td>0</td>
</tr>
<tr>
<td>24 (M)</td>
<td>Membrane disruptors (uncouplers) (e.g. dinoterb)</td>
<td>0</td>
</tr>
<tr>
<td>29 (L)</td>
<td>Inhibitors of cell wall synthesis site C (e.g. indaziflam)</td>
<td>0</td>
</tr>
<tr>
<td>30 (R)</td>
<td>Tyrosine Aminotransferase (e.g. cinmethylin)</td>
<td>0</td>
</tr>
<tr>
<td>NC* (Unknown)</td>
<td>Not Classified (e.g. cacodylic acid, endothall)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Not Classified.

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Table I-2. Herbicide Mechanisms of Action of Moderate Concern for Herbicide Resistance Development. As of March 2016, there are 86 herbicides in these MOAs with 29 total herbicide-resistant weeds in MOAs of Moderate Concern.

<table>
<thead>
<tr>
<th>MOA Classification by WSSA (HRAC)</th>
<th>Mechanism Of Action (MOA) of Moderate Concern</th>
<th>Resistant Species in U.S. (#)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 (K1) Inhibitors of microtubule assembly (e.g. trifluralin)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>8 (N) Inhibitors of lipid synthesis; not ACCase inhibition (plus old Group 16) (e.g. EPTC, bensulide)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>22 (D) Photosystem I electron diverters (e.g. paraquat)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>27 (F2 and Z) Inhibitors of 4-hydroxyphenyl-pyruvatedioxygenase (4-HPPD) and Unknown site of action (e.g. isoxaflutole, mesotrione)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>14 (E) Inhibitor of protoporphyrinogen oxidase (Protox, PPO) (e.g. fomesafen, oxyfluorfen)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>26 (Z) Unknown site of action (e.g. difenzoquat, metham)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>6 (C3) Inhibitors of photosynthesis at photosystem II site B (e.g. bentazon, pyridate)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>12 (F1) Inhibitors of phytoene desaturase (PDS) (e.g. fluridone)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>13 (F3) Inhibitor of 1-deoxy-D-xyulose 5-phosphate synthatase (DOXP synthase) (e.g. clomazone)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>15 (K3) Mitosis Inhibitors (e.g. acetochlor, s-metolachlor)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>11 (F3) Inhibitors of carotenoid biosynthesis (unknown target) (e.g. amitrole)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>28 (F3) Unknown site of action (e.g. MSMA)</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Table I-3. Herbicide Mechanisms of Action of High Concern for Herbicide Resistance Development. As of March 2016, there are 116 herbicides in these MOAs with 126 total herbicide-resistant weeds in MOAs of High Concern.

<table>
<thead>
<tr>
<th>MOA Classification by WSSA (HRAC)</th>
<th>Mechanism Of Action (MOA) of High Concern</th>
<th>Resistant Species in U.S. (#)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (B)</td>
<td>AcetoLactate Synthase (ALS) or Acetohydroxy Acid Synthase (AHAS) inhibitors (e.g. chlorsulfuron, imazaquin)</td>
<td>49</td>
</tr>
<tr>
<td>5 (C1)</td>
<td>Inhibitors of photosynthesis at photosystem II site A (e.g. triazines, uracils)</td>
<td>26</td>
</tr>
<tr>
<td>1 (A)</td>
<td>Acetyl CoA Carboxylase (ACCase) Inhibitors (e.g. fluazifop-p, sethoxydim)</td>
<td>15</td>
</tr>
<tr>
<td>9 (G)</td>
<td>Inhibitor of 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS) (e.g. glyphosate)</td>
<td>16</td>
</tr>
<tr>
<td>7 (C2)</td>
<td>Inhibitors of photosynthesis at photosystem II site A; different binding behavior from group 5 (e.g. ureas and amides)</td>
<td>11</td>
</tr>
<tr>
<td>4 (O)</td>
<td>Synthetic Auxins (e.g. 2,4-D)</td>
<td>8</td>
</tr>
<tr>
<td>10 (H)</td>
<td>Inhibitor of glutamine synthetase (e.g. glufosinate)</td>
<td>1</td>
</tr>
</tbody>
</table>
APPENDIX II. Elements of an herbicide-resistance management and stewardship plan.
Elements 1 through 4 are proposed for MOAs of Low Concern, elements 1 through 8 are proposed for MOAs of Moderate Concern, and elements 1 through 11 are proposed for MOAs of High Concern. Appendix I lists the MOAs that fall into the low, moderate and high categories.

<table>
<thead>
<tr>
<th>Element Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Element 1.</strong> List Mechanism of Action (MOA) Group Number on label.</td>
</tr>
<tr>
<td><strong>Element 2.</strong> List seasonal and annual maximum number of applications and amounts.</td>
</tr>
<tr>
<td><strong>Element 3.</strong> Provide Resistance Management language from PR Notice 2016-X, and/or Best Management Practices language from Weed Science Society of America (WSSA) &amp; Herbicide Resistance Action Committee (HRAC), and/or HRAC proposed guidelines for herbicide labels. Note that BMPs should be appropriate to crop and production system.</td>
</tr>
<tr>
<td><strong>Element 4.</strong> Instruction to user to scout before and after application.</td>
</tr>
<tr>
<td><strong>Element 5.</strong> Provide definition of Likely Resistance.</td>
</tr>
<tr>
<td><strong>Element 6.</strong> Instruction to user to report lack of performance to registrant or their representative.</td>
</tr>
<tr>
<td><strong>Element 7.</strong> List confirmed resistant weeds in a separate table and list recommended rates for these weeds with the table.</td>
</tr>
<tr>
<td><strong>Element 8.</strong> Registrant report new cases of likely and confirmed resistance to EPA and users yearly. This is in addition to any adverse effects reporting.</td>
</tr>
<tr>
<td><strong>Element 9.</strong> Provide growers with:</td>
</tr>
<tr>
<td>• Resistance Management Plan</td>
</tr>
<tr>
<td>• Remedial Action Plan (to control resistant weeds this season or next season)</td>
</tr>
<tr>
<td>• Educational materials on resistance management.</td>
</tr>
<tr>
<td>Plans should be locally developed and easily modified. EPA recommends that registrants work with Extension, Consultants, Crop Groups, HRAC, &amp; USDA.</td>
</tr>
<tr>
<td><strong>Element 10.</strong> For combination products with multiple MOA, list which herbicide is controlling which weed (a 3-way mixture may only have one effective MOA for some problem weeds). List minimum recommended rate if resistance is suspected.</td>
</tr>
<tr>
<td><strong>Element 11.</strong> Any additional specific requirements (e.g. mandatory crop rotation, unique agronomic aspects, additional training, time limited registration, etc.).</td>
</tr>
</tbody>
</table>
APPENDIX III. Best Management Practices for Herbicide-Resistant Weeds (modified from the Herbicide Resistance Action Committee / Weed Science Society of America\textsuperscript{19})

Crop Selection and Cultural Practices:

1. Understand the biology of the weeds present.
2. Use a diversified approach toward weed management focused on preventing weed seed production and reducing the number of weed seeds in the soil seed-bank.
3. Emphasize cultural practices that suppress weeds by using crop competitiveness.
4. Plant into weed-free fields, keep fields as weed-free as possible, and note areas where weeds were a problem in prior seasons.
5. Incorporate additional weed-control practices whenever possible, such as mechanical cultivation, biological management practices, crop rotation, and weed-free crop seeds, as part of an integrated weed-control program.
6. Do not allow weed escapes to produce seeds, roots or tubers.
7. Manage weed seed at harvest and post-harvest to prevent a buildup of the weed seed-bank.
8. Prevent field-to-field and within-field movement of weed seed or vegetative propagules.
9. Thoroughly clean plant residues from equipment before leaving fields.
10. Prevent an influx of weeds into the field by managing field borders.
11. Fields should be scouted before application to ensure herbicides and application rates will be appropriate for the weed species and weed sizes present.
12. Fields should be scouted after application to confirm herbicide effectiveness and to detect weed escapes.
13. If resistance is suspected, treat weed escapes with an alternate mode of action or use non-chemical methods to remove escapes.
14. Avoid outcrossing to weedy relatives, in crops that outcross. Control weedy relatives in surrounding field margins. Research has demonstrated that the pollen can move many feet.

Herbicide Selection:

Use a broad spectrum soil-applied herbicide with a mechanism of action that differs from this product as a foundation in a weed-control program.

1. A broad-spectrum weed-control program should consider all of the weeds present in the field. Weeds should be identified through scouting and field history.
2. Difficult to control weeds may require sequential applications of herbicides with alternative mechanisms of action.
3. Fields with difficult to control weeds should be rotated to crops that allow the use of herbicides with alternative mechanisms of action.
4. Apply full rates of this herbicide for the most difficult to control weed in the field. Applications should be made when weeds are at the correct size to minimize weed escapes.

\textsuperscript{19} The list of best management practices is modified from Norsworthy et al., 2012. \textit{op. cit.}
5. Do not use more than two applications of “this herbicide” or any herbicide with the same mechanism of action within a single growing season unless mixed with another mechanism of action herbicide with overlapping spectrum for the difficult to control weeds.

6. Report any incidence of non-performance of this product against a particular weed species to the registrant or their representative (list contact information here).
there are 205 new a.i. and new use applications, of which 167 are for conventional pesticides; the
remaining are for antimicrobial pesticides and biocides. Of the conventional pesticides, the
historical distribution of pesticide types indicates slightly less than half are herbicides.
Therefore, EPA estimates that there will be about 78 new herbicide a.i. and new uses. Because
several new uses may be requested for a single a.i., EPA estimates fewer than 17 actions per year
will involve implementing herbicide resistance measures and only about 10 actions, including
four new a.i., will be of a high level of concern such that resistance management and remedial
action plans will be part of the burden. Given the relatively few number of actions involving
these plans, EPA is not revising the overall average burden associated with 205 new a.i. and new
use applications.

The ICR document for Submission of Unreasonable Adverse Effects Information under Section
6(a)(2) has been assigned EPA ICR Number 1204.12 and is approved under OMB control
number 2070-0039. This ICR captures the burden associated with activity 3, reporting cases of
resistance. The average annual incident reporting burden for a registrant is an estimated 2.37
hours per submission. The paperwork burden consists of processing and reviewing the
information about the incident and submitting the report to EPA. Investigation of the incident is
not considered paperwork.

8. FOR FURTHER INFORMATION

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

Bill Chism,
Biological and Economic Analysis Division (7503P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460-0001
Telephone: 703-308-8136
E-mail: chism.bill@epa.gov

Date: 5/14/16

Jack Houssen, Director
Office of Pesticide Programs
U.S. Environmental Protection Agency