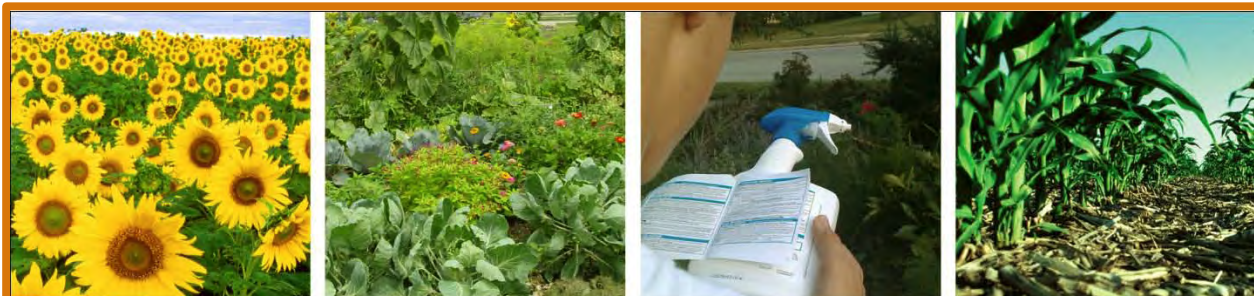


Revised December 2011



# Label Review Manual

## Chapter 4: Types of Label Reviews



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## I. Introduction

Label reviews are conducted for many types of submissions. How a reviewer proceeds with a label review depends on the type of action proposed by the registrant and whether the submission is a new submission (first time submitted to the Agency) or a follow-up to a previous submission.

When a registrant submits information pertaining to several products that are similar in composition or a series of dilutions (products that have the same active ingredient (a.i.) and other ingredients so when diluted they may be considered identical), every effort should be made to route and review these submissions together to ensure consistency of labeling decisions.

Labeling use patterns (sites and pests) are captured for the purpose of registration, re-registration and registration review and are internally available in the Office of Pesticides Program Information Network (OPPIN) database. This will soon become PRISM, the “Pesticide Registration Improvement System”. It is very important that the Agency be able to easily and accurately identify the registered uses for pesticide products. OPPIN/PRISM captures registration numbers, active ingredients, use sites, etc. from approved Section 3 and Section 24(c) labels. OPPIN/PRISM provides the basis for determining what products are currently registered and their use patterns. The registrant must submit and maintain a “Master Label” bearing all registered uses for each registered product (whether or not they use sub-labels or split-labels as described in Chapter 3 IV.B). The regulations allow the reviewer to request the complete text of the proposed amended label at any time. *40 CFR 152.50(e)*.

### Electronic Label Review

OPP has begun to use electronic label review to assist in the review and approval of pesticide labels.

#### ***Q: What is E-Label Review?***

A: Use of a text searchable .pdf label during EPA review of any label submission. The label reviewer will use a computer to:

- a) *compare* the proposed e-label to the last version to quickly identify changes,
- b) *comment* directly on label to indicate any revisions required on the label.

#### ***Q: How are e-labels submitted?***

A: Registrants should submit a text searchable .pdf of the label on a CD-ROM along with the usual paper application. The paperwork should also include a signed affidavit (see website for form) that states that the paper label matches the e-label. Alternately, the entire application can be submitted in electronic XML format on a CD-ROM. E-labels can be submitted for an initial product application, a label amendment, or a label notification. Resubmission of corrected labels per EPA comments can be sent via email directly to the label reviewer.

**Q: What are the technical requirements for e-labels?**

A: See website: <http://www2.epa.gov/pesticide-registration/electronic-submissions-pesticide-applications>

Critical requirements for e-labels:

- a) must be a text searchable .pdf (not image)
- b) use of filename syntax: *reg#.yyyymmdd.anything else.pdf*.
- c) embed the fonts used in label in the .pdf

**Q: What are the benefits to using E-Label Review?**

A: The use of electronic labels will help to increase EPA review efficiency and improve the quality of labeling. The comparison function can quickly identify changes (intentional and unintentional) in the proposed version of a label and can be used to ensure conformance to any standardized text requirements. The commenting function allows the reviewer to pinpoint where changes are needed to the label and provide text which the registrant can copy/paste into a revised label. Using email, rather than paper mail, to exchange comments and revised labels makes the process more efficient and saves paper. Ultimately, e-label review allows the label reviewer and registrant to work interactively to achieve a label stamped "accepted" without any qualifying comments.

## II. Labeling and labeling changes that do not require submission or review

### A. Distributor Labeling

After a registrant has obtained registration for its pesticide product, a second person or company may then distribute or sell the basic registrant's product under the second person or company's name and address. Such distribution and sale is termed "supplemental distribution" and the product is referred to as a "distributor product". Supplemental distribution requires an agreement between the basic registrant and the second company (usually referred to as the "distributor"). The registrant confirms the agreement, both the registrant and the distributor company sign the Notice of Supplemental Distribution of a Registered Pesticide Product form (EPA Form 8570-5) for each distributor product, and the registrant submits the original signed form to the Agency. The distributor does not submit the form. (See [40 CFR 152.132](#) for other requirements). The distributor is considered an agent of the registrant for all purposes under FIFRA and both the distributor and the registrant can be held liable for violations pertaining to the distributor product. [40 CFR 152.132](#). The basic registrant is requested to notify EPA in writing if it terminates its agreement with a distributor (See the [Pesticide Registration Manual](#) (Blue Book)). Distributor labels should *not* be submitted to EPA for review even though distributor products are subject to FIFRA and its implementing regulations. If submitted they will *not* be stamped "Accepted", or even retained in Agency files (See [Chapter 14](#) for more information on distributor labeling).

**B. Minimum Risk Pesticide Exemptions**

*FIFRA section 25(b)* authorizes the Agency to exempt from FIFRA regulation any pesticide which the Agency determines either (1) to be adequately regulated by another Federal agency or (2) to be a character which is unnecessary to be subject to FIFRA. In either case, the pesticide labels do not need to be submitted to the Agency. The Agency has exempted certain minimum risk pesticides by regulations, which are listed at *40 CFR 152.25(f)(1)*, *40 CFR 152.25(f)(3)* and *PR Notice 2000-6* describe additional conditions required to be met in order for the product to be exempt. No false or misleading labeling statements, including those listed in *40 CFR 156.10(a)(5)(i) through (viii)* may appear on an exempt pesticide product. *40 CFR 152.25(f)(3)(iii)*. Only minimum risk inerts from the current updated list may be used to formulate exempt pesticides. *40 CFR 152.25(f)(2)*. The list can be found at <http://www2.epa.gov/minimum-risk-pesticides/inert-ingredients-approved-use-minimum-risk-pesticide-products>.

**C. Non-Notification**

There are changes to labels that can be made without notification to the Agency. See *40 CFR 152.46(b)*. PR Notice 98-10 identifies those label topics that can be amended through “non-notification”, Please note that other PR Notices may permit certain label modifications by notification for specific Agency initiated label changes. Also be aware that the Antimicrobials Division’s notification process is different in some respects from other Divisions. See *PR Notice 98-10* for details relating to notification pursuant to *FIFRA § 3(c)(9)*.

**D. Devices**

A device is defined by Section 2(h) of FIFRA as any instrument or contrivance (other than a firearm) intended for trapping, destroying, repelling, or mitigating any pest or any other form of plant or animal life (other than man and other than a bacterium, virus, or other microorganism on or in living man or living animals) but not including equipment used for the application of pesticides (such as tamper-resistant bait boxes for rodenticides) when sold separately therefrom.

A device is not required to be registered under *FIFRA sec. 3*. The Agency has issued a policy statement concerning its authority and activities with respect to devices, which was published in the Federal Register of November 19, 1976 (*41 FR 51065*).

A device *is* subject, however, to the requirements set forth in:

- (1) *FIFRA sec. 2(q)(1)* and Part 156 of this chapter, with respect to labeling;
- (2) *FIFRA sec. 7* and Part 167 of this chapter, with respect to establishment registration and reporting;
- (3) *FIFRA sec. 8* and Part 169 of this chapter, with respect to books and records;
- (4) *FIFRA sec. 9*, with respect to inspection of establishments;

- (5) *FIFRA sec. 12, 13, and 14*, with respect to violations, enforcement activities, and penalties;
- (6) *FIFRA sec. 17*, with respect to import and export of devices;
- (7) *FIFRA sec. 25(c)(3)*, with respect to child-resistant packaging; and
- (8) *FIFRA sec. 25(c)(4)*, with respect to the Agency's authority to declare devices subject to certain provisions of the Act.

### III. Labeling and Labeling Changes that require review

The following types of submissions require label review:

- ▶ New Active Ingredients and New Uses
- ▶ Technical Grade and Manufacturing Use Products
- ▶ New Products Containing Existing Active Ingredients
- ▶ Labeling Changes by Notification
- ▶ Amendments
- ▶ Identical or Substantially Similar Products
- ▶ Products for which Efficacy Data Must be Submitted
- ▶ Special Local Needs, state FIFRA section 24(c) labels
- ▶ Experimental Use Permits
- ▶ Re-registration

#### A. New Active Ingredients and New Uses

This type of submission involves a new active ingredient (a.i.) that is currently not registered by the Agency as a pesticide or a new use. The registrant must propose the labeling for such products. The labeling should, however, follow the general label format discussed in Chapter 3. The proposed label text may be modified as a result of the science review.

#### B. Technical Grade and Manufacturing Use Products

This type of submission involves a product that is used to manufacture or formulate other pesticides (MP). Normally, a technical grade product is registered concurrently with other manufacturing use products or end use products that can be formulated from it. (See description of these types of products below).

1. A technical grade active ingredient (TGAI) is the pesticide chemical in pure form (with impurities) as it is manufactured by a chemical company prior to being formulated into other pesticide products.
2. An MP contains the technical grade active ingredient and may contain intentionally added inerts. A TGAI product is considered an MP, but not all MPs are technical grade products. (See *40 CFR 158.300*; *40 CFR 161.155 (h) and (k)*). The following statement in item 3 below applies to TGAI and MP products.
3. MP registrants are required to identify in their labeling which uses they are supporting for reformulation into end use products. For example:

*“For formulating only into end-use products for (list the use patterns and sites)”.*

*PR Notice 94-1* recommends specific language. OPP requires that registrants identify at a minimum, the relevant sites, which are listed in the *Pesticide Use Site Index*. See also, Appendix A, part 161 of the CFR (Use Pattern Index for Antimicrobial Pesticides). *40 CFR 156.10(i)(2)(iii)*. Some MPs list very specific use patterns including pests and in some cases site limitations to assist their formulators in preparing their application for registration.

The labeling of the MP source product used to produce the applicant’s product must either:

- ▶ List the uses sought by the applicant *or*
- ▶ Allow the applicant to formulate the MP product for the uses sought if the applicant satisfies the applicable EPA data requirements for such uses (see *PR Notice 94-1*).

If an applicant wishes to use an MP product for a use that requires the applicant to first satisfy EPA data requirements in order to reformulate the MP product, the applicant must comply with EPA data submission/compensation obligations to support that use.

4. The labeling of the technical grade or manufacturing use product should include a listing of the use patterns and sites for the end use products to be formulated from the MP, and will also include a statement such as:

*“For Manufacturing or Formulating Use Only”*

At the registrant’s discretion, one of the two statements listed below may be added to an MP label under “Directions for Use” to permit the reformulation of the product for a specific use or all additional uses supported by a formulator or a user group.

*“This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator, user group, or grower has complied with the U.S. EPA data submission requirements regarding the support of such use(s)”.*

or

“This product may be used to formulate products for any additional uses not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA data submission requirements regarding the support of such uses”. See [PRN 94-1](#).

### C. New Products Containing Existing Active Ingredients

This type of submission involves an application for registration of a product containing an active ingredient (a.i.) that is currently registered for use as a pesticide. Label reviewers should consult label recommendations specified in the latest relevant Agency decision documents. Such documents may include the Reregistration Eligibility Decisions (REDs), Interim Reregistration Eligibility Decisions (IREDs), Biopesticide Registration Action Documents (BRADs), Registration Review Decisions, Registration Review Interim Decisions.

### D. Labeling Changes by Notification

PR Notice 98-10 sets forth what actions can be done through notification and non-notification. Some of these changes can be made simply by “Notification”; which generally involves an Application for Pesticide Registration/Amendment form (EPA Form 8570-1) marked “Notification”, a copy of the labeling with changes highlighted, and a certified statement of the notification, submitted to the Document Processing Desk. [PR Notice 98-10](#). Notifications are processed separately from amendments. The Agency will respond in writing as it is able to do so. If the “notification” documents raise a concern with the label reviewer, he or she may require the registrant to submit an application for amendment when necessary. [40 CFR 152.46\(a\)\(2\)](#). The following modifications are some that can be made by notification. Refer to [PR Notice 98-10](#) for specific information on the circumstances under which the Agency has determined notification is appropriate and for additional topics that can be modified through notification.

- ▶ Adding or changing alternate brand names
- ▶ Changing primary product name
- ▶ Adding or deleting pests (exceptions include, but are not limited to, pests of public health significance, termites or pests under USDA quarantine)
- ▶ Adding indoor, nonfood sites to antimicrobial products
- ▶ Changes in packaging and related labeling statements
- ▶ Use deletions related to Data Call-Ins
- ▶ Storage and disposal statements
- ▶ Use of symbols and graphics (except Skull & Crossbones)

- ▶ Changes in Warranty Statements
- ▶ Addition of certain relevant information to the labeling of an antimicrobial pesticide product regarding product efficacy, product composition, container composition or design, or other characteristics that do not relate to a pesticidal claim or pesticidal activity (see *FIFRA § 3(c)(9)*)

**Please note that registrants may no longer add or change advisory label statements by notification.** (See *PR Notice 2000-5*). Please also note that there is a separate process for antimicrobials (See *FIFRA 3(h)(3)(f)*).

### E. Amendments

#### 1. No Data Review Required

This type of submission involves an application for an amendment to a currently registered pesticide where no data is required for review of the action. An example is an amendment for the addition to the label of a new site or pest, which has been previously approved by the Agency for other products containing the same active ingredient. For products composed of multiple active ingredients, the proposed new site must be previously approved for all of the a.i.'s. For certain pests, such as public health pests, quarantine pests, and structural pests, data are required to demonstrate efficacy.

#### 2. Data Review Required

This type of submission involves an application for amendment of a currently registered pesticide where the request involves the need to review data. For example, the request may involve a new use, a new application rate, or a change in precautionary statements. A data review is also required to be expanded when there is a new public health claim (such as control of a human pathogen or control of mosquitoes) or when the environmental or human exposures are changed (e.g., a residential assessment is needed when turf/lawns are added to a label that has sod grass as a use site). This is an action not previously approved by the Agency, and a data submission and review is necessary. Review of the label will be based upon the conclusions of the data reviews. Generally, the specific reviews will only affect a small portion of the label; the rest of the text should remain unchanged from the originally accepted label.

### F. Identical or Substantially Similar Products

For identical or substantially similar product (formerly known as “me-too”) submissions, the pesticide product and the proposed use must be identical or substantially similar to a currently registered pesticide or may differ only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment. *FIFRA 3(c)(7)(A)*. Identical or substantially similar products may be a “repack”, if the product is manufactured by simply repackaging from another registered product, with no changes to its composition. As a “repack,” a product may not include use sites that are merely similar to use sites on the



label of the product being repackaged. For example, if the product being repackaged includes directions for use on commercial apple orchards, it would not be acceptable for the new product to include directions for use on apple trees in residential areas. The sites must be the same. The label does not necessarily have to have all the uses but the repacked product cannot have more uses on the label than the product from which it is repacked.

The applicant must cite the currently registered pesticide product by EPA registration number. The Agency must first ensure that the two products *are* substantially similar or identical in formulation before the label review can begin.

The label reviewer must also ensure that the new product's use patterns, including any public health claims, are the same as those of the cited product. In addition, if the label under review is a rodenticide, repellent, or antimicrobial bearing a public health claim, any changes in the other intentionally added ingredients must be cleared by the efficacy reviewers to make certain that these changes will not affect the efficacy of the product (i.e., change of bait color, smell, texture, etc.) No changes to the composition of the rodenticide baits or repellents may be accepted without an efficacy review.

### **G. Products for Which Efficacy Data Must Be Submitted**

Efficacy studies document how well pesticide products perform as pest control agents. These studies may include tests to determine the lethality of a formulation against a certain pest species, to document effectiveness under actual use situations, and/or to determine whether claims beyond mere control are supported (i.e., length of a residual effect).

Although the Agency routinely waives the submission (but not the requirement to conduct the study) of efficacy data for most products (except for the types of products listed below), the applicant or registrant is required to have such data on file for each product. EPA reserves the request that the data be submitted at any time, either during initial review or subsequent to registration. The reviewer should be alert to label claims that seem to promise control or performance beyond that of similar products. Examples of products with such claims include herbicides that claim control of weeds in lawns for one full year, and cotton insecticides that claims total season-long elimination of pink bollworm with just one application. When a reviewer identifies questionable or unusual efficacy claims, the PM/team leader should be consulted and, if warranted, the applicant should be told to delete the claims or to submit efficacy data that support the claims. If the reviewer is not sure whether proposed claims are appropriate, the submission should be routed to an efficacy reviewer for assessment.

#### **1. Some Types of Products Requiring Submission of Efficacy Data**

- a. Antimicrobials.** Pesticide products intended to control microorganisms infectious to humans or animals.
- b. Invertebrate Control.** Products intended for use in or on humans (or in or on pets for control of pests which attack humans such as fleas, ticks, mosquitoes, and biting flies) and in premises or in the environment to control pests of sanitary or public

health significance such as those above as well as termites, wasps, scorpions, poisonous spiders, fire ants, cockroaches, centipedes, and bedbugs. See [PR Notice 96-7](#) for important information on termiticide labeling and efficacy data requirements for termiticides.

- c. Rodenticides and Repellents.** Rat and mouse control products; products used to disperse or control birds that pose health threats; products used to control rabies vectors such as bats, skunks, raccoons, foxes, coyotes; products used to control rodents considered to be disease vectors; and products used to control vertebrate animals such as poisonous snakes, dogs, and bears that can injure humans by direct attacks.
- d. New Actives Ingredients with Public Health Uses or New Public Health Uses.** Formulated products that either contain new active ingredients or have proposed use patterns that differ from any previously accepted for a similar formulation, and that have public health uses.
- e. Products to Control Mycotoxin-Producing Organisms.** Products intended to control organisms that produce mycotoxins (organic compounds produced by the fungi which may be highly toxic and carcinogenic to mammals).

## 2. Product Team Structures/Roles Regarding Efficacy Data

Within the Office of Pesticide Programs, product performance (efficacy) data are specific to and evaluated by the three product Divisions: Antimicrobial Division (AD), Registration Division (RD), and Biopesticides and Pollution Prevention Division (BPPD).

The Antimicrobial Division has developed guidance documents called DIS/TSS enclosures for the review of antimicrobial pesticides, including determination of health-related and non-health-related issues and label requirements. Efficacy issues including label review are handled by the Product Science Branch in the Antimicrobial Division. The microbiologists within this branch are responsible for determining whether the product claims are supported by the data and that the directions for use are appropriate for the claims.

Within the Fungicide and Herbicide Branches in RD, submission of efficacy data are generally not required since the target pests seldom affect human health. Because efficacy data is necessary for registration of certain insecticides and rodenticides, technical reviewers within the Insecticide-Rodenticide Branch review the product performance data submitted with these products.

Within the Biopesticides and Pollution Prevention Division (BPPD) science reviewers evaluate efficacy and may consult other efficacy reviewers in other parts of OPP as needed.

**H. Special Local Needs (SLN)**

States have authority under *FIFRA Section 24(c)* to register additional uses for a federally registered pesticide. Such registrations are for distribution and use only within a particular state to meet a “Special Local Need” (“SLN”). Although SLNs can be approved for many different reasons and application sites, most involve use on crops. A certain crop grown within a state may be attacked by a new pest not on a current label, or state officials may expect it to be attacked sometime during the growing season, thereby creating a special pest problem. The pesticide ingredients must have an established tolerance associated with the crop, or be exempted from the requirement of a tolerance for that crop. *FIFRA 24(c)(3)*. Although most 24(c) registrations consist of adding a use to a federally registered product, the state may also register a new end-use product (not federally registered) as a 24(c) registration with a stand-alone label. See *40 CFR 162.152(b)(2)* for information on the types of new end-use products for which a state may issue a 24(c) registration.

SLN registrations are effective unless EPA takes action to disapprove such registrations. If the Agency determines the SLN must be disapproved, EPA must provide notice of the disapproval, in writing, to the state within 90 days of the effective date of the registration. See disapproval process at *40 CFR 162.154*. SLN registrations that are issued without following the procedures laid out in 40 CFR 162.152 may be invalidated by the Agency. *40 CFR 162.156(a)(3)*. In such cases, EPA will attempt to provide this information to the state no later than 90 days from the effective date of the registration.

Special Local Need labels are not stamped “Accepted”, but are reviewed for the required, pertinent information. EPA sends the State an acknowledgement letter. If there is a problem with the SLN (e.g., no established tolerance), a notice of intent to disapprove or invalidate, if appropriate, is sent to the State by the PM/team leader. If something is omitted from the label, the State is informed; however, the SLN is not disapproved. Occasionally, it is necessary to send the SLN for science review depending on the use pattern.

The Section 24(c) review process is described in further detail in OPP’s Standard Operating Procedure #4007.1, February 9, 1996.

**I. Experimental Use Permits**

Experimental Use Permits (EUP) authorize testing (such as greater than ten acres terrestrial; one acre aquatic; or on a case-by-case basis as EPA determines that an EUP is required) of unregistered pesticides or registered pesticides unregistered use. See *40 CFR 172.3* for a description of the types of tests that generally require a permit. The EUP label follows the standard label format, except that the label must also include:

- ▶ The EPA Experimental Use Permit No. *40 CFR 172.6(a)(2)*.
- ▶ The statement: “*Not for sale to any person other than a participant or cooperator of the EPA-approved Experimental Use program*”, *40 CFR 172.6(a)(3)*.
- ▶ The statement “*For Experimental Use Only*”. *40 CFR 172.6(a)(1)*.

- ▶ The name and address of the permittee, producer or registrant. *40 CFR 172.6(a)(5)*. Refer to *40 CFR 172.6* for additional labeling requirements. EUP's are usually issued for a period of one year for a specific number of pounds to be used on a specific acreage, but may be extended for longer periods. *40 CFR 172.5*.

### **J. Re-registration**

The 1988 amendments to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) authorized EPA to conduct a comprehensive pesticide reregistration program in order to completely review the human health and environmental effects of pesticides first registered before November 1, 1984, and make decisions about these pesticides' future use. The goal of the reregistration program is to mitigate risks associated with the use of older pesticides while preserving their benefits. Pesticides that meet current scientific and regulatory standards may be declared "eligible" for reregistration. The results of EPA's reviews are summarized in Reregistration Eligibility Decision (RED) documents. Products undergoing reregistration receive a product-specific data call-in (PDCI) that requires product chemistry and acute toxicity data on that product. Compliance with RED label changes is required during reregistration, and companies have to submit copies of labels with the changes required in the RED with the PDCI responses for review.

## **IV. When a use is deleted**

Use deletions are published in the Federal Register according to the requirements of *FIFRA 6(f)(1)(B)*. When a use is voluntarily deleted from the label, the label is not stamped accepted even if it is found to be acceptable upon review until the use cancellation FR notice comment period has concluded with no substantial comments. Registrants that intend to delete uses must submit a request to voluntarily terminate the use as described in section 6(f)(1) of FIFRA, an application for amended registration and five copies of revised labeling requesting the deletion of uses. See *40 CFR 152.44* and *152.50*. Two copies of a marked-up version of the previously approved labeling highlighting the deletions should be included.