



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

**Response Letter for Extension
of the Exclusive Use
Data Protection Period for
Acetamiprid and Acetamiprid
Technical**

April 6 , 2010



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

John Wrubel
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Subject: Petition for Extension of the Exclusive Use Data Protection
Period for Acetamidrid, Acetamidrid Technical (EPA Reg. 8033-20)

Dear Mr. Wrubel,

The Agency **GRANTS** your petition for an extension of exclusive use data protection for Acetamidrid Technical (EPA Reg. 8033-20) for an **additional three (3) years**. The initial registration of acetamidrid occurred on March 15, 2002. Exclusive use protection for data submitted in support of this registration which complies with 40 CFR 152.83(c) **will expire on March 15, 2015**.

This letter is in response to your petition for extension of the exclusive use data period for acetamidrid dated August 11, 2008 and supplemental information to the petition provided to the Agency on June 2, 2009 and November 3, 2009. You cited FIFRA section 3(c)(1)(F)(ii) as the authority for the Agency to make such a determination.

The 1996 Food Quality Protection Act (FQPA) amendments to FIFRA incorporated provisions under 3(c)(1)(F), the section that provides certain data protection, to provide additional data protection for minor use registrations. FIFRA section 3(c)(1)(F)(ii) sets forth the criteria for extending the period of exclusive use protection. If the Administrator determines that one of four criteria are met, the period of exclusivity can be extended one year for every three minor uses registered within the first seven years of the exclusive use period of the original registration. The maximum number of years the exclusivity period may be extended is three years.

The first step in determining whether data qualifies for an extension of its exclusive use period is to ascertain which data have exclusive use protection. FIFRA section 3(c)(1)(F)(i) and its implementing regulations carefully circumscribe the set of data that are eligible for exclusive use protection. A study entitled to exclusive use protection is defined in 40 CFR 152.83(c).

Pursuant to the 40 CFR 152.83 definition of exclusive use study, the following requirements must be met for a study to be considered an exclusive use study:

- (1) The study pertains to a new active ingredient (new chemical) or new combination of active ingredients (new combination) first registered after September 30, 1978; and
- (2) The study was submitted in support of, or a condition of approval of, the application resulting in the first registration of a product containing such new chemical or new combination (first registration), or an application to amend such registration to add a new use; and
- (3) The study was not submitted to satisfy a data requirement imposed under FIFRA Section 3(c)(2)(B);

Provided that, a study is an exclusive use study only during the 10-year period following the date of first registration.

The following describes our analysis for determining whether the data associated with Acetamiprid Technical (EPA Reg. 8033-20) contains exclusive use data. First, we determine whether there are data associated with this registration that do pertain to, or have been derived from testing on, a new active ingredient. We have determined that there are data associated with this registration that pertain to a new active ingredient.

Second, the data must have been submitted in support of the first registration of the new chemical.¹ The first registration for acetamiprid, Acetamiprid Technical (EPA Reg. 3033-20), was granted on March 15, 2002.

Please note, because exclusive use protection is not available for studies that the Agency requires to maintain registration in effect under FIFRA section 3(c)(2)(B), any such data associated with this registration will not receive exclusive use protection under FIFRA section 3(c)(1)(F)(ii).

Now that the Agency has determined that studies associated with this registration are exclusive use studies², we must determine whether you have met the criteria for extending the exclusive use protection period pursuant to FIFRA section 3(c)(1)(F)(ii), and if so by how many years.

FIFRA section 3(c)(1)(F)(ii) states in pertinent part:

¹ Data are not protected solely because they pertain to the new chemical, but because they are submitted in support of a particular product registration of a new chemical. Thus, data submitted to support an application for the second (and later) registrations, by whatever applicant, of a product containing the same new chemical acquire no exclusive use protection. Additionally, data submitted in support of subsequent amendments to add new uses to the first registration of a product containing the new chemical gain such protection, but the protection is limited to data that pertain solely to the new use. Thus, for example, if the new use is approved after eight years of registration, the data supporting that use would gain exclusive use protection for only two years. See 49 FR 30884, 30889

² This response is general in nature. For purposes of this petition, EPA did not determine which data associated with this registration have/had exclusive use data protection, only that at least some data are entitled to exclusive use data protection.

The period of exclusive data use provided under clause (i) shall be extended 1 additional year for each 3 minor uses registered after the date of enactment of this clause and within 7 years of the commencement of the exclusive use period, up to a total of 3 additional years for all minor uses registered by the Administrator if the Administrator, in consultation with the Secretary of Agriculture, determines that, based on information provided by an applicant for registration or a registrant, that-

- (I) there are insufficient efficacious alternative registered pesticides available for the use; or
- (II) the alternatives to the minor use pesticide pose a greater risk to the environment or human health; or
- (III) the minor use pesticide plays or will play a significant part in managing pest resistance; or
- (IV) the minor use pesticide plays or will play a significant part in an integrated pest management program.

The registration of a pesticide for a minor use on a crop grouping established by the Administrator shall be considered for purposes of this clause 1 minor use for each representative crop for which data are provided in the crop grouping. Any additional exclusive use period under this clause shall be modified as appropriate or terminated if the registrant voluntarily cancels the product or deletes from the registration the minor uses which formed the basis for the extension of the additional exclusive use period or if the Administrator determines that the registrant is not actually marketing the product for such minor uses.

Nisso America Inc. requested 3 years extension of exclusive use data protection for acetamiprid based on registrations of 30 minor crops; broccoli, cabbage, mustard greens, grapefruit, lemon, pear, eggplant, pepper, celery, head lettuce, leaf lettuce, spinach, cantaloupe, cucumber, squash, green beans (snap beans), green peas, lima beans, edible-pod pea, peach, plum, sweet cherry, tart cherry, pecan, blackberry, blueberry, raspberry, strawberry, bulb onion, and green onion. After reviewing the Agency's files we found the following: On March 15, 2002 the following 12 minor crops were registered for acetamiprid: broccoli, cabbage, mustard greens, grapefruit, lemon, pear, eggplant, pepper, celery, head lettuce, leaf lettuce, and spinach. On November 15, 2007 the following 12 minor crops were registered for acetamiprid: cantaloupe, cucumber, squash, green beans (snap beans), green peas, lima beans, edible-pod peas, peach, plum, sweet cherry, tart cherry, and pecan. On January 1, 2008, the following 6 minor crops were registered for acetamiprid: blackberry, blueberry, raspberry, strawberry, bulb onion, and green onion. The initial registration of acetamiprid occurred on March 15, 2002 and as required by the statute, the aforementioned minor uses were all registered within the requisite seven-year period.

Residue data were generated by Nisso America Inc. to support all of the 30 minor crop registrations listed above except strawberries. IR-4 generated data to support the registration of strawberries. Minor crop registrations supported by IR-4 data are eligible to be counted towards minor use registrations for extension of exclusive use, but the data will not receive exclusive use

protection. The Agency has determined that all 30 of the minor uses in the petition qualify towards extension of exclusive use data protection.

In addition to meeting the minor use requirements, FIFRA section 3(c)(1)(F)(ii) requires that one of the criteria I-IV as stated above be met. Nisso America Inc. submitted information for criteria II, III and IV. The Agency reviewed the information submitted by Nisso America Inc. and elected to evaluate for criterion III, “the minor use pesticide plays or will play a significant part in managing pest resistance”. The Agency concluded that criterion III has been met for 12 of the minor uses in the petition; broccoli, cabbage, cantaloupe, celery, cucumbers, eggplant, head lettuce, leaf lettuce, mustard greens, peppers, squash, spinach. The Agency’s evaluation follows.

First, EPA reviewed the acetamiprid labels. We found that acetamiprid is labeled to control a number of resistance-prone insect pests on minor crops including; Sweet potato whitefly (*Bemisia tabaci*), silverleaf whitefly (*Bemisia argentifolii*), greenhouse whiteflies (*Trialeurodes vaporariorum*) and western flower thrips. Nisso’s acetamiprid end use products contain general and site specific resistance management labeling for these pests. With regard to the minor crops in the petition, the following table indicates the minor crops for which acetamiprid has use-specific labeling for control of these resistance-prone insects:

NISSO’S Acetamiprid Labels: Resistance-Prone Pests

Minor Crop	Sweet Potato Whitefly	Silverleaf Whitefly	Greenhouse Whitefly	Western Flower Thrip
Broccoli	x *	x	x	x
Cabbage	x	x	x	x
Mustard Greens	x	x	x	x
Eggplant	x	x	x	x
Pepper	x	x	x	x
Head lettuce	x	x	x	
Leaf lettuce	x	x	x	
Celery	x	x	x	
Spinach	x	x	x	
Cantaloupe	x	x		
Cucumber	x	x		
Squash	x	x		

* x indicates acetamiprid is labeled for control of this pest

Second, EPA reviewed pesticide resistance databases. Michigan State University provides the Arthropod Pesticide Resistance Database (ARPD). This comprehensive public database reports worldwide resistance cases from 1914 to present, when the resistance is first discovered for a specific time and place. The APRD indicates that *Bemisia* whiteflies (i.e., sweet potato and silverleaf whiteflies) have developed resistance to 41 insecticidal active ingredients with 274 confirmed cases of resistance reported worldwide. The APRD database also indicates that greenhouse whiteflies have developed resistance to 19 insecticides and 86 confirmed cases of resistance have been reported worldwide. Western flower thrips (*Frankliniella occidentalis*) are

also prone to developing resistance to insecticides. The APRD indicates that this species of thrip has developed resistance to 20 insecticides with 100 confirmed cases of resistance reported worldwide. According to the APRD, these resistance-prone pests have not developed resistance to acetamiprid in the United States.

The Agency also reviewed the Insecticide Resistance Action Committee (IRAC) database for information about acetamiprid regarding resistance management. The IRAC is an international group with over 150 members of the crop protection industry organized by sector and region that advises on prevention and management of insecticide/acaricide resistance. The mission of the IRAC is to promote the development of insecticide/acaricide resistance management strategies to maintain efficacy and support sustainable agriculture and improved public health. The IRAC developed an internationally recognized and accepted classification system for insecticides/acaricides for resistance management based on pesticide mode of action and potential of a pest to develop resistance. The IRAC database is publically available. It indicates that acetamiprid is a member of the neonicotinoid group of insecticides and classifies them as group 4A insecticides. The neonicotinoid/4A class of insecticides includes imidacloprid, thiomethoxam, acetamiprid, dinotefuran, thiacloprid and clothianidin. The IRAC prepared guidelines for resistance management for the neonicotinoid insecticides in July 2008. The guidelines target certain insect pests which are prime targets for neonicotinoid insecticides and have been shown to possess a high potential resistance development. The resistance-prone pests listed in the guidelines include sweet potato whitefly, greenhouse whitefly, green peach aphid, cotton aphid, Colorado potato beetle and codling moth among others. Resistance management recommendations for the neonicotinoids include rotating active ingredients with different modes of action in treatment regimens and not relying exclusively on neonicotinoids for control of multi-generational pests. IRAC resistance management recommendations are based on research from academia and industry.

The resistance-prone insects discussed above develop resistance to pesticides as a result of several factors. First, multiple applications of pesticides are required to control or suppress these pests because they reproduce quickly and inhabit areas of plants that can be difficult to reach with pesticides. Second, some individuals within the pesticide-treated population are genetically capable of overcoming the toxic effects of one or more pesticides and survive after being treated with a pesticide(s). The survivors reproduce and the succeeding population has a larger percentage of resistant biotypes than the initially treated population. Pesticide resistance occurs when the same pesticide or pesticides with the same mode of action/same class are used exclusively or consecutively to control a pest. In some cases, cross resistance occurs when insects that have developed resistance to a pesticide exhibit resistance to pesticides in the same or different class of pesticide without having been previously exposed to the pesticide. Resistance management programs call for rotating treatments with insecticides with a different mode of action (from a different class of pesticide). This has been shown to delay or prevent development of resistance and cross-resistance (National Academy of Science).

The APRD and IRAC indicate that these pests can develop resistance to an insecticide quickly if alternative insecticides with different modes of action are not available and used as rotational treatments for resistance management. Some of the newer pesticides have already lost their effectiveness to control these pests due to resistance and others are likely to lose their

effectiveness unless resistance management techniques are adopted by users (APRD). Historically, pesticide resistance has resulted in the use of higher rates and/or more applications of pesticides to provide control. When this happens, more pesticide ends up being applied to the field/site, pests develop resistance at a faster rate and growers' pesticide costs are increased. In addition, newer insecticides typically have less risky environmental and human health toxicity end points compared to organo-phosphate and carbamate insecticides. When resistance develops to the newer, less risky pesticides, growers lose the use of them and may need to rely on riskier alternatives.

A number of insecticides are registered in the United States to control the above resistance-prone insect pests including; azadirachtin, flonicamid, chlorantraniliprole, buprofezin, pymetrozine, cyfluthrin, lambda and gamma cyhalothrin, imidacloprid, spiromesifen, thiamethoxam, endosulfan, spirotetramat, zeta-cypermethrin, *Chenopodium ambrosioides*, and dinotefuran for control of *Bemisia* whiteflies in head lettuce and imidacloprid, azadirachtin, beta-cyfluthrin, petroleum and vegetable oils, spinosad, pyrethrins, piperonyl butoxide, methomyl, potassium salts of fatty acids, rotenone, spinetoram, dinotefuran and neem oil for western flower thrip control in leaf lettuce. However, these pests have developed resistance to many if not most of these pesticides (APRD). As these pests are highly prone to developing resistance to most pesticides, it is necessary to have various, effective pesticides with different modes of action available for rotational treatment within a resistance management program. Although there are other group 4A neonicotinoid insecticides besides acetamiprid labeled for use for *Bemisia* whitefly control, i.e., imidacloprid, thiamethoxam and dinotefuran, and for western flower thrip control, i.e., imidacloprid and dinotefuran, it is valuable to have all of them available for resistance management as they vary in their effectiveness on these pests depending on locality and in optimal application timings. Of the four neonicotinoid insecticides registered for control of *Bemisia* whiteflies, resistance has only been reported for imidacloprid in the United States (California). Testing was conducted by the University of California and the United States Department of Agriculture (USDA)-Agricultural Research Service to determine if there is cross resistance from the California strain of imidacloprid resistant *Bemisia* whiteflies to acetamiprid, thiamethoxam and dinotefuran and cross resistance was not exhibited. Western flower thrip resistance has not been reported to acetamiprid, imidacloprid or dinotefuran in the United States and no cross resistance has been reported between class 4A neonicotinoids and other conventional insecticides. Acetamiprid provides an effective option for rotational treatments in resistance management programs for these pests.

Resistance management is used to maintain the effectiveness of pesticides and includes both reactive strategies and proactive initiatives to prevent future pesticide resistance development. The Agency is concerned about pesticide resistance and is developing a resistance management initiative to help delay or prevent pesticide resistance. The Agency is working with stakeholders to identify and address key resistance management issues. The initiative includes encouraging registrants to adopt voluntary resistance management labeling as described in Pesticide Notice (PR) 2001-5. Pesticide users are more likely to use resistance management programs if product labeling alerts them to the possibility of pesticide resistance and provides them with resistance management practices.

Nisso adopted the general, voluntary pesticide resistance management labeling recommended by Pesticide Registration (PR) Notice 2001-5 for acetamiprid end use products (ASSAIL 70 WP and ASSAIL 30SG) and added use-specific resistance management labeling for the above resistance-prone insect pests. The 'General Use' portions of the acetamiprid end use product labels contain the following voluntary resistance management instructions as recommended by PR Notice 2001-5:

Acetamiprid is the active ingredient in ASSAIL 70WP/ASSAIL 30SG insecticide. It is a member of a class of chemicals known as neonicotinoids and within the mode of action Group 4A. Rotating ASSAIL 70WP/ASSAIL 30SG insecticide with insecticides with a different mode of action (other than Group 4A insecticides) may delay or prevent development of resistance and cross-resistance to ASSAIL and other Group 4A insecticides. Avoid making more than two (2) consecutive applications of ASSAIL 70WP/ASSAIL 30SG insecticide before rotating to an alternative mode of action insecticide. Foliar applications of ASSAIL 70WP/ASSAIL 30SG insecticide should be avoided on crops treated with a Group 4A seed treatment or soil-applied insecticide until a foliar application of a non-Group 4A insecticide (insecticide with a different mode of action) has been applied between these applications. Use recommended IPM practices in your pest management system. Consult your agricultural advisor, PCA, university or extension personnel for recommended pest and resistance management practices for your area. The use of ASSAIL 70WP insecticide should conform to the resistance management practices for your area.

In addition to the above labeling, Assail 70WP contains the following mandatory resistance labeling, "To prevent development of insect resistance, do not apply Assail 70WP insecticide to crops listed on this label when grown in a greenhouse." This is a sound proactive recommendation as resistance has been known to develop rapidly in field grown crops which were treated with the same pesticides while they were being grown as transplants in greenhouses.

Acetamiprid also has use-specific resistance management labeling for whitefly and western flower thrips as follows:

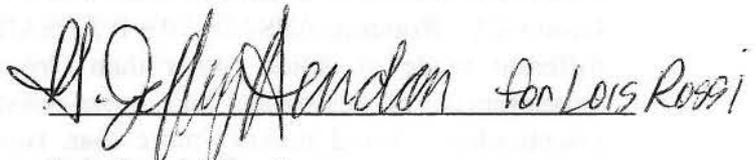
Whiteflies have shown a tendency to develop resistance. For resistance management purposes, alternating applications of different chemical classes reduces the potential for resistance development.

(For western flower thrips) - For resistance management purposes, alternating applications of different chemical classes reduces the potential for resistance development.

Nisso's use of the voluntary resistance management labeling from PR Notice 2001-5 and use-specific labeling further supports their case for criterion III.

In summary, the Agency concludes that acetamiprid meets criterion III, plays or will play a significant part in managing resistance for resistance-prone pests, *Bemisia* and/or greenhouse whiteflies and/or western flower thrips in 12 minor crops; broccoli, cabbage, cantaloupe, celery,

cucumber, eggplant, head lettuce, leaf lettuce, mustard greens, peppers, spinach and squash. Therefore the Agency **GRANTS** your request for an extension of exclusive use data protection under EPA registration No. 8033-20 for an additional three (3) years. Exclusive use protection for data submitted in support of this registration which complies with 40 CFR 152.83(c) will expire on March 15, 2015.

A handwritten signature in black ink, appearing to read "Lois Rossi" followed by "for Lois Rossi". The signature is written over a horizontal line.

Lois Rossi, Director
Registration Division
Office of Pesticide Programs

cc: Meredith Laws
Venus Eagle
Julie Chao
Michele Knorr
Nicole Williams
Pat Cimino

REFERENCES

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