

**Formal Recommendation by the
National Organic Standards Board (NOSB)
to the National Organic Program (NOP)**

Date: April 29, 2011
Subject: Tetracycline Petition
Chair: Tracy Miedema

The NOSB hereby recommends to the NOP the following:

Rulemaking Action X
Guidance Statement
Other

Statement of the Recommendation (Including Recount of Vote):

Adopt of the petition to amend the listing for tetracycline to remove the expiration date of October 21, 2012 and be annotated as follows:
§205.601 Synthetic substances allowed for use in organic crop production.
 (i) As plant disease control.
 (12) Tetracycline, for fire blight control in apples and pears only until October 21, 2014.

The Board expects that members of the industry will collaborate and coordinate efforts in preparing for the eventual removal of this material from the National List, specifically optimizing the use of resistant rootstocks and cultivars, preventive management methods, and the use of alternative, allowed biological and chemical controls whenever warranted.

Rationale Supporting Recommendation (including consistency with OFPA and NOP):

The Crops Committee originally requested, but did not receive, prior to adopting its recommendation on tetracycline, an updated Technical Review (TR), noting deficiencies in the previous reviews. The committee had a 2006 TR and a 1995 Technical Advisory Panel (TAP) for tetracycline. The committee proceeded based on its own research, pending the receipt of the new TR, which was reviewed when it is received and found to support the committee's research.

The antibiotic tetracycline was first approved in November 1995. Tetracycline and another antibiotic, streptomycin, were each listed with a split vote. The

issue of engendering antibiotic resistance in human pathogens and in workers was raised in the 1995 TAP review. The annotation that permitted use for “fire blight control in apples and pears only” was adopted. Streptomycin antibiotics were to be reviewed again in two years, and there was to be a task force to further explore antibiotic use in fruit production.

The 1998 proposed rule would have allowed “antibiotics as pesticides.” There was public opposition to the use of antibiotics as pesticides. When the USDA published the next draft rule in early 2000, it removed the NOSB recommendations allowing streptomycin and tetracycline in order to be consistent with the prohibition of antibiotics in livestock. The two antibiotics were reinstated in the December 2000 final rule in response to comments from growers.

Thus, from the very beginning, there has been controversy over allowing these chemicals to be used in organic agriculture. The Board discussion regarding the 2006 sunset included concerns about:

- Promotion of resistance in human pathogens
- Natural substitutes
- Inconsistency with the prohibition of antibiotics in livestock
- Inconsistency with organic principles
- Disagreement with the prophylactic use of antibiotics
- The Centers for Disease Control and Prevention (CDC) opposition to the use of streptomycin and tetracycline in crop production
- Failing to give an incentive for alternatives
- Reaction against organic fruit by consumers
- Possibility that antibiotics might be taken up by fruit trees
- Need for more research
- Restrictions on sales of fruit in Europe
- Disruption of the organic system.

And on the other hand,

- Lack of data showing impact on resistance in human pathogens
- Dependency of growers on the materials

Ultimately, after expressing concern and the wish that someone might petition to remove them sooner than the next sunset, the two antibiotics were renewed with a vote of 7 yes, 4 no, 1 abstention, and 2 absent.

At its November 2008 meeting, the Board took up a petition to add a second form of tetracycline —oxytetracycline hydrochloride, by removing the tetracycline annotation that limited its use to the “oxytetracycline calcium complex.” This would have reset the clock on the tetracycline sunset. However, because there was a general belief that tetracycline should be phased-out, the

Board voted down the proposal; 1 yes, 13 no, and 1 absent. However, after that vote, a motion to reconsider resulted in hydrochloride being added (“to level the playing field”), as well as an annotation that turned the sunset date into an expiration date —October 21, 2012— thus seeking to prevent any additional extensions of the sunset period.

Now tetracycline has come to Board again in a petition that requests the removal of the annotation, the 2012 expiration date. The committee found that the case against the antibiotic has grown stronger and that removal from 601 should be delayed no longer than necessary.

The Crops Committee was presented with evidence that tetracycline can contribute to antibiotic resistance in human pathogens when used as pesticides on plants. At the same time, additional products are available for use against fire blight. Serenade Max, Bloomtime Biological FD, BlightBan C9-1 and Blightban A506 are relatively new biological controls. Surround is a kaolin clay product that has had some success in controlling fire blight.

Many in the public believe that the first line of defense is the choice of resistant varieties and rootstocks, a concept that the committee majority stated is a critical organic principle, essential to disease or pest prevention in organic systems. Despite this, the pattern of growth in organic apple and pear varieties in certain areas of the country has been skewed toward those varieties most susceptible to fire blight. In 2010, the leading organic apple varieties grown in Washington state were Fuji, Gala, and Granny Smith and accounted for approximately 54% of organic apple acreage—all highly susceptible to fire blight. (Some other widely-planted varieties are also highly susceptible.) The leading varieties in organic pear production were Bartlett, D’Anjou, and Bosc—80% of organic pear acreage—again among the most susceptible to fire blight. On the other hand, there are numerous apple and pear varieties that are not susceptible to fire blight.

Given the public health threat associated with antibiotic resistance, there is a history of Board and public concern that organic production not contribute in a small or large way to antibiotic resistance. The Committee originally passed a motion denying the petition, but based on comments that more time is needed to make a transition, proposed that the expiration date be postponed until October 21, 2014.

The options for new antibiotics with efficacy are eluding us as resistance continues to increase, and the committee feels antibiotic resistance in human pathogens is an issue that should drive a process to speedy adoption of alternative management of fire blight.

NOSB Vote:

Moved: John Foster		Second: Steve DeMuri		
Yes: 13	No: 1	Abstain: 0	Absent: 0	Recusal: 0

EVALUATION CRITERIA FOR SUBSTANCES ADDED TO THE NATIONAL LIST

Category 1. Adverse impacts on humans or the environment? Substance: Tetracycline

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. Are there adverse effects on environment from manufacture, use, or disposal? [§205.600 b.2]			X	.
2. Is there environmental contamination during manufacture, use, misuse, or disposal? [§6518 m.3]	X			TR1 ¹ 149-164 Daniels, 1982. ² Manufacture results in discharges of solvents, detergents, disinfectants. Treated plants exude tetracycline.
3. Is the substance harmful to the environment and biodiversity? [§6517c(1)(A)(i);6517(c)(2)(A)i]	X			Thiele-Bruhn and Beck, 2005. ³ See #6 below.
4. Does the substance contain List 1, 2, or 3 inerts? [§6517 c (1) (B)(ii); 205.601(m)2]	?			
5. Is there potential for detrimental chemical interaction with other materials used? [§6518 m.1]	X			Burgos et al, 2003. ⁴ Bacteria with multiple resistance.
6. Are there adverse biological and chemical interactions in agro-ecosystem? [§6518 m.5]	X			Thiele-Bruhn and Beck, 2005 Shifts fungal-bacterial balance at environmentally relevant concentrations.
7. Are there detrimental physiological effects on soil organisms, crops, or livestock? [§6518 m.5]	X			Xiujie Xie et al, 2010. ⁵ Tetracycline may be genotoxic to plant cells.
8. Is there a toxic or other adverse action of the material or its breakdown products? [§6518 m.2]	X			See #10 below.
9. Is there undesirable persistence or concentration of the material or breakdown products in environment?[§6518 m.2]	X			Daniels, 1982. Chander et al, 2005. ⁶ Halling-Sørensen et al, 2002. ⁷ Tetracycline is taken up by plants and appears in all tissues and in exudates. Soil-bound tetracycline maintains biological activity.

¹ TR1 is TR dated January 27, 2006.

² MJ Daniels, 1982. Editorial: Possible effects of antibiotic therapy in plants. *Reviews of Infectious Diseases* 4 (Supp): 167-170.

³ Sören Thiele-Bruhn and Iris-Constanze Beck, 2005. Effects of sulfonamide and tetracycline antibiotics on soil microbial activity and microbial biomass. [Chemosphere, Volume 59, Issue 4](#), April 2005, Pages 457-465

⁴ Burgos JM, Ellington BA, Varela MF., 2005. Presence of multidrug-resistant enteric bacteria in dairy farm topsoil. [J Dairy Sci](#). 2005 Apr;88(4):1391-8.

⁵ Xie, X., Zhou, Q., Bao, Q., He, Z. and Bao, Y. , Genotoxicity of tetracycline as an emerging pollutant on root meristem cells of wheat (*Triticum aestivum* L.). *Environmental Toxicology*, n/a. doi: 10.1002/tox.20567

⁶ Chander Y, Kumar K, Goyal SM, Gupta SC, 2005. Antibacterial activity of soil-bound antibiotics. [J Environ Qual](#). 2005 Oct 12;34(6):1952-7. Print 2005 Nov-Dec.

⁷ Halling-Sørensen B; Sengeløv G; Tjørnelund J, 2002. Toxicity of tetracyclines and tetracycline degradation products to environmentally relevant bacteria, including selected tetracycline-resistant bacteria.

Archives of environmental contamination and toxicology 2002;42(3):263-71.

				Degradation products have same activity as parent.
10. Is there any harmful effect on human health? [§6517 c (1)(A) (i) ; 6517 c(2)(A)I; §6518 m.4]	X			<p>TR163-71, 279-293 Lugo-Melchor et al, 2010.⁸ Levy et al, 1976.⁹ http://en.wikipedia.org/wiki/Tetracycline_antibiotics “Prop 65 list” http://www.oehha.org/prop65/prop65_list/files/P65single3405.pdf</p> <p>Workers are at risk of contracting tetracycline-resistant disease and suffering from allergic reactions. As a consequence of the widespread use of tetracyclines, the emergence and spread of tetracycline-resistant bacterial pathogens, among them the foodborne pathogen <i>Salmonella enterica</i>, has become a serious health hazard worldwide.</p> <p>Workers who handle feed with tetracycline have tetracycline-resistant flora in their intestines.</p> <p>Tetracyclines remain the treatment of choice for infections caused by chlamydia (trachoma, psittacosis, salpingitis, urethritis, and <i>L. venereum</i> infection), <i>Rickettsia</i> (typhus, Rocky Mountain spotted fever), brucellosis, and spirochetal infections (borreliosis, syphilis, and Lyme disease). In addition, they may be used to treat anthrax, plague, tularemia, and Legionnaires' disease.</p> <p>They may have a role in reducing the duration and severity of cholera, although drug-resistance is occurring, and their effects on overall mortality is questioned.</p> <p>Developmental toxin listed by the state of California.</p>
11. Is there an adverse effect on human health as defined by applicable Federal regulations? [205.600 b.3]			X	
12. Is the substance GRAS when used according to FDA’s good manufacturing practices? [§205.600 b.5]			X	
13. Does the substance contain residues of heavy metals or other contaminants in excess of FDA tolerances? [§205.600 b.5]			X	

¹ If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

⁸ Lugo-Melchor, Y., Quinones, B., Amezcuita-Lopez, B.A., Leon-Felix, J., Garcia-Estrada, R., Chaidez, C. 2010. Characterization of tetracycline resistance in *Salmonella enterica* strains recovered from irrigation water in the Culiacan Valley, Mexico. *Microbial Drug Resistance*. 6(3):185-190.

⁹ Stuart B. Levy, M.D., George B. FitzGerald, Ph.D., and Ann B. Macone, B.S., 1976. Changes in Intestinal Flora of Farm Personnel after Introduction of a Tetracycline-Supplemented Feed on a Farm. *N Engl J Med* 1976; 295:583-588.

Category 2. Is the Substance Essential for Organic Production? Substance:

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. Is there a natural source of the substance? [§205.600 b.1]			X	.
2. Is there an organic substitute? [§205.600 b.1]			X	
3. Is the substance essential for handling of organically produced agricultural products? [§205.600 b.6]			X	
4. Is there a wholly natural substitute product? [§6517 c (1)(A)(ii)]	X			TR1 304-312. Stockwell and Stack, 2007 ¹⁰
5. Is the substance used in handling, not synthetic, but not organically produced? [§6517 c (1)(B)(iii)]			X	
6. Are there any alternative substances? [§6518 m.6]	X			TR1 317-330
7. Is there another practice that would make the substance unnecessary? [§6518 m.6]	X			TR1 297-302, 335-343. Aldwinckle et al, 1998 ¹¹ . “Fireblight Management in the Pacific Northwest USA” (http://www.ncw.wsu.edu/treefruit/fireblight/principles.htm)

If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

¹⁰ Stockwell, V. O., and Stack, J. P. 2007. Using *Pseudomonas* spp. for integrated biological control. *Phytopathology* 97:244-249.

¹¹ H. Aldwinckle, J Norelli, and MT Momol, 1998. Fire blight: the search for better control. *IDFTA Compact Fruit Tree*, Vol. 31, No. 4

Category 3. Is the substance compatible with organic production practices?

Substance:

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. Is the substance compatible with organic handling? [§205.600 b.2]			X	
2. Is the substance consistent with organic farming and handling, and biodiversity? [§6517 c (1)(A)(iii); 6517 c (2)(A)(ii)]				
3. Is the substance compatible with a system of sustainable agriculture? [§6518 m.7]				
4. Is the nutritional quality of the food maintained with the substance? [§205.600 b.3]			X	
5. Is the primary use as a preservative? [§205.600 b.4]			X	
6. Is the primary use to recreate or improve flavors, colors, textures, or nutritive values lost in processing (except when required by law, e.g., vitamin D in milk)? [205.600 b.4]			X	
7. Is the substance used in production, and does it contain an active synthetic ingredient in the following categories:				
a. copper and sulfur compounds;				
b. toxins derived from bacteria;			X	
c. pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals?				
d. livestock parasiticides and medicines?				
e. production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleaners?				

¹ If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

Category 4. Is the commercial supply of an agricultural substance as organic, fragile or potentially unavailable? [§6610, 6518, 6519, 205.2, 205.105 (d), 205.600 (c) 205.2, 205.105 (d), 205.600 (c)]

Substance - _____

Question	Yes	No	N/A	Comments on Information Provided (sufficient, plausible, reasonable, thorough, complete, unknown)
1. <u>Is the comparative description provided</u> as to why the non-organic form of the material /substance is necessary for use in organic handling?			X	
2. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate form to fulfill an essential function in a system of organic handling?			X	
3. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate quality to fulfill an essential function in a system of organic handling?			X	
4. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate quantity to fulfill an essential function in a system of organic handling?			X	
5. Does the industry information provided on material / substance non-availability as organic, include (but not limited to) the following: a. Regions of production (including factors such as climate and number of regions);			X	
b. Number of suppliers and amount produced;			X	
c. Current and historical supplies related to weather events such as hurricanes, floods, and droughts that may temporarily halt production or destroy crops or supplies;			X	
d. Trade-related issues such as evidence of hoarding, war, trade barriers, or civil unrest that may temporarily restrict supplies; or			X	
e. Are there other issues which may present a challenge to a consistent supply?			X	