

**Sunset 2022**  
**Meeting 1 - Request for Public Comment**  
**Livestock Substances §§ 205.603 & 205.604**  
**April 2020**

**Introduction**

As part of the [Sunset Process](#), the National Organic Program (NOP) announces substances on the National List of Allowed and Prohibited Substances (National List) that are coming up for sunset review by the National Organic Standard Board (NOSB). The following list announces substances that are on the National List for use in organic livestock production that must be reviewed by the NOSB and renewed by the USDA before their sunset dates. This document provides the substance's current status on the National List, use description, references to past technical reports, past NOSB actions, and regulatory history, as applicable. If a new technical report has been requested for a substance, this is noted in this list. To see if any new technical report is available, please check for updates under the substance name in the [Petitioned Substances Database](#).

**Request for Comments**

While the NOSB will not complete its review and any recommendations on these substances until the Fall 2020 public meeting, the NOP is requesting that the public provide comments about these substances to the NOSB as part of the Spring 2020 public meeting. Comments should be provided via Regulations.gov at [www.regulations.gov](http://www.regulations.gov) by April 3, 2020 as explained in the meeting notice published in the Federal Register.

These comments are necessary to guide the NOSB's review of each substance against the criteria in the Organic Foods Production Act (7 U.S.C. 6518(m)) and the USDA organic regulations (7 CFR 205.600). The current substances on the National List were originally recommended by the NOSB based on evidence available to the NOSB at the time of their last review, which demonstrated that the substances were found to be: (1) not harmful to human health or the environment, (2) necessary because of the unavailability of wholly nonsynthetic alternatives, and (3) consistent and compatible with organic practices.

Public comments should focus on providing new information about a substance since its last NOSB review. Such information could include research or data that may support a change in the NOSB's determination for a substance. Public comment should also address the continuing need for a substance or whether the substance is no longer needed or in demand.

**Guidance on Submitting Your Comments**

Comments should clearly indicate your position on the allowance or prohibition of substances on the list and explain the reasons for your position. You should include relevant information and data to support your position (e.g., scientific, environmental, manufacturing, industry impact information, etc.).

**For Comments That Support Substances under Review:**

If you provide comments in support of an allowance of a substance on the National List, you should provide information demonstrating that the substance is:

- (1) not harmful to human health or the environment;
- (2) necessary to the production of the agricultural products because of the unavailability of wholly nonsynthetic substitute products; and
- (3) consistent with organic livestock production.

**For Comments That Do Not Support Substances under Review:**

If you provide comments that do not support a substance on the National List, you should provide reasons why the use of the substance should no longer be allowed in organic production or handling. Specifically, comments that support the removal of a substance from the National List should provide new information since its last NOSB review to demonstrate that the substance is:

- (1) harmful to human health or the environment;
- (2) unnecessary because of the availability of alternatives; and
- (3) inconsistent with livestock production.

**For Comments Addressing the Availability of Alternatives:**

Comments may present information about the viability of alternatives for a substance under sunset review. Viable alternatives include, but are not limited to:

- Alternative management practices that would eliminate the need for the specific substance;
- Other currently exempted substances that are on the National List, which could eliminate the need for this specific substance; and
- Other organic or nonorganic agricultural substances.

Your comments should address whether any alternatives have a function and effect equivalent to or better than the allowed substance, and whether you want the substance to be allowed or removed from the National List. Assertions about alternative substances, except for those alternatives that already appear on the National List, should, if possible, include the name and address of the manufacturer of the alternative. Further, your comments should include a copy or the specific source of any supportive literature, which could include product or practice descriptions; performance and test data; reference standards; names and addresses of producers or handlers who have used the alternative under similar conditions and the date of use; and an itemized comparison of the function and effect of the proposed alternative(s) with substance under review.

Written public comments will be accepted through April 3, 2020 via [www.regulations.gov](http://www.regulations.gov). Comments received after that date may not be reviewed by the NOSB before the meeting.

**Sunset 2022**  
**Meeting 1 - Request for Public Comment**  
**Livestock Substances §§ 205.603 & 205.604**  
**April 2020**

**Reference: 7 CFR 205.603 Synthetic substances allowed for use in organic livestock production**

Butorphanol  
Flunixin  
Magnesium hydroxide  
Poloxalene  
Formic Acid  
EPA List 4 - Inerts of Minimal Concern  
Excipients

**Livestock 205.604 Prohibited nonsynthetic substances**

Strychnine

## Butorphanol

**Reference: §205.603(a)** As disinfectants, sanitizer, and medical treatments as applicable

(5) Butorphanol (CAS #-42408-82-2) - federal law restricts this drug to use by or on the lawful written or oral order of a licensed veterinarian, in full compliance with the AMDUCA and 21 CFR part 530 of the Food and Drug Administration regulations. Also, for use under 7 CFR part 205, the NOP requires:

- (i) Use by or on the lawful written order of a licensed veterinarian; and
- (ii) A meat withdrawal period of at least 42 days after administering to livestock intended for slaughter; and a milk discard period of at least 8 days after administering to dairy animals.

**Technical Report:** 2002 TR

**Petition(s):** 2002 Petition

**Past NOSB Action:** 2002 Livestock Subcommittee recommendation; 09/2002 Meeting minutes and vote; 04/2010 sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** National List Amended 12/12/2007 ([72 FR 7049](#)); Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

### Background from Subcommittee:

#### Use:

Butorphanol is used in livestock production as a pre-operative treatment of pain before surgery. Butorphanol belongs to a general class of drugs known as opiate agonists. It is commonly used as an anesthetic used to treat patients prior to surgery. Other related drugs in this class include buprenorphine, fentanyl, meperidine, and morphine. Xylazine, acepromazine, and butorphanol serve similar functions but each has its own specific advantages that make it the preferred treatment at the time: acepromazine has no analgesic activity, it is only a sedative; xylazine has both analgesic and sedative properties; and butorphanol is a pain killer with no real sedative activity” (TAP p24.) Although, “there are non-synthetic opiates (refers to a group of drugs used for treating pain), butorphanol is preferred for several reasons: it is associated with fewer adverse effects for the animal; it has less abuse potential in humans thereby reducing unwanted consequences if the drug is “diverted” to illicit use.”

#### Manufacture:

Butorphanol is an opioid analgesic derived from morphine. Known for the ability to reduce the perception of pain without a loss of consciousness, the original opioids were derived from opium, which is a partially dried latex harvested from the opium poppy, *Papaver somniferum*.

#### International Acceptance:

*Canadian General Standards Board Permitted Substances List*

Table 5.3 of the Permitted Substances List includes butorphanol under the entry for botanical compounds, noting it shall be used according to label specifications.

*CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)*

While butorphanol is not specifically listed, the standard states that when veterinary drugs are used, the withholding period shall be twice the period of conventional standards.

*European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008*

Article 14 notes that “suffering shall be kept to a minimum during the entire life of the animal, including at the time of slaughter.” The regulation further notes “disease shall be treated immediately to avoid suffering to the animal; chemically synthesized allopathic veterinary medicinal products including

antibiotics may be used where necessary and under strict conditions, when the use of phytotherapeutic, homeopathic and other products is inappropriate. In particular restrictions with respect to courses of treatment and withdrawal periods shall be defined.”

#### *Japan Agricultural Standard (JAS) for Organic Production*

While butorphanol is not specifically listed, the standard states that when veterinary drugs are used, the withholding period shall be twice the period of conventional standards.

#### *International Federation of Organic Agriculture Movements (IFOAM) Norms*

While butorphanol is not specifically listed, the general principles state management practices should be directed to the well-being of animals, achieving maximum resistance against disease and preventing infections. Sick and injured animals must be given prompt and adequate treatment. Further, the standards note the well-being of the animals is the primary consideration in the choice of illness treatment. The use of conventional veterinary medicines is allowed when no other justifiable alternative is available. Withdrawal periods shall not be less than double of that required by legislation.

#### **Ancillary substances:**

Butorphanol tartrate includes sodium chloride, sodium citrate, and citric acid.

#### **Environmental Issues:**

Impacts of manufacture of butorphanol are unknown (TAP p25.) Butorphanol is used by injection. Butorphanol and metabolites are not considered toxic if released. Although the fate of butorphanol in the environment is not known, the metabolites that are excreted via urine and bile are water-soluble which will not likely accumulate in the local environment. Butorphanol disposal in city water drainage/sewer systems is accepted practice (TAP pp19, 25).

#### **Discussion:**

Butorphanol has been FDA approved for use as an anesthetic in non-food animals. Its use in food animals is an extra-label use (ELU) governed by the Animal Medicinal Drug Use Clarification Act, which allows animal drugs to be used for ELUs when, “limited to treatment modalities when the health of an animal is threatened or suffering, or death may result from failure to treat.” The material must be administered by a licensed veterinarian. If all precautions are followed and the drug is administered appropriately, the NOSB judged that there will be no harm done to humans who consume the meats from these animals—and the livestock are able to tolerate surgery, recover quickly, and grant the farmer economic satisfaction, according to the 2002 TAP.

The withdrawal periods for butorphanol in the organic regulations are twice those in the Food Animal Residue Avoidance Databank (FARAD). FARAD is a university-based national program that serves as the primary source for scientifically-based recommendations regarding safe withdrawal intervals of drugs and chemicals in food-producing animals.

In its last review, the NOSB judged butorphanol to be consistent with consumer perceptions of organic products. The NOSB’s 2002 votes were 11 favored, 1 absent, and 2 abstained and the NOSB’s 2010 vote was unanimous to retain this material on the NL.

Comments received generally supported the continued listing of butorphanol. Two dairy organizations, one dairy cooperative, and one former NOSB member commented in favor of continued use. One organization requested that the LS determine the impacts of the metabolites of butorphanol in milk and when excreted; and determine the legality of the use under the Animal Medicinal Drug Use Clarification Act (AMDUCA), since labels prohibit the use in food-use animals. With regard to the legality of the use and the presence of butorphanol and its metabolites in milk, USDA did determine that butorphanol is

listed in the Food Animal Residue Avoidance Databank (FARAD), and the listed meat withdrawal and milk discard times are twice those listed in FARAD (2007 FR Notice). With regard to the impacts of the excreted metabolites, the TAP review did not consider them problematic.

However, reliance on AMDUCA's exemption of ELUs can be problematic (Wren, 2008), and at the time of last review, the Livestock Subcommittee encouraged the Food and Drug Administration to address these uses directly through labeling.

**Additional information or questions requested by Subcommittee:**

1. Is butorphanol considered the preferred choice for its use at this time, or are there other options?
2. Are there nonsynthetic materials that would serve the same purpose as Butorphanol?

## Flunixin

**Reference:** **§205.603(a)** As disinfectants, sanitizer, and medical treatments as applicable (9) Flunixin (CAS #-38677-85-9)—in accordance with approved labeling; except that for use under 7 CFR part 205, the NOP requires a withdrawal period of at least two-times that required by the FDA

**Technical Report:** 2007 TAP Report

**Petition(s):** N/A

**Past NOSB Actions:** 10/2002 NOSB recommendation; 10/2010 NOSB sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** National List Amended 12/12/2007 ([72 FR 7049](#)); Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

**Background from Subcommittee:**

**Use:**

Flunixin, in its compounded state called flunixin meglumine is a potent, non-narcotic, nonsteroidal analgesic agent with anti-inflammatory and antipyretic activity. Flunixin, in its drug form, Banamine®, exists for intravenous or intramuscular use in horses and for intravenous use in beef and non-lactating dairy cattle only to treat inflammation and pyrexia.

Banamine® has been used to rapidly reduce the fever and lung inflammation that typically accompany Bovine Respiratory Disease (BRD). As a result of usage, cattle feel better faster and have fewer lung lesions in comparison to treatment with other remedies. Additionally, Banamine® has been used to reduce inflammation associated with endotoxemia.

If all precautions are followed and the drug is administered appropriately, there will be no harm done to humans who consume the meats from these animals - and the livestock are able to cope with the disorder and actually heal from it, quickly recovering, and granting the farmer economic satisfaction.

**Manufacture:**

Flunixin is a synthetic drug more commonly made into flunixin meglumine, which is the primary component of Banamine® (the injectable flunixin meglumine solution). It has been FDA approved and used in horses for intravenous or intramuscular injections and as intramuscular injections for beef and non-lactating dairy cattle for many years to help cope with inflammation, pyrexia, and colic.

Administered intravenously and intramuscularly, flunixin is quickly broken down internally and cleared from the bloodstream in urine

Flunixin meglumine is a potent inhibitor of the enzyme cyclooxygenase and is often classified as a non-steroidal anti-inflammatory drug (NSAID) and it functions by reducing the production of mediators of the inflammatory process. It acts as an anti-inflammatory by inhibiting the effect of prostaglandins by inhibiting cyclooxygenase (COX), the enzyme responsible for the direct synthesis of prostaglandins.

**International Acceptance:**

**Canada - Canadian General Standards Board Permitted Substances List:**

<http://www.tpsgc-pwgsc.gc.ca/ongc-cgsb/programme-program/normes-standards/internet/bio-org/permises-permitted-eng.html>. Flunixin is permitted in Table 5.3 as inflammatories. Preference shall be given to non-synthetic alternatives to reduce inflammation.

**European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008**

<http://www.organic-world.net/news-eu-regulation.html>; [http://eur-lex.europa.eu/LexUriServ/site/en/oj/2007/l\\_189/l\\_18920070720en00010023.pdf](http://eur-lex.europa.eu/LexUriServ/site/en/oj/2007/l_189/l_18920070720en00010023.pdf). Flunixin does not explicitly appear in the EU Council Regulation, EC No. 834/2007 or 889/2008. However, EC No. 889/2008 Section 4, Article 24 permits the use of chemically synthesized, allopathic veterinary treatments (including antibiotics) when phytotherapeutic, homeopathic products, trace elements and products listed in Annex V, part 3 and in Annex VI, part 1.1 are ineffective. Flunixin is a drug that has been specifically approved for use in swine.

**Japan Agricultural Standard (JAS) for Organic Production;**

<http://www.ams.usda.gov/nop/NOP/TradeIssues/JAS.html>

Flunixin does not explicitly appear in the Japanese Agricultural Standard for Organic Livestock Production; (Notification No. 1608); however, Article 4 allows the use of veterinary drugs including biological drugs and antibiotics. Article 3 defines three types of drugs and incorporates by reference other Japanese laws pertinent to animal health care and drugs.

**International Federation of Organic Agriculture Movements (IFOAM)**

<http://www.ifoam.org/standard/norms/cover.html> Flunixin does not explicitly appear in the IFOAM NORM (Version 2014). However, Section 5.6 permits the use of chemical allopathic medical products when natural and alternative medicines and treatments are unlikely to be effective. Vaccines are also permitted in some cases. The norm also states that operators shall give preference to natural medicines, including homeopathy, Ayurvedic medicine and acupuncture.

**Environmental Issues:**

Generally, Flunixin has been declared fairly safe and the probability of environmental contamination during use or disposal of flunixin is very low. EPA stated in a report on PPCP (Pharmaceuticals and Personal Care Products) that are found in the environment, particularly in the water, flunixin was not among the other NSAIDs (i.e. aspirin, ibuprofen, etc.) that had residues left in the waters.

**Discussion:**

Based on prior Subcommittee review and public comments, the NOSB found flunixin compliant with OFPA criteria, and does not recommend removal from the National List.

**Additional information or questions requested by Subcommittee:**

1. Is flunixin, listed in §205.603(a), still deemed necessary for organic livestock production?
2. Are there other non-synthetic materials that would serve the same purposes as flunixin?

## Magnesium hydroxide

**Reference: §205.603(a)** As disinfectants, sanitizer, and medical treatments as applicable (15) Magnesium hydroxide (CAS #-1309-42-8)—federal law restricts this drug to use by or on the lawful written or oral order of a licensed veterinarian, in full compliance with the AMDUCA and 21 CFR part 530 of the Food and Drug Administration regulations. Also, for use under 7 CFR part 205, the NOP requires use by or on the lawful written order of a licensed veterinarian.

**Technical Report:** 2007 TR

**Petition(s):** 2002 Petition

**Past NOSB Actions:** 2002 NOSB recommendation; 11/2005 NOSB sunset recommendation; 10/2010 sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

### Background from Subcommittee:

#### Use:

Magnesium hydroxide is used as an antacid for temporary relief of an upset stomach and as a laxative for short-term relief of constipation. Magnesium hydroxide is used as a flame retardant and smoke depressant for temperatures exceeding 400 degrees Fahrenheit. It is also a general food additive used as a color-retention agent, drying agent, pH control agent, or processing aid. Magnesium hydroxide is also used as a fertilizer (in the form of lime) as a substitute for more expensive chemical fertilizers.

#### Manufacture:

The TR states magnesium hydroxide (Brucite) is found naturally in serpentine, chlorite or dolomitic schists, or in crystalline limestones as an alteration product of periclase (magnesium oxide). It is prepared by mixing sodium hydroxide with a water-soluble magnesium salt. It is also formed by the hydration of reactive magnesium oxide. Either case produces a white precipitate.

#### International Acceptance:

IFOAM: Basic standards 2002- not explicitly listed as approved food additive or processing aid.

CODEX: Magnesium hydroxide meets the requirements set forth in the Food Chemical Codex, 3rd ed. Assuming good manufacturing practices, magnesium hydroxide is recognized as an acceptable, safe food ingredient.

NORWAY: Magnesium hydroxide is listed as a chemical requiring a much-reduced discharge rate, despite the full known toxicology of the compound. The discharge of unused chemicals is strictly forbidden and enforced in Norway.

The European Union (EU) and the US vary greatly in their limitations on sludge and how it should be treated to prevent disease in livestock. The EU allows more freedom when considering how sludge will be used for treatment. The US requires disposal classification of the sludge before it can be used for treatment. Magnesium hydroxide/oxide are listed as permitted substances in the EU standards.

JAPAN: not specifically listed in Japanese Rule.



**Environmental Issues:**

According to the TR, the EPA has deemed magnesium hydroxide environmentally safe. This assessment is based on toxicology reports provided by the Centers for Disease Control. Magnesium hydroxide is not listed on the EPA's list of regulated chemicals.

**Discussion:**

Based on prior Subcommittee review and public comments, the NOSB found magnesium hydroxide compliant with OFPA criteria, and did not recommend removal from the National List.

**Additional information or questions requested by Subcommittee:**

None

## Poloxalene

**Reference: §205.603(a)** As disinfectants, sanitizer, and medical treatments as applicable (21) Poloxalene (CAS #-9003-11-6)—for use under 7 CFR part 205, the NOP requires that poloxalene only be used for the emergency treatment of bloat

**Technical Report:** 2001 TAP

**Petition(s):** 2000 Petition

**Past NOSB Actions:** 03/2001 NOSB minutes and vote; 11/2005 sunset recommendation; 10/2010 sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

**Background from Subcommittee:****Use:**

Poloxalene (chemical formula:  $C_5H_{10}O_2$ ) is a copolymer of polyethylene and polypropylene ether glycol that is a non-ionic polyol surface-active agent. Poloxalene is a fast-acting synthetic material approved under the organic regulations only for emergency treatment of bloat. In conventional agriculture, it is also used medically as a fecal softener and in cattle for prevention of bloat.

**Manufacture:**

According to the 2001 NOSB TAP review of poloxalene, "There are two principal processes used [to manufacture poloxalene] the traditional chlorhydrin process and indirect oxidation by the hydroperoxide process that uses a molybdenum catalyst. Both processes start with propylene (propene) derived from cracking of petroleum. The chlorhydrin process involves reaction of propylene ( $CH_3CH=CH_2$ ) and chlorine in the presence of water to produce two isomers of propylene chlorhydrin. This is followed by dehydrochlorination using caustic soda or lime to produce propylene oxide and salt. The hydroperoxide process involves oxidation of propylene to PO by an organic hydroperoxide, producing an alcohol as a co-product. One of the possible alcohols (tert-butanol, TBE) produced as a by-product from this process is used as feedstock for MTBE, a gasoline additive. (Kirk-Othmer 1996b)"

**International acceptance:**

- Poloxalene is not mentioned specifically in *the Codex Alimentarius*; however, the Codex states that in certain defined circumstances "veterinary drugs or antibiotics may be used under the

responsibility of a veterinarian” provided that “withholding periods [are] double of that required by legislation with, in any case, a minimum of 48 hours.”

- Poloxalene is not mentioned specifically the Canadian standards; however, “the standards encourage the use of alternative treatments (e.g., homeopathy and herbal treatments) over regular veterinary drugs. However, if the animal is not responding to alternative treatments or if alternatives are known to be ineffective, the use of antibiotics, parasiticides and other medications is allowed with the additional restrictions outlined here. ‘Chemical, allopathic veterinary drugs’ refer to synthetic drugs used in mainstream veterinary practice.”
- The Japanese Agricultural Standard for Organic Livestock etc. does not specifically mention poloxalene; however, like the Codex and Canadian standards, there is some allowance for use of allopathic veterinary drugs when organic approaches are not effective.
- According to the 2001 TAP:
  - EU 2092/91 – Similar to Codex, with an additional proviso that animals treated more than 2 times or maximum of 3 times per year with chemical veterinary drugs can no longer be marketed as organic (Annex I, Section B 4).
  - IFOAM – similar to Codex and EU, natural products and preventive methods preferred, but use of veterinary medicines is permitted under control of certification agency.

#### **Ancillary substances:**

No clear information on ancillary substances was available.

#### **Environmental/Health Issues:**

According to the 2001 TAP review, “The production of organic polymers from petroleum sources is a large volume chemical manufacturing process that has significant environmental impact.” The 2001 TAP also states that the “FDA does not list any withdrawal times or residue tolerances for poloxalene. (21CFR)” and also the following in regard to human health: “Poloxalene is listed by USP for use as pharmaceutical aid. It is reported to have no known toxicity (Winters, 99) and is not listed in the National Toxicology Program Database.”

#### **Discussion:**

The 2001 TAP review stated that “Clearly, there are many preventive measures that can be taken to avoid pasture bloat. Organic farmers seeking to establish a pasture based system for ruminants may occasionally experience unforeseen incidence of pasture bloat that requires an emergency remedy. Use of this synthetic material could be justified to alleviate animal suffering on a very occasional basis.”

The following was the conclusion stated in the 2001 TAP review: “Poloxalene is clearly synthetic and prohibited unless added to the National List for medical use. The TAP reviewers are divided and do not have a consensus recommendation. Two of the reviewers favor its allowance for emergency use only based on a need to prevent suffering and promote animal welfare. The third reviewer finds the rare emergency use not to be a compelling reason for considering as a permitted synthetic and does not see it as indispensable given that other treatments are available for cases of mild bloat, and other emergency treatments are called for in life threatening circumstances. This is supported by the lack of historic allowance, or demonstrated need by existing certification agencies. The two reviewers who favor limited allowance also suggested either an extended withdrawal time, or a limited allowance for a permitted number of emergency treatments per year for organic animals. No data to support an extended withdrawal time has been presented, but the NOSB may want to consider an overall policy for frequency of emergency treatment or develop criteria for emergency use medication in general.”

**Additional information or questions requested by Subcommittee:**

1. Are organic approaches to dealing with bloat (e.g., use of oils) sufficient to address this healthcare issue or is poloxalene an essential tool for organic livestock production?
2. Is poloxalene consistent with the OFPA criteria and the organic regulations?

**Formic acid**

**Reference: §205.603(b)** As topical treatment, external parasiticide or local anesthetic as applicable  
(2) Formic acid (CAS # 64-18-6) - for use as a pesticide solely within honeybee hives

**Technical Report:** 2011 TR

**Petition(s):** 2010 Petition

**Past NOSB Actions:** 2010 NOSB recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** Added to National List, effective August 3, 2012 ([77 FR 45903](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

**Background from Subcommittee:****Use:**

Formic acid has been registered by the EPA as a pesticide since 1999 to control varroa and tracheal mites in honeybee. It is formulated into a pad that is placed in the hive and as the formic acid volatilizes the vapors kill the mites attached to bees, inside bees and in some cases in uncapped and capped brood cells. The mites die of asphyxiation, and they fall off the bees after exposure to the formic acid fumes. The lifespan and behavior of the honeybees are not negatively affected by the treatment. Mite mortality from formic acid treatment can be as high as 95%. Formic acid is present in nature in the stings and bites of many insects including ants and bees, and found in some nectars and fruits of plants including coffee and nettles. The natural form of formic acid is not available in sufficient quantities for commercial use. Its other uses include processing latex sap into rubber, or can be used to remove limescale as well as other uses in the textile industry as well as an antibacterial agent and preservative in livestock feed. Formic acid is an alternative to synthetic pyrethroids and organophosphates that have been used to kill mites. Label use requirements require no honey supers can be used on the hive during the 21-day treatment period. Honey supers may be placed on the hive after the 21-day treatment period and the formic acid gel pack has been removed. The honey in these supers cannot be extracted for harvest sooner than two weeks after placing on the hive. Formic acid can be used after honey supers have been removed from the hive at the end of the honey collecting season.

**Manufacture:**

Formic acid is produced through the hydrolysis of methyl formate, which also produces methanol. The methanol and carbon monoxide are combined with a strong base such as sodium methoxide, in the liquid phase and at elevated pressure to produce methyl formate. The methyl formate is then hydrolyzed to produce formic acid. Formic acid is also produced as byproduct in the manufacture of other chemicals, such as acetic acid, but this production is insufficient to meet demand, and so the first method is used as well to meet market demand.

**International Acceptance:**

Allowed by Canadian Organic Standards with a 30-day withdrawal time between use and addition of honey supers on the hive, as well as for organic silage preservation. The European Economic Community Council Regulation Organic Standards allows formic acid to be used to control varroa mite in honeybee hives as well as for silage preservation. The FDA considers formic acid “generally recognized as safe” GRAS (21CFR 186.1316). It is permitted to be used in the feed and drinking water of nonorganic livestock, as well as a flavoring agent in human consumed beverages and foods at permitted concentrations (21 CFR 573.480).

**Ancillary substances:**

Mite-Away Quick Strip lists the product as containing 46.7% formic acid and 53.3% inert ingredients. The only other information that was available, was that the formic acid is impregnated into a gel encased in a plastic wrap.

**Environmental Issues:**

Honeybees can produce minute levels of formic acid and it is found naturally in honey. Since formic acid is used only within the hive, no residues of formic acid are found outside the hive and no negative effects on the environment have been found when used according to package instructions. Plants can be killed when exposed to high concentrations of formic acid. Human health can be negatively affected through oral ingestion or inhalation, and it is highly irritating to the respiratory tract, eyes and mucous membranes of the mouth and throat. Chronic skin contact may cause sensitization dermatitis. The label requires the use of personal protection equipment including coveralls, long sleeve shirt, long pants, socks and shoes, acid resistant gloves and protective eyewear. A respirator is required only if working with the formic acid product indoors. Beekeepers typically wear protective equipment around their hives to prevent stings, even when not applying formic acid.

**Discussion:**

The introduction of the non-native varroa mites and tracheal mites to North American honeybees in the 1980s has been devastating to both domestic and feral honeybees. While hygienic behavior can be encouraged through breeding, and bees then do what they can to clean themselves and remove the mites, this breeding activity is insufficient to control these destructive parasites. Use of screened bottom boards where mites drop off bees and cannot crawl back into the hive, drone trap frames where mites tend to congregate and then removal before the drone brood hatches, and various types of essential oils including thymol can all be used to lessen mite populations, but these strategies are insufficient to control the mites to acceptable levels. Major losses of honeybee colonies are attributed to these two parasites. Oxalic acid was recently recommended by the NOSB to be added to the National List as another control for formic acid, and can be used in package bees (formic acid cannot) as well as in rotation with formic acid to prevent mite resistance. There is concern that a product that addresses organic apiculture production should not be on the National List since there are no NOP apiculture standards.

**Additional information or questions requested by Subcommittee:**

1. Are there natural sources of formic acid that are commercially available to beekeepers for use in their hives?
2. Are there other natural products that are effective in controlling varroa and tracheal mites in honeybees, that would make formic acid no longer necessary in organic production?
3. When formic acid is used in the hive as a miticide, would there be higher than the natural levels of formic acid in the propolis, royal jelly, or beeswax?

## EPA List 4—Inerts of Minimal Concern

**Reference:** §205.603(e) As synthetic inert ingredients as classified by the Environmental Protection Agency (EPA), for use with non-synthetic substances or synthetic substances listed in this section and used as an active pesticide ingredient in accordance with any limitations on the use of such substances.

(1) EPA List 4 -Inerts of Minimal Concern

**Technical Report:** 2015 TR Nonylphenol Ethoxylates (NPEs) (one group only of List 4 inerts)

**Petition(s):** N/A

**Past NOSB Actions:** 02/1999 NOSB minutes and vote; 11/2005 sunset recommendation; 10/2010 sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

### Background from Subcommittee:

#### Use:

EPA List 4 Inerts are used for a wide range of applications including surfactants and adjuvants in pesticide, herbicide and fungicide formulations.

#### Manufacture:

As this listing covers a wide range of substances, manufacture varies.

#### International:

*Canadian General Standards Board Permitted Substances List*

The Permitted Substances List does not individually list inerts, or “formulants” as noted in the Canadian text. Formulants as a class are not subject to the restrictions and prohibitions in the standard.

*CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)*

While section 5 outlines criteria for the inclusion of substances, the guidelines do not specifically address or include inerts.

*European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008*

The regulation does not specifically address the use of inerts.

*Japan Agricultural Standard (JAS) for Organic Production*

The standard does not specifically address the use of inerts.

*International Federation of Organic Agriculture Movements (IFOAM) Norms for Organic Production and Processing*

Section 3.1 of the norms state organic crop production ensure co-formulants (e.g. inerts) in formulated farm input products are not carcinogens, mutagens, teratogens or neurotoxins.

#### Ancillary Substances:

Given the wide range of substances, presence of ancillaries will vary.

#### Discussion:

While the EPA categorized lists (1, 2, 3, 4, 4A, 4B) provided guidance for evaluation of inert substances in organic production, these lists are no longer updated and have limited utility. The NOSB has devoted

considerable time to discussing and debating how to address the placement of inerts on the National List.

The Inerts Working Group (IWG), made up of NOSB members and NOP and EPA staff, was established in June 2010 and reported to the Crops Subcommittee. The group collected information regarding current classification of the former List 3 and 4 inerts and presented a discussion document at the November 2011 NOSB meeting. At that time, the NOSB and the IWG were working toward a solution to review the inerts that were formerly on EPA List 4 by collaborating with the Safer Choice Program (SCP) of the EPA.

In 2015, the Crops Subcommittee requested a Technical Report (TR) on the class of inerts known as Nonylphenol Ethoxylates (NPEs). The Livestock Subcommittee also reviewed this TR as part of the 2017 Sunset review of the EPA List 4 Inerts of Minimal Concern listed at §205.603. As highlighted in the TR, the US EPA is encouraging industry to eliminate the use of NPEs (TR 2015, line 137) because of toxicity concerns and persistence in the environment. It is unlikely that the NPEs would pass favorably through the SCP screening process. The Crops and Livestock Subcommittees have considered removing NPEs through an annotation, while maintaining the general listing for EPA List 4 while the new SCP review program starts up.

Because of concerns about the adverse health and environmental effects of NPEs, the SCP completed an [alternatives assessment](#) for synthetic surfactants, like NPEs, that are not endocrine disrupting chemicals. SCP's goal was to assist in the voluntary phase-out of NPEs used in industrial detergents. The SCP assessment for NPEs reviewed several alternatives to NPE surfactants that are comparable in cost, readily available, and rapidly biodegrade to non-polluting, lower hazard compounds in aquatic environments. Since this assessment, many formulators have reformulated their products without the use of NPEs.

The Crops Subcommittee drafted a proposal outlining the steps for implementation of the Safer Choice Program for inert review. Once initiated, inert manufacturers would have to submit their products to Safer Choice to be reviewed. A long implementation phase would be proposed, so that industry and manufacturers have enough time for submittal of inerts for screening and any required formulation change. The Livestock and Crops Subcommittees have noted that some inerts currently in use in organic products would likely not pass the Safer Choice review, and strongly encourage manufacturers to consider the likelihood of the need for reformulation.

Past public comments at sunset weighed heavily in favor of robust reviews of inert ingredients, due in large part to the fact that the original listing of inerts relied upon an EPA screening process which does not consider the OFPA criteria. Additionally, public comments indicated significant concern that, while inerts are not listed as active ingredients in many pesticide, herbicide and fungicide formulations, they nevertheless exert significant impact on the environment, terrestrial and aquatic ecosystems and human health. The Livestock Subcommittee recognizes the public's deep concerns regarding these materials, while also acknowledging the significant impact that wholesale removal of EPA List 4 Inerts from the National List would have on the organic industry.

In the last two sunset reviews, the Board has voted to retain the listing of EPA List 4 Inerts while the organic industry, the NOP, and the EPA worked together to create a path forward that adequately reviews inerts for compatibility with organic production. In October 2015, the Board passed a recommendation proposing an annotation to remove the reference to EPA List 4, and move forward with a formal relationship to work with the EPA Safer Choice Program. The recommendation acknowledges the current nomenclature in use by the EPA regarding FIFRA 25(b) and 40 CFR 180.1122, while laying a framework for some inerts to be reviewed individually.

**To date, the 2015 recommendation has not been implemented.** The 2015 recommendation presents options for moving forward that are still relevant and necessary. **The board strongly encourages the NOP to move forward on this recommendation and add it to the regulatory agenda.**

**Additional information or questions requested by Subcommittee:**

1. How can the Safer Choice Program be used to evaluate inerts? How can the Board help facilitate this in moving forward?
2. If the NOSB and NOP use the Safer Choice Program, would *all* inerts reviewed and approved by Safer Choice be allowed? Would only certain criteria established by Safer Choice or those criteria established by an MOU with the NOP be allowed?
3. How should the NOSB establish review criteria based on the Safer Choice Program while also ensuring it is consistent with OFPA criteria and the regulation?
4. If Safer Choice is not the ideal path forward, or a formal relationship with EPA cannot be established, how should the Board proceed with addressing inerts?
5. Should the Board focus on inerts of greatest toxicity? If so, how should the Board identify and prioritize these for review?

## Excipients

**Reference:** §205.603(f) Excipients, only for use in the manufacture of drugs used to treat organic livestock when the excipient is: Identified by the FDA as Generally Recognized As Safe; Approved by the FDA as a food additive; or Included in the FDA review and approval of a New Animal Drug Application or New Drug Application

**Technical Report:** [2015 TR](#)

**Petition(s):** N/A

**Past NOSB Actions:** 10/2002 NOSB minutes and vote; 10/2010 sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

**Background from Subcommittee:**

**Use:**

There are more than 8,000 food, drug, and cosmetic excipients available to conventional production; however, excipients currently appear in the USDA National Organic Program (NOP) regulations at §205.603 only for use in the manufacture of drugs used to treat organic livestock when the excipient is identified by the FDA as: 1) Generally Recognized As Safe (GRAS); 2) approved by the FDA as a food additive; or 3) included in the FDA review and approval of a New Animal Drug Application or New Drug Application. In 2009, the National Organic Standards Board (NOSB) recommended a fourth criterion for their allowance: “Approved by APHIS” for vaccines.

Excipients are defined in §205.2 as “any ingredients that are intentionally added to livestock medications but do not exert therapeutic or diagnostic effects at the intended dosage, although they may act to improve product delivery (e.g., enhancing absorption or controlling release of the drug substance). Excipients are used in New Animal Drug Applications (NADAs) approved by FDA, and in animal health care products that do not carry NADA registration. They are also used in New Drug

Applications (NDAs) in drugs marketed for human consumption that may be administered to animals, such as aspirin.

Excipients are used for a great number of applications in animal drug and health care products but are delineated into broad categories based on the major reasons the excipient is used. Examples of such ingredients include fillers, extenders, diluents, wetting agents, solvents, emulsifiers, preservatives, flavors, absorption enhancers, sustained- release matrices, and coloring agents.”

#### **Manufacture:**

Excipients are common in almost all therapeutic products for veterinary use, and in some cases the total amount of excipients used is greater than the active substances in the dose. They are derived from natural sources or are synthetically manufactured by chemicals, derived from genetically modified organisms, or manufactured by other means. They range from simple, whole food products, to highly characterized organic and inorganic molecules, to complex materials that are difficult to fully characterize chemically.

Excipients can be added to the active substance individually or together in a formulated excipient package, depending on the drug. Excipients serve many functions but are typically comprised of suspending and viscosity-modifying agents, pH modifiers and buffering agents, preservatives, antioxidants, chelating agents, sequestrants, colorants, flavors, fillers, and diluents. While it is clear the functions that excipients serve, very few of them have been chemically described in any detail.

Because excipients are manufactured for a wide variety of purposes, the source and origin are highly variable. They range from whole food products such as wheat middlings and yeast to synthetic food additives such as sodium benzoate and sodium lauryl sulfate. They may be agricultural, non-synthetic or synthetic. Some are extracted or produced from plants, animals, minerals or microorganisms, and others are manufactured entirely from chemicals.

#### **International Acceptance:**

**Canada - Canadian General Standards Board Permitted Substances List:** <http://www.tpsgc-pwgsc.gc.ca/ongc-cgsb/programme-program/normes-standards/internet/bio- org/permises-permitted-eng.html> Excipients are permitted under the Canadian Organic Standards, appearing in Table 5.3 as Formulants (inerts, excipients), and can only be used in conjunction with substances listed in Table 5.3. The listing in Table 5.3 does not specify any criteria for further compliance of such excipients.

#### **CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)**

<ftp://ftp.fao.org/docrep/fao/005/Y2772e/Y2772e.pdf> 263 Excipients do not explicitly appear in the tables of permitted substances for organic livestock production; however, the use of veterinary medicinal products is permitted under certain conditions according to Health Care, Section 22, including chemical allopathic drugs. Excipients are not specifically mentioned in this section.

#### **European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008**

<http://www.organic-world.net/news-eu-regulation.html>; [http://eur-lex.europa.eu/LexUriServ/site/en/oj/2007/l\\_189/l\\_18920070720en00010023.pdf](http://eur-lex.europa.eu/LexUriServ/site/en/oj/2007/l_189/l_18920070720en00010023.pdf) 271.

Excipients do not explicitly appear in the EU Council Regulation, EC No. 834/2007 or 889/2008. However, EC No. 889/2008 Section 4, Article 24 permits the use of chemically synthesized, allopathic veterinary treatments (including antibiotics) when phytotherapeutic, homeopathic products, trace elements and products listed in Annex V, part 3 and in Annex VI, part 1.1 are ineffective.

#### **Japan Agricultural Standard (JAS) for Organic Production**

<http://www.ams.usda.gov/nop/NOP/TradeIssues/JAS.html>



Excipients do not explicitly appear in the Japanese Agricultural Standard for Organic Livestock Production; (Notification No. 1608); however, Article 4 allows the use of veterinary drugs including biological drugs and antibiotics. Article 3 defines three types of drugs and incorporates by reference other Japanese laws pertinent to animal health care and drugs.

### **International Federation of Organic Agriculture Movements (IFOAM)**

<http://www.ifoam.org/standard/norms/cover.html> Excipients do not explicitly appear in the IFOAM NORM (Version 2014). However, Section 5.6 permits the use of chemical allopathic medical products when natural and alternative medicines and treatments are unlikely to be effective. Vaccines are also permitted in some cases. The norm also states that operators shall give preference to natural medicines, including homeopathy, Ayurvedic medicine and acupuncture.

**Environmental Issues:** The primary mechanism through which excipients appear in the environment is via manure application to cropland. There is little known about the actual effects, adverse or not, on the environment from excipients. Only a handful of studies have even identified the presence of specific excipients in the environment, while most studies focus on pharmaceuticals without making a distinction between active and excipient ingredients. Since most excipients used in organic livestock production are GRAS or FDA approved food additives, the potential for environmental and human health effects has been evaluated by the FDA as part of their legal status. No literature was found to show definitive harmful effects on the environment when excipients are used in animal health care products.

On the other hand, there are environmental concerns related to the manufacture of excipients. Because of the great variety of substances permitted for use as excipients and the methods of manufacture, some of the excipients could have detrimental environmental effects. Raw material extraction of petroleum products, solvents and mined minerals pose negative environmental effects; the FDA has gone as far as recommend to the pharmaceutical industry to avoid certain solvents (e.g., benzene, carbon tetrachloride, 1,2-dichloroethane, 1,1-dichloroethane, 1,1,1-trichloroethane) that pose exceptional environmental and human health risks. Further processing of certain ingredients like starches and starch derivatives can lead to environmental degradation, air pollution, and exploitation of resources. A great number of excipients may be derived from GMOs; i.e., soy, corn, cotton, etc.

### **Health Issues:**

There is no literature to indicate specific human health effects through the use of excipients in livestock health care products; but there is significant literature to show that certain excipients can have detrimental and even lethal consequences when administered directly to human beings, especially infants. This is one reason the FDA assesses the safety of excipients as part of each NADA application, rather than individually in a separate program. New excipients undergo a series of preclinical tests recommended by FDA and the International Pharmaceutical Excipients Council that include acute oral and dermal toxicity, teratology, genotoxicity assays, and skin sensitization studies in rodents. These tests may be conducted on the excipient in combination with the active ingredient, or as a stand-alone ingredient.

The most likely route of exposure of humans to excipients in animal drugs is through consumption of residues in milk and meat products of treated animals. Most of the research on contamination has focused upon traces of antibiotics, but formulations specifically allowed in §205.603 can also appear in milk and meat. Presumably, both the active ingredient and the excipients are cleared from commercial products by the withdrawal times dictated by the NOSB on the active ingredients. However, since the majority of excipients used in organic livestock production are GRAS or food additives, the FDA assessment would include human and animal effects of ingestion of such ingredients, including their metabolism and breakdown pathways. Adulterated excipients pose some potential risk to human

health; as a result, the FDA identified a partial list of excipients and active ingredients that may also be adulterated and need further testing.

**Discussion:**

Based on prior Subcommittee review and public comments, the NOSB found excipients compliant with OFPA criteria, and does not recommend removal from the National List.

**Additional information or questions requested by Subcommittee:**

1. Are excipients listed in §205.603(f) still deemed necessary for organic livestock production?
2. How are excipients currently being reviewed in livestock health products by the certifiers?
3. Since the previous TR and NOSB Subcommittee reviews, has there been any further research completed to document environmental or health issues that would justify removing excipients used in organic production?
4. Are there any specific excipients that cause more concern to the public than others? If so, how should the review of those excipients be addressed separately?

## Strychnine

**Reference:** §205.604 Nonsynthetic substances prohibited for use in organic livestock production. The following nonsynthetic substances may not be used in organic livestock production:

(a) Strychnine

**Technical Report:** None

**Petition(s):** N/A

**Past NOSB Actions:** 04/1995 NOSB minutes and vote (crops only); 11/2005 sunset recommendation; 10/2010 sunset recommendation; [10/2015 sunset recommendation](#)

**Recent Regulatory Background:** Sunset renewal notice published 06/06/12 ([77 FR 33290](#)); Sunset renewal notice published 03/21/2017 ([82 FR 14420](#))

**Sunset Date:** 3/15/2022

**Background from Subcommittee:**

**Use:**

Strychnine is a toxic alkaloid that is a transparent crystal or white, crystalline powder. It was widely used in poison (toxic) baits to kill rodents and other mammals and is a common adulterant of many illicit (street) drugs. Exposure to strychnine can be fatal. It is colorless, odorless and has a bitter taste.

Strychnine can be absorbed into the body by inhalation or ingestion. It can also be injected into the body when mixed with a liquid. Strychnine is rapidly metabolized and detoxified by the liver. This substance is also well-absorbed and acts very rapidly, producing muscular hyperactivity, which can quickly lead to respiratory failure and death.

Strychnine has been placed in Toxicity Category I, indicating the greatest degree of acute toxicity, for oral and ocular effects; inhalation toxicity is also presumed to be high.

According to the USDA, above-ground uses were canceled in 1988; however, it remains registered for below-ground use to control damage caused by pocket gophers.

**Environmental Issues:**

According to the EPA, acute toxicity of strychnine to birds is assumed to be very high. Subacute dietary data indicate that strychnine ranges from slightly to highly toxic to avian species. Strychnine may pose a threat to birds who may be subject to repeated or continuous exposure from spills.

Mammalian studies indicate that strychnine is very highly toxic to small mammals on both an acute oral basis and dietary basis. The signs of toxicity, including death, occurring within one hour. Acute freshwater fish data reveal that strychnine ranges from moderately to highly toxic to freshwater fish. Aquatic invertebrate acute toxicity data indicate that strychnine is moderately toxic to aquatic invertebrates.

**Discussion:**

In 2017, The Livestock Subcommittee determined that strychnine did not meet the OFPA criteria and saw no reason to remove it from its prohibited status on the National List. Both the Livestock Subcommittee and the full NOSB voted to not remove strychnine from §205.604, non-synthetic substances prohibited for use in organic crop production.

**Additional information or questions requested by Subcommittee:**

None

