Sunset 2022
Meeting 2 - Review
Livestock Substances §205.603, §205.604
October 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

Written public comments will be accepted through October 1, 2020 via www.regulations.gov. Comments received after that date may not be reviewed by the NOSB before the meeting.

Sunset 2022
Meeting 2 - Review
Livestock Substances §205.603, §205.604
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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

Subcommittee Review:
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, merperidine, 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.

During its first review at the April 2020 meeting, the Board received a majority of comments that support butorphanol's continued listing. Certifiers provided data that shows a small number of operations using this, but several conveyed its importance as a veterinary medicine tool. Several dairy and dairy organizations advocated for its continued listing to ensure the welfare of their animals and the safety of their vets during procedures. As noted in the last sunset review, one organization indicated that information in the TAP about impacts of butorphanol and its metabolites when excreted were not covered and that additional info would be helpful to understand any impacts that may exist. The commenter proposes that all metabolites be evaluated, as well as the extra-label use as described in the discussion above. Xylazine was noted as an alternative but with a caveat that it is not effective.

Based on the comments received, the Livestock Subcommittee considers butorphanol to still be an important veterinary tool for organic producers and supports its relisting at this time.

Subcommittee Vote:
Motion to remove butorphanol from §205.603 of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Scott Rice
Seconded by: Dan Seitz
Yes: 0 No: 5 Abstain: 0 Absent: 1 Recuse: 0

Flunixin

Reference: §205.603(a) As disinfectants, sanitizer, and medical treatments as applicable
(12) 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
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

Subcommittee Review:
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. 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.

The Spring 2020 Public Comments were overwhelmingly supportive of keeping Flunixin on the National List. Several certifiers conducted surveys of their clients and reported to the NOSB that their clients used Flunixin on their operations and desired to keep it in their 'toolbox" to use when needed for their livestock's well-being**.** 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.

Subcommittee Vote:
Motion to remove flunixin from §205.603 of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Sue Baird
Seconded by: Dan Seitz
Yes: 0 No: 5 Abstain: 0 Absent: 1 Recuse: 0

Magnesium hydroxide

Reference: §205.603(a) As disinfectants, sanitizer, and medical treatments as applicable
(18) 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

Subcommittee Review:
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.

Subcommittee Review:
Based on the Subcommittee review and public comment, the Livestock Subcommittee finds magnesium hydroxide compliant with OFPA criteria and does not recommend removal from the National List.

Subcommittee Vote:
Motion to remove magnesium hydroxide from §205.603.
Motion by: Jesse Buie
Seconded by: Kim Huseman
Yes: 0 No: 5 Abstain: 0 Absent: 1 Recuse: 0

Poloxalene

Reference: §205.603(a) As disinfectants, sanitizer, and medical treatments as applicable
(26) 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

Subcommittee Review:

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 chlorohydrin 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 (CH3CH=CH2) 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 in 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, the 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 pharmeuceutic 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."

Altogether, about a dozen written comments on poloxalene were submitted prior to the April 2020 NOSB meeting. The large majority of comments either supported continued listing of the substance as necessary in emergencies when natural approaches to treating bloat are not effective, or stated that the substance was used by organic farming operations for emergency situations. The general consensus was that while poloxalene is rarely needed, in certain emergency situations it is essential. Two commenters stated that the NOSB should not relist poloxalene unless there is strong evidence of need; however, these commenters did not offer any conclusions in this regard.

Based on the comments received, the Livestock Subcommittee considers poloxalene to still be an important veterinary tool for organic producers and supports its relisting at this time.

Subcommittee Vote:
Motion to remove poloxalene from §205.603(a) of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Dan Seitz
Seconded by: Nate Powell-Palm
Yes: 0 No: 5 Abstain: 0 Absent: 1 Recuse: 0

Formic acid

Reference: §205.603(b) As topical treatment, external parasiticide or local anesthetic as applicable
(3) 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

Subcommittee Review:

Use:

Formic acid is a pesticide employed to control Varroa and tracheal mites in honeybee hives. Deployed in the form of a compressed pad inside the hive, the material volatilizes to kill mites throughout the hive including mites attacking broods, and located externally on and internally in the adult bees.

The EPA first registered formic acid as a pesticide in 1999 as material control for Varroa and tracheal mites in honeybees. Formic acid kills mites by asphyxiation while not causing harm to the bees. Typically employed over a 21-day treatment period (per label instructions), the efficacy of formic acid in killing mites has been found to be as high as 95%. Label recommendations instruct producers who treat hives with formic acid to not harvest honey from the hive for two weeks after the introduction of the formic acid pads.

Natural sources of formic acid, which include coffee, nectars, some fruits, as well as the stings of ants and bees, have proven insufficient to extract commercially viable quantities.

Manufacture:

Primarily produced through the hydrolysis of methyl formate. Formic acid may be produced as a byproduct of other chemicals (e.g. acetic acid) though these have not proven to be commercially viable.

International Acceptance:

Canada: The Canadian Organic Standards require a 30-day withdrawal time. Also allowed for use silage preservation.

European Economic Community: Formic acid is allowed to control Varroa mites in honeybees. Also allowed for use in silage preservation.

FDA: Formic acid is generally recognized as safe GRAS (21CFR 186.1316)

Environmental Issues:

Due to its localized use inside the beehives, no residue is found outside the hive environment. Human health may be adversely affected if formic acid is inhaled or ingested. Respirators and skin covering personal protective equipment is recommended to protect against applicator contact.

Subcommittee Vote:

Motion to remove formic acid at § 205.603 (b) of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Nathaniel Powell-Palm
Seconded by: Scott Rice
Yes: 0 No: 6 Abstain: 0 Absent: 0 Recuse: 0

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 Limited Scope 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

Subcommittee Review:
Use:
EPA List 4 Inerts are used for a wide range of applications including surfactants and adjuvants in pesticide formulations.

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

International:
Since this listing covers many different materials, a specific listing of international acceptance cannot be provided. However, it is worth pointing out how other standards address inerts.

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.

Environmental Issues:
Some of the materials listed on List 4 may have negative environmental and human health consequences, while others may be relatively benign. A complete review of materials listed as to environmental issues is not possible without Technical Reviews of each material.

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. A comprehensive timeline authored by Terry Shistar of Beyond Pesticides is included in the Crops Subcommittee's EPA List 4 Inerts sunset review.

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 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.**

During the spring 2020 comment period, the Board again heard overwhelmingly from stakeholders that the inertia around this issue is unacceptable. As one comment noted, "It has now been five years since NOP committed to implementing the NOSB recommendation; ten years since EPA directly requested NOP to remove the reference in its regulations; and about 15 years since EPA Lists became obsolete. Yet the NOP regulations still refer to EPA Lists that were last updated in August 2004." Commenters expressed support for removing the reference in the annotation to EPA List 4 Inerts and moving the 2015 recommendation forward. Several comments provided detailed steps for how the NOP, NOSB and EPA Safe Choice Program can work together to accomplish this.

Though a path forward is well-defined, the timeline required to enact the 2015 recommendation is likely a lengthy one. Many EPA List 4 inerts used in compliant crop and livestock input formulations also appear on the EPA Safer Chemicals Ingredient List (SCIL), thus providing a viable transition to this more relevant list. Other inputs with inerts of known toxicity or other concerns would not move to the SCIL list and require reformulation and the subsequent registration and approval that is required of new regulated inputs. Ultimately, the reformulation of inputs to safer ingredients is a positive direction in which to move, one which meets consumer expectations and strengthens the integrity of the organic label. However, removal of the EPA List 4 reference with no immediate substitute will in the interim cause potential disruption to organic operations that rely on materials formulated with these inerts, removing essential tools in an already limited toolbox.

With these concerns recognized, the Subcommittee on a whole is hesitant to recommend removing EPA List 4 at 205.603(e) from the National list. However, we are unanimous in our request that the NOP immediately initiate steps to implement the 2015 NOSB recommendation to use the Safer Chemical Ingredient List for inerts as an evaluative tool in an expedited manner where possible. It is the intent that the NOP and NOSB work, as recommended by this Board in 2015, with EPA's Safer Choice Program and move to evaluate inerts in a manner that fulfills the requirements laid out in the Organic Foods Production Act.

Subcommittee Vote:
Motion to remove EPA List 4—Inerts of Minimal Concern from §205.603 of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Scott Rice
Seconded by: Sue Baird
Yes: 2 No: 4 Abstain: 0 Absent: 0 Recuse: 0

Excipients

Reference: §205.603(f) Excipients—only for use in the manufacture of drugs and biologics used to treat organic livestock when the excipient is: (1) Identified by the FDA as Generally Recognized As Safe; (2) Approved by the FDA as a food additive; (3) Included in the FDA review and approval of a New Animal Drug Application or New Drug Application; or (4) Approved by APHIS for use in veterinary biologics.
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 renewal notice published 12/27/2018 (83 FR 66559)
Sunset Date: 3/15/2022

Subcommittee Review:
Use:
There are more than 8,000 food, drug, and cosmetic excipients available for conventional production; however, excipients currently appear in the USDA National Organic Program (NOP) regulations at §205.603 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; 3) included in the FDA review and approval of a New Animal Drug Application or New Drug Application; or 4) Approved by APHIS (Animal and Plant Health Inspection Service) for use in veterinary biologics. Additionally, excipients are allowed in "nutritive supplements" listed at § 205.603(a)(21).

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." (§ 205.2)

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 (TR- 54-56).

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 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.

There were many comments from the public during the Spring 2020 NOSB meeting. Most of the comments addressed inconsistencies amongst certifiers about how to determine which excipients for livestock use are allowable and which are not. The NOSB was asked to commit to identifying and reviewing individual excipients to bring the clarity needed.

Nevertheless, the NOSB heard resoundingly that the public desired that excipients remain on the National List. Several Certifiers sent results of surveys that they had conducted with their clients, and the results showed that the numbers of uses of excipients in livestock health products were in the thousands.

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.

Subcommittee Vote:
Motion to remove excipients from §205.603 of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Sue Baird
Seconded by: Jesse Buie
Yes: 0 No: 5 Abstain: 0 Absent: 1 Recuse: 0

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

Subcommittee Review:
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 by the EPA, 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 Crops 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 Crops Subcommittee and the full NOSB voted to not remove strychnine from § 205.604 - non-synthetic substances prohibited for use in organic crop production.

Based on prior Subcommittee reviews and public comments, the NOSB found Strychnine non-compliant with OFPA criteria, and does not recommend removal from the National List §205.604.

Subcommittee Vote:
Motion to remove strychnine from §205.604 of the National List based on the following criteria in the Organic Foods Production Act (OFPA) and/or 7 CFR 205.600(b): N/A
Motion by: Nathaniel Powell-Palm
Seconded by: Jesse Buie
Yes: 0 No: 6 Abstain: 0 Absent:0 Recuse: 0