Sunset 2027
Meeting 1 - Request for Public Comment
Livestock Substances § 205.603 & § 205.604
Spring 2025

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 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, annotation, references to past technical reports, past NOSB actions, and regulatory history, as applicable. If a new technical report has been requested for a substance, it is noted in this list. Substances included in this document may also be viewed in the NOP's Petitioned Substances Index.

Request for Comments
While the NOSB will not complete its review and any recommendations on these substances until the Fall 2024 public meeting, the NOP requests that the public provide comments about these substances to the NOSB as part of the Spring 2025 public meeting. Written comments should be submitted via Regulations.gov at www.regulations.gov during the comment period as explained in the meeting notice published in the Federal Register.

Public 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: (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 clearly indicate the commentor's position on the allowance or prohibition of substances on the National List and explain the reasons for the position. Public comments should focus on providing relevant 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 (e.g., scientific, environmental, manufacturing, industry impact information, etc.). Public comment should also address the continuing need for a substance or whether the substance is no longer needed or in demand.

For Comments that Support the Continued Use of §205.603 Substances in Organic Production:
If you provide comments supporting the allowance of a substance at §205.603, 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 the Continued Use of §205.603 Substances in Organic Production:
If you provide comments that do not support a substance at §205.603, you should provide reasons why the use of the substance should no longer be allowed in organic production. 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/or
3. inconsistent with organic livestock production.

For Comments that Support the Continued Prohibition of §205.604 Substances in Organic Production:
If you provide comments supporting the prohibition of a substance on the §205.604 section of the National List, you should provide information demonstrating that the substance is:

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

For Comments that Do Not Support the Continued Prohibition of §205.604 Substances in Organic Production:
If you provide comments that do not support the prohibition of a substance at §205.604, you should provide reasons why the use of the substance should no longer be prohibited in organic production. Specifically, comments that support the removal of a substance from the §205.604 section of the National List should provide new information since its last NOSB review to demonstrate that the substance is:

1. not harmful to human health or the environment; and/or
2. consistent with organic livestock production.

For Comments Addressing the Availability of Alternatives:
Comments may include 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 substances that are on the National List that are better alternatives, which could eliminate the need for this specific substance; and/or
- 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 organic operations 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 via www.regulations.gov during the open comment period noted in the Federal Register. Comments received after that date may not be reviewed by the NOSB before the meeting.

§205.603 Sunsets: Synthetic substances allowed for use in organic livestock production:
Butorphanol
Flunixin
Magnesium hydroxide

Oxytocin
Poloxalene
Formic acid
Sucrose octanoate esters
EPA List 4 Inerts
Excipients

§205.604 Sunsets: Nonsynthetic substances prohibited for use in organic livestock production:
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 TAP
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; 10/2020 sunset recommendation
Recent Regulatory Background: National List Amended 12/12/2007 (72 FR 7049); Sunset renewal notice published 06/06/2012 (77 FR 33290); Sunset renewal notice published 03/21/2017 (82 FR 14420); Sunset renewal notice published 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

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 (2002 TAP, page 24). 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 and it has less abuse potential in humans, thereby reducing unwanted consequences if the drug is diverted to illicit use (2002 TAP, page 26).

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* (2002 TAP, page 3).

International Acceptance

Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Substances that appear in CAN/CGSB-32.311, *Organic production systems — Permitted substances lists,* are subject to the FDA when used in Canada as veterinary drugs destined to food producing animals and to the Feeds Act (FA) when used in Canada as livestock feed. Health Canada's Veterinary Drugs Directorate is the federal authority responsible for the regulation of veterinary drugs under the FDA Regulations (Introduction, CAN/CGSB-32.311-2020).
- Botanical compounds: Botanical preparations, such as atropine, butorphanol, and other medicines from herbaceous plants shall be used according to label specifications (Table 5.3 – Health care products and production aids, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Butorphanol is not explicitly mentioned in the regulations.
- Disease prevention shall be based on breed and strain selection, husbandry management practices, high-quality feed, exercise, appropriate stocking density and adequate and appropriate housing maintained in hygienic conditions. Immunological veterinary medicinal products may be used. Chemically synthesised allopathic veterinary medicinal products, including antibiotics and boluses of synthesised allopathic chemical molecules, shall not be used for preventive treatment (Disease prevention, EC No. 2018/848).
- Disease shall be treated immediately to avoid suffering of the animal. Chemically synthesised allopathic veterinary medicinal products, including antibiotics, may be used where necessary, under strict conditions and under the responsibility of a veterinarian, 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. The withdrawal period between the last administration to an animal of a chemically synthesised allopathic veterinary medicinal product, including of an antibiotic, under normal conditions of use, and the production of organically produced foodstuffs from that animal shall be twice the withdrawal period referred to in Article 11 of Directive 2001/82/EC, and shall be at least 48 hours (Veterinary treatment, EC No. 2018/848).

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

- Butorphanol is not explicitly mentioned in the regulations.
- The basis for organic livestock husbandry is the development of a harmonious relationship between land, plants and livestock, and respect for the physiological and behavioural needs of livestock. This is achieved by a combination of providing good quality organically grown feedstuffs, appropriate stocking rates, livestock husbandry systems appropriate to behavioural needs, and animal management practices that minimize stress and seek to promote animal health and welfare, prevent disease, and avoid the use of chemical allopathic veterinary drugs (including antibiotics) (Description and Definitions, CXG 32-1999).
- Organic livestock management should aim to utilize natural breeding methods, minimize stress, prevent disease, progressively eliminate the use of chemical allopathic veterinary drugs (including antibiotics), reduce the feeding of animals with products of animal origin (e.g. meat meal), and maintain animal health and welfare (Livestock and Livestock Products, CXG 32-1999).
- The use of veterinary medicinal products in organic farming shall comply with the following principles: a) where specific disease or health problems occur, or may occur, and no alternative permitted treatment or management practice exists, or, in cases required by law, vaccination of livestock, the use of parasiticides, or therapeutic use of veterinary drugs are permitted; b) phytotherapeutic (excluding antibiotics), homeopathic or ayurvedic products and trace elements shall be used in preference to chemical allopathic veterinary drugs or antibiotics, provided that

their therapeutic effect is effective for the species of animal and the condition for which the treatment is intended; c) if the use of the above products is unlikely to be effective in combating illness or injury, chemical allopathic veterinary drugs or antibiotics may be used under the responsibility of a veterinarian; withholding periods should be the double of that required by legislation with, in any case, a minimum of 48 hours; d) the use of chemical allopathic veterinary drugs or antibiotics for preventative treatments is prohibited (Health care, CXG 32-1999).

International Federation of Organic Agriculture Movements (IFOAM)

- Butorphanol is not explicitly mentioned in the regulations.
- Organic animal management does not practice any prophylactic use of synthetic allopathic veterinary drugs. Organic animal management strictly limits use of antibiotic and other allopathic chemical veterinary drugs for animals to the treatment of illness and injuries under the supervision of qualified personnel, and subject to defined withdrawal periods. Common withdrawal period: at least twice the legislated withdrawal period or 48 hours, whichever is longer (Animal Production, IFOAM NORMS 2014).
- Organic animal management systems follow the principle of positive health, which consist of a graduated approach of prevention (including vaccinations and anti-parasite treatments only when essential), then natural medicines and treatment, and finally if unavoidable, treatment with allopathic chemical drugs (Livestock production, IFOAM NORMS 2014).
- Use of synthetic allopathic veterinary drugs or antibiotics will cause the animal to lose its organic status. Producers shall not withhold such medication where doing so will result in unnecessary suffering of the livestock. Regional or other exception: The animal may retain its organic status if: a) the operator can demonstrate compliance with 5.6.1, and; b) natural and alternative medicines and treatments are unlikely to be effective to cure sickness or injury, or are not available to the operator, and; c) the chemically synthetized allopathic veterinary medical products or antibiotics are used under the supervision of a veterinarian, and; d) withdrawal periods shall be not less than double of that required by legislation, or a minimum of 14 days, whichever is longer; e) this exception is granted for a maximum of three courses of remedial treatments with chemically synthesized allopathic veterinary medicinal products or antibiotics within 12 months, or one course of treatment if the productive lifecycle of the animal is less than one year (Veterinary Medicine, IFOAM NORMS 2014).

Japan Agricultural Standard (JAS) for Organic Production

- Butorphanol is not explicitly mentioned in the regulations.
- Do not use veterinary medicinal products unless a specific disease or health problem has occurred or is likely to occur and no other appropriate treatment or control method is available, or unless required by laws and regulations (including orders and dispositions based on the provisions of laws; the same applies hereinafter). In the case where veterinary medicinal products are used, veterinary medicinal products other than medicines requiring medical examination or antibiotics are to be used. Vitamins, minerals, veterinary biological drugs, or any veterinary medicinal products other than parasiticides, should be used only for the therapeutic treatment of livestock or poultry (Health management, JAS for Organic Livestock Products).

Ancillary Substances

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

Human Health and Environmental Issues

Impacts of manufacture of butorphanol are unknown (2002 TAP, page 25). Butorphanol is administered via

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 an accepted practice (2002 TAP, page 25).

Discussion
The NOSB has reviewed several substances related to pain relief in livestock over the past 2 years. The community consistently highlights the necessity of having adequate pain relief materials available to organic livestock producers. Butorphanol is effective at managing pain in mild to moderate pain scenarios.

Questions to our Stakeholders
1. In what circumstances is Butorphanol commonly used on organic livestock operations?
2. Is the pain relief material toolbox for managing pain in surgical applications sufficient?

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; 10/2020 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 renewal notice published 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

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 (2007 TAP, pages 1-2).

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 (2007 TAP, page 3).

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 (2007 TAP, page 1).

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 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 (2007 TAP, page 1).

Flunixin meglumine is a potent inhibitor of the enzyme cyclooxygenase (2007 TAP, page 19), 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 (2007 TAP, page 3).

International Acceptance

Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Flunixin is not explicitly mentioned in the regulations.
- Substances that appear in CAN/CGSB-32.311, *Organic production systems — Permitted substances lists,* are subject to the FDA when used in Canada as veterinary drugs destined to food producing animals and to the Feeds Act (FA) when used in Canada as livestock feed. Health Canada's Veterinary Drugs Directorate is the federal authority responsible for the regulation of veterinary drugs under the FDA Regulations (Introduction, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Flunixin is not explicitly mentioned in the regulations.
- Disease prevention shall be based on breed and strain selection, husbandry management practices, high-quality feed, exercise, appropriate stocking density and adequate and appropriate housing maintained in hygienic conditions. Immunological veterinary medicinal products may be used. Chemically synthesised allopathic veterinary medicinal products, including antibiotics and boluses of synthesised allopathic chemical molecules, shall not be used for preventive treatment (Disease prevention, EC No. 2018/848).
- Disease shall be treated immediately to avoid suffering of the animal. Chemically synthesised allopathic veterinary medicinal products, including antibiotics, may be used where necessary, under strict conditions and under the responsibility of a veterinarian, 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. The withdrawal period between the last administration to an animal of a chemically synthesised allopathic veterinary medicinal product, including of an antibiotic, under normal conditions of use, and the production of organically produced foodstuffs from that animal shall be twice the withdrawal period referred to in Article 11 of Directive 2001/82/EC, and shall be at least 48 hours (Veterinary treatment, EC No. 2018/848).

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

- Flunixin is not explicitly mentioned in the regulations.
- The basis for organic livestock husbandry is the development of a harmonious relationship between land, plants and livestock, and respect for the physiological and behavioural needs of livestock. This is achieved by a combination of providing good quality organically grown feedstuffs, appropriate stocking rates, livestock husbandry systems appropriate to behavioural needs, and animal management practices that minimize stress and seek to promote animal health and welfare, prevent disease, and avoid the use of chemical allopathic veterinary drugs (including antibiotics) (Description and Definitions, CXG 32-1999).

- Organic livestock management should aim to utilize natural breeding methods, minimize stress, prevent disease, progressively eliminate the use of chemical allopathic veterinary drugs (including antibiotics), reduce the feeding of animals with products of animal origin (e.g. meat meal), and maintain animal health and welfare (Livestock and Livestock Products, CXG 32-1999).
- The use of veterinary medicinal products in organic farming shall comply with the following principles: a) where specific disease or health problems occur, or may occur, and no alternative permitted treatment or management practice exists, or, in cases required by law, vaccination of livestock, the use of parasiticides, or therapeutic use of veterinary drugs are permitted; b) phytotherapeutic (excluding antibiotics), homeopathic or ayurvedic products and trace elements shall be used in preference to chemical allopathic veterinary drugs or antibiotics, provided that their therapeutic effect is effective for the species of animal and the condition for which the treatment is intended; c) if the use of the above products is unlikely to be effective in combating illness or injury, chemical allopathic veterinary drugs or antibiotics may be used under the responsibility of a veterinarian; withholding periods should be the double of that required by legislation with, in any case, a minimum of 48 hours; d) the use of chemical allopathic veterinary drugs or antibiotics for preventative treatments is prohibited (Health care, CXG 32-1999).

International Federation of Organic Agriculture Movements (IFOAM)

- Flunixin is not explicitly mentioned in the regulations.
- Organic animal management does not practice any prophylactic use of synthetic allopathic veterinary drugs. Organic animal management strictly limits use of antibiotic and other allopathic chemical veterinary drugs for animals to the treatment of illness and injuries under the supervision of qualified personnel, and subject to defined withdrawal periods. Common withdrawal period: at least twice the legislated withdrawal period or 48 hours, whichever is longer (Animal Production, IFOAM NORMS 2014).
- Organic animal management systems follow the principle of positive health, which consist of a graduated approach of prevention (including vaccinations and anti-parasite treatments only when essential), then natural medicines and treatment, and finally if unavoidable, treatment with allopathic chemical drugs (Livestock production, IFOAM NORMS 2014).
- Use of synthetic allopathic veterinary drugs or antibiotics will cause the animal to lose its organic status. Producers shall not withhold such medication where doing so will result in unnecessary suffering of the livestock. Regional or other exception: The animal may retain its organic status if: a) the operator can demonstrate compliance with 5.6.1, and; b) natural and alternative medicines and treatments are unlikely to be effective to cure sickness or injury, or are not available to the operator, and; c) the chemically synthetized allopathic veterinary medical products or antibiotics are used under the supervision of a veterinarian, and; d) withdrawal periods shall be not less than double of that required by legislation, or a minimum of 14 days, whichever is longer; e) this exception is granted for a maximum of three courses of remedial treatments with chemically synthesized allopathic veterinary medicinal products or antibiotics within 12 months, or one course of treatment if the productive lifecycle of the animal is less than one year (Veterinary Medicine, IFOAM NORMS 2014).

Japan Agricultural Standard (JAS) for Organic Production

- Flunixin is not explicitly mentioned in the regulations.
- Do not use veterinary medicinal products unless a specific disease or health problem has occurred or is likely to occur and no other appropriate treatment or control method is available, or unless required by laws and regulations (including orders and dispositions based on the provisions of laws; the same applies hereinafter). In the case where veterinary medicinal products are used, veterinary medicinal products other than medicines requiring medical examination or antibiotics are to be

used. Vitamins, minerals, veterinary biological drugs, or any veterinary medicinal products other than parasiticides, should be used only for the therapeutic treatment of livestock or poultry (Health management, JAS for Organic Livestock Products).

Ancillary Substances
Flunixin is an ancillary substance in other pain relief drug formulations.

Human Health and Environmental Issues
Generally, flunixin has been declared 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
The Livestock Subcommittee has generally heard over the past 4 meetings that pain management in organic livestock is a top priority.

Questions to our Stakeholders
1. What are the common applications of this material?
2. Are the tools available for surgical pain relief sufficient to manage pain in organic animals?

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 TAP
Petition(s): 2002 Petition
Past NOSB Actions: 2002 NOSB recommendation; 03/2005 NOSB sunset recommendation; 10/2010 sunset recommendation; 10/2015 sunset recommendation; 10/2020 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 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

Subcommittee Review

Use
Magnesium hydroxide, also referred to as milk of magnesia, 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.

Manufacture
The TAP 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 magnesium hydroxide as a white precipitate (2007 TAP, page 3).

International Acceptance

Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Magnesium hydroxide is not explicitly mentioned in the regulations.

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Magnesium hydroxide is not explicitly mentioned in the regulations.

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

- Magnesium hydroxide is not explicitly mentioned in the regulations.

International Federation of Organic Agriculture Movements (IFOAM)

- Magnesium hydroxide is not explicitly mentioned in the regulations.

Japan Agricultural Standard (JAS) for Organic Production

- Magnesium hydroxide is permitted when obtained by grinding natural ores (Table A.1 Fertilizers and soil improvement substances, JAS for Organic Products of Plant Origin).

Ancillary Substances

N/A

Human Health and Environmental Issues

According to the TAP, the EPA has deemed magnesium hydroxide environmentally safe. This assessment is based on toxicology reports provided by the Center for Disease Control. Magnesium hydroxide is not listed on the EPA's list of regulated chemicals (2007 TAP, page 8). In addition, magnesium hydroxide is allowed for extra-label use in livestock under the provisions of AMDUCA.

Discussion

The reference material for this substance is from 2007. While the substance appears to remain necessary for organic livestock production and there does not appear to be any new information to suggest it now fails any of the National List criteria, future boards may want to consider requesting an updated Technical Review for its use in livestock production.

Questions to our Stakeholders

None

Oxytocin

Reference: 205.603(a) As disinfectants, sanitizer, and medical treatments as applicable
(17) Oxytocin—use in post parturition therapeutic applications
Technical Report: 1995 TAP; 2005 TR
Petition(s): N/A
Past NOSB Actions: 10/1995 NOSB minutes and vote; 11/2005 sunset recommendation; 10/2010 sunset recommendation; 10/2015 sunset recommendation; 11/2017 sunset recommendation to remove
Recent Regulatory Background: Sunset renewal notice published 03/21/2017 (82 FR 14420); Sunset renewal notice published 02/28/2022 (87 FR 10930)
Sunset Date: 03/15/2027

Subcommittee Review

Use
Oxytocin is a hormone produced primarily in two discrete locations in the brains of all male and female mammals (2005 TR, lines 18-19). In nonorganic production, it can be used regularly to help nonorganic dairy cows relax and "let down their milk" (1995 TAP, page 9). There are some concerns with overuse of oxytocin in nonorganic production systems. In the USDA organic regulations, it is used "in post parturition therapeutic applications," which is ambiguous.

Manufacture
Oxytocin is chemically manufactured as a both a veterinary and medical synthetic hormone. It is identical in structure ($C_{44}H_{68}N_{12}O_{12}S_2$) to the naturally occurring hormone. In brief, oxytocin's peptide synthesis goes through multiple steps and involves a series of condensation reactions using various solvents (e.g., triethylamine, ether) to form amide bonds. Biologically active oxytocin exists in a cyclic configuration formed by oxidation of two thiol groups to form a disulfide bond between the cysteine and asparagine amino acids. Other molecular configurations (e.g., non-cyclic) also may exist (2005 TR, lines 95-101).

International Acceptance
Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Oxytocin is permitted for post-parturition therapeutic use. Meat from treated animals will not lose its organic status. See 6.6.10 d) of CAN/CGSB-32.310, for criteria pertaining to the mandatory withdrawal period (Table 5.3 – Health care products and production aids, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Oxytocin is not explicitly mentioned in the regulations.
- Disease shall be treated immediately to avoid suffering of the animal. Chemically synthesised allopathic veterinary medicinal products, including antibiotics, may be used where necessary, under strict conditions and under the responsibility of a veterinarian, when the use of phytotherapeutic, homeopathic and other products is inappropriate.

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

- Oxytocin is not explicitly mentioned in the regulations.
- The use of veterinary medicinal products in organic farming shall comply with the following principles: a) where specific disease or health problems occur, or may occur, and no alternative permitted treatment or management practice exists, or, in cases required by law, vaccination of livestock, the use of parasiticides, or therapeutic use of veterinary drugs are permitted; b) phytotherapeutic (excluding antibiotics), homeopathic or ayurvedic products and trace elements shall be used in preference to chemical allopathic veterinary drugs or antibiotics, provided that their therapeutic effect is effective for the species of animal and the condition for which the treatment is intended; c) if the use of the above products is unlikely to be effective in combating illness or injury, chemical allopathic veterinary drugs or antibiotics may be used under the responsibility of a veterinarian; withholding periods should be the double of that required by legislation with, in any case, a minimum of 48 hours; d) the use of chemical allopathic veterinary drugs or antibiotics for preventative treatments is prohibited (Health care, CXG 32-1999).

International Federation of Organic Agriculture Movements (IFOAM)

- Oxytocin is not explicitly mentioned in the regulations.

- Organic animal management does not practice any prophylactic use of synthetic allopathic veterinary drugs. Organic animal management strictly limits use of antibiotic and other allopathic chemical veterinary drugs for animals to the treatment of illness and injuries under the supervision of qualified personnel, and subject to defined withdrawal periods.
- Use of synthetic allopathic veterinary drugs or antibiotics will cause the animal to lose its organic status. Producers shall not withhold such medication where doing so will result in unnecessary suffering of the livestock. Regional or other exception: The animal may retain its organic status if: a) the operator can demonstrate compliance with 5.6.1, and; b) natural and alternative medicines and treatments are unlikely to be effective to cure sickness or injury, or are not available to the operator, and; c) the chemically synthetized allopathic veterinary medical products or antibiotics are used under the supervision of a veterinarian, and; d) withdrawal periods shall be not less than double of that required by legislation, or a minimum of 14 days, whichever is longer; e) this exception is granted for a maximum of three courses of remedial treatments with chemically synthesized allopathic veterinary medicinal products or antibiotics within 12 months, or one course of treatment if the productive lifecycle of the animal is less than one year (Veterinary Medicine, IFOAM NORMS 2014).

Japan Agricultural Standard (JAS) for Organic Production

- Oxytocin is not explicitly mentioned in the regulations.
- Do not use veterinary medicinal products unless a specific disease or health problem has occurred or is likely to occur and no other appropriate treatment or control method is available, or unless required by laws and regulations.

Ancillary Substances
None

Human Health and Environmental Issues
In general, the acute toxicity of oxytocin is considered low. The lethal dose (LD_{50}) of oxytocin has been determined by the oral route of administration in rats (> 20.5 mg/kg) and mice (> 514 mg/kg). Its LD_{50} in rats via intravenous administration is much lower and has been reported in the literature to range from > 2.275 mg/kg to 5.8 mg/kg. Veterinary oxytocin is not available in oral form because it is destroyed in the stomach and intestines of mammals. More specifically, the nonapeptide is degraded into biologically inactive smaller peptides and amino acids by enzymes of the gastrointestinal tract (2005 TR, lines 164-170).

Because oxytocin is used in small doses on a case-by-case basis and only by or under the direction of a veterinarian in organic livestock production, it is unlikely to reach significant concentrations in the environment (agro-ecosystem) through normal use (2005 TR, lines 133-135).

Oxytocin consumed by humans in contaminated milk or drinking water would likely be destroyed in their stomach and intestines (2005 TR, lines 248-249).

Discussion
Oxytocin has been on the National List of approved synthetics since the USDA organic regulations were implemented.
In comments received for the 2020 sunset review, the two largest organic milk buyers in the U.S., CROPP Cooperative/Organic Valley and White Wave/Horizon, did not support renewal of this material. Numerous comments stated the current annotation of “use in post parturition therapeutic applications” is unclear, leading to uses on organic milk animals that do not meet the intention of this annotation. Commenters asked for clarity detailing what time frame is considered “post parturition,” and which therapeutic

applications are allowed. Some certifiers would not allow its use for "milk let down," others would not allow its use for displaced abomasum, while other certifiers would. Two different certifiers, Pennsylvania Certified Organic (PCO) and California Certified Organic Farmers (CCOF), noted a total of 47 operations had used it, while others noted it was not commonly used. Those in favor of relisting stated this is an important material in the dairy health toolkit to assist animals after giving birth. Those not in favor stated there were preventative measures, as well as other activities that could be performed post birthing, that make oxytocin unnecessary in organic livestock production.

In 2020, the NOSB voted to remove oxytocin from the National List, but this recommendation was not implemented. The NOP stated, "By retaining oxytocin on the National List, organic livestock producers will continue to be permitted to use the drug to treat specific conditions within a limited timeframe following parturition without forfeiting the animal's organic status." And, "The current annotation allows producers to use oxytocin to treat conditions related to labor and to an animal's postpartum survival. Its use is not permitted on a routine basis (*i.e.,* as protocol). Instead, it is available for emergency situations and severe complications in the immediate postpartum (following birth of young) period. It may not be administered to increase an animal's milk production (volume) or for milk letdown. As previously noted in this document, Federal law restricts this drug to use by or on the order of a licensed veterinarian (21 CFR 522.1680(c)(3))."

In the current review, the LS discussed the 2020 recommendation as well as possible reasons for relisting. It was pointed out that some dairy processors do not allow their dairy farms to use oxytocin, and thus can make the labeling claim of "no synthetic hormones." For other livestock farmers, the use of oxytocin is part of their approach to birthing problems. The LS recommends that oxytocin be relisted, on the balance of these considerations.

Questions to our Stakeholders

1. Is oxytocin an essential material for safe and humane treatment of animals in organic production and why?
2. Are there nonsynthetic alternatives, or other methods that can be used to accomplish the same results as oxytocin?

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; 2025 Limited Scope TR
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; 10/2020 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 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

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 ruminants, such as cattle and sheep. Poloxalene destabilizes foam and allows gas to release from the rumen.

Manufacture

A limited scope TR was completed in 2024 to evaluate the manufacturing process of poloxalene. As stated in the TR, the process for synthesizing poloxalene always involves the polymerization of ethylene oxide (EO) and propylene oxide (PO) to form a block copolymer. However, the process manufacturers use to produce the monomers can vary. PO and EO manufacturing is further described in the TR, as well as the steps involved in the polymerization reaction used to synthesize poloxalene. Once both monomers (PO and EO) are available, they are copolymerized to form poloxalene. Manufactures typically do this in the presence of a catalyst – such as KOH – which facilitates the polymerization reaction. The process consists of three steps: initiation, propagation, and termination. Poloxalene is not created using excluded methods.

Prior to the updated TR, manufacturing information was derived from the 2001 NOSB TAP review of poloxalene, which stated "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 chlorohydrin process involves reaction of propylene ($CH_3CH=CH_2$) and chlorine in the presence of water to produce two isomers of propylene chlorohydrin. 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 (2001 TAP, page 1).

International Acceptance

Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Poloxalene is not explicitly mentioned in the regulations.
- Substances that appear in CAN/CGSB-32.311, *Organic production systems — Permitted substances lists,* are subject to the FDA when used in Canada as veterinary drugs destined to food producing animals and to the Feeds Act (FA) when used in Canada as livestock feed. Health Canada's Veterinary Drugs Directorate is the federal authority responsible for the regulation of veterinary drugs under the FDA Regulations (Introduction, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Poloxalene is not explicitly mentioned in the regulations.
- Disease prevention shall be based on breed and strain selection, husbandry management practices, high-quality feed, exercise, appropriate stocking density and adequate and appropriate housing maintained in hygienic conditions. Immunological veterinary medicinal products may be used. Chemically synthesised allopathic veterinary medicinal products, including antibiotics and boluses of synthesised allopathic chemical molecules, shall not be used for preventive treatment (Disease prevention, EC No. 2018/848).
- Disease shall be treated immediately to avoid suffering of the animal. Chemically synthesised allopathic veterinary medicinal products, including antibiotics, may be used where necessary, under strict conditions and under the responsibility of a veterinarian, 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. The withdrawal period between the last administration to an animal of a chemically synthesised allopathic veterinary medicinal product, including of an antibiotic, under normal conditions of use, and the production of organically produced foodstuffs from that animal shall be twice the withdrawal period referred to in Article 11 of Directive 2001/82/EC, and shall be at least 48 hours (Veterinary treatment, EC No. 2018/848).

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

- Poloxalene is not explicitly mentioned in the regulations.
- The basis for organic livestock husbandry is the development of a harmonious relationship between land, plants and livestock, and respect for the physiological and behavioural needs of livestock. This is achieved by a combination of providing good quality organically grown feedstuffs, appropriate stocking rates, livestock husbandry systems appropriate to behavioural needs, and animal management practices that minimize stress and seek to promote animal health and welfare, prevent disease, and avoid the use of chemical allopathic veterinary drugs (including antibiotics) (Description and Definitions, CXG 32-1999).
- Organic livestock management should aim to utilize natural breeding methods, minimize stress, prevent disease, progressively eliminate the use of chemical allopathic veterinary drugs (including antibiotics), reduce the feeding of animals with products of animal origin (e.g. meat meal), and maintain animal health and welfare (Livestock and Livestock Products, CXG 32-1999).
- The use of veterinary medicinal products in organic farming shall comply with the following principles: a) where specific disease or health problems occur, or may occur, and no alternative permitted treatment or management practice exists, or, in cases required by law, vaccination of livestock, the use of parasiticides, or therapeutic use of veterinary drugs are permitted; b) phytotherapeutic (excluding antibiotics), homeopathic or ayurvedic products and trace elements shall be used in preference to chemical allopathic veterinary drugs or antibiotics, provided that their therapeutic effect is effective for the species of animal and the condition for which the treatment is intended; c) if the use of the above products is unlikely to be effective in combating illness or injury, chemical allopathic veterinary drugs or antibiotics may be used under the responsibility of a veterinarian; withholding periods should be the double of that required by legislation with, in any case, a minimum of 48 hours; d) the use of chemical allopathic veterinary drugs or antibiotics for preventative treatments is prohibited (Health care, CXG 32-1999).

International Federation of Organic Agriculture Movements (IFOAM)

- Poloxalene is not explicitly mentioned in the regulations.
- Organic animal management does not practice any prophylactic use of synthetic allopathic veterinary drugs. Organic animal management strictly limits use of antibiotic and other allopathic chemical veterinary drugs for animals to the treatment of illness and injuries under the supervision of qualified personnel, and subject to defined withdrawal periods. Common withdrawal period: at least twice the legislated withdrawal period or 48 hours, whichever is longer (Animal Production, IFOAM NORMS 2014).
- Organic animal management systems follow the principle of positive health, which consist of a graduated approach of prevention (including vaccinations and anti-parasite treatments only when essential), then natural medicines and treatment, and finally if unavoidable, treatment with allopathic chemical drugs (Livestock production, IFOAM NORMS 2014).
- Use of synthetic allopathic veterinary drugs or antibiotics will cause the animal to lose its organic status. Producers shall not withhold such medication where doing so will result in unnecessary suffering of the livestock. Regional or other exception: The animal may retain its organic status if: a) the operator can demonstrate compliance with 5.6.1, and; b) natural and alternative medicines and treatments are unlikely to be effective to cure sickness or injury, or are not available to the operator, and; c) the chemically synthetized allopathic veterinary medical products or antibiotics are used under the supervision of a veterinarian, and; d) withdrawal periods shall be not less than double of that required by legislation, or a minimum of 14 days, whichever is longer; e) this exception is granted for a maximum of three courses of remedial treatments with chemically

synthesized allopathic veterinary medicinal products or antibiotics within 12 months, or one course of treatment if the productive lifecycle of the animal is less than one year (Veterinary Medicine, IFOAM NORMS 2014).

Japan Agricultural Standard (JAS) for Organic Production

- Poloxalene is not explicitly mentioned in the regulations.
- Do not use veterinary medicinal products unless a specific disease or health problem has occurred or is likely to occur and no other appropriate treatment or control method is available, or unless required by laws and regulations (including orders and dispositions based on the provisions of laws; the same applies hereinafter). In the case where veterinary medicinal products are used, veterinary medicinal products other than medicines requiring medical examination or antibiotics are to be used. Vitamins, minerals, veterinary biological drugs, or any veterinary medicinal products other than parasiticides, should be used only for the therapeutic treatment of livestock or poultry (Health management, JAS for Organic Livestock Products).

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 added the following in regard to human health: "Poloxalene is listed by USP for use as pharmaceutics aid. It is reported to have no known toxicity and is not listed in the National Toxicology Program Database" (2001 TAP, page 3).

Discussion
Many preventive measures 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, and the use of this synthetic material could be justified to alleviate animal suffering on an emergency basis.

In previous NOSB meetings, many 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 consensus was that while poloxalene is rarely needed, in certain emergency situations it is essential.

Questions to our Stakeholders

1. Are there any non-synthetic, approved, and effective bloat remedies for ruminants that are commercially available to ranchers?

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; 10/2020 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 renewal notice published 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

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 those 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 (2011 TR, lines 89-95). Formic acid kills mites by asphyxiation while not causing harm to the bees (2011 TR, lines 121-125). 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 (2011 TR, lines 223-224).

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 (2011 TR, lines 199-203).

International Acceptance
Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Hay or silage preservation products are permitted: Preference should be given to bacterial or enzymatic additives derived from bacteria, fungi and plants and food by-products (such as molasses and whey). The following acids may be used: lactic, propionic and formic (Table 5.2 – Feed, feed additives and feed supplements, CAN/CGSB-32.311-2020).
- Acids: Ascorbic, acetic, propionic, citric, formic and lactic acids and vinegar. Permitted for all uses such as treatment of water and bedding (Table 5.3 – Health care products and production aids, CAN/CGSB-32.311-2020).
- Formic acid is permitted for apicultural use, to control parasitic mites. This substance may be used after the last honey harvest of the season and shall be discontinued 30 days before the addition of honey supers (Table 5.3 – Health care products and production aids, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Formic acid, lactic acid, acetic acid and oxalic acid, as well as menthol, thymol, eucalyptol or camphor, may be used in cases of infestation with *Varroa destructor* (Health care, EC No. 2018/848).
- Soft ground rock phosphate is permitted. Product obtained by grinding soft mineral phosphates and containing tricalcium phosphate and calcium carbonate as essential ingredients. Minimum content of nutrients (percentage by weight): 25% P_2O_5. Phosphorus expressed as P_2O_5 soluble in

mineral acids, at least 55% of the declared content of P_2O_5 being soluble in 2% formic acid (Authorised fertilisers, soil conditioners and nutrients, EC No. 2021/1165).
- Formic acid is permitted as a preservative (Authorised feed additives and processing aids used in animal nutrition, EC No. 2021/1165).

CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)
- Silage additives and processing aids may not be derived from genetically engineered/modified organisms or products thereof, and may be comprised of only: sea salt; coarse rock salt; yeasts; enzymes; whey; sugar or sugar products such as molasses; honey; lactic, acetic, formic and propionic bacteria, or their natural acid product when the weather conditions do not allow for adequate fermentation, and with approval of the competent authority (Livestock and Livestock Products, CXG 32-1999).
- For pest and disease control the following are allowed: lactic, oxalic, acetic acid; formic acid; sulphur; natural etheric oils (e.g. menthol, eucalyptol, camphor); *Bacillus thuringiensis*; steam and direct flame (Beekeeping and bee products, CXG 32-1999).

International Federation of Organic Agriculture Movements (IFOAM)
- Fodder preservatives such as the following may be used: a) bacteria, fungi and enzymes; b) natural products of food industry; c) plant-based products; and d) vitamins and minerals subject to 5.5.6. Synthetic chemical fodder preservatives such as acetic, formic, and propionic acid are permitted in severe weather conditions (Animal Nutrition, IFOAM NORMS 2014).
- For pest and disease control the following are permitted: a) lactic acid, formic acid; b) oxalic acid, acetic acid; c) sulfur; d) natural essential oils (e.g. menthol, eucalyptol, camphor); e) *Bacillus thuringiensis;* f) steam, direct flame and caustic soda for hive disinfection (Bee Keeping, IFOAM NORMS 2014).
- Formic acid is permitted (Table 2 - Indicative List of Equipment Cleansers and Equipment Disinfectants, IFOAM NORMS 2014).
- Citric, peracetic acid, formic, lactic, oxalic and acetic acid are permitted (Appendix 5 - Substances for Pest and Disease Control and Disinfection in Livestock Housing and Equipment, IFOAM NORMS 2014).

Japan Agricultural Standard (JAS) for Organic Production
- Formic bacteria is permitted (Table A.1 Substances used in the preparation etc., JAS for Organic Feed).
- Natural acids are permitted: limited to those made from lactic bacteria, acetic acid bacteria, formic bacteria or propionic acid bacteria (Table A.1 Substances used in the preparation etc., JAS for Organic Feed).

Environmental Issues

Due to its localized use inside the beehives, no residue is found outside the hive environment. Formic acid is generally recognized as safe (GRAS) by the FDA (21 CFR 186.1316) (2011 TR, lines 99-100). Human health may be adversely affected if formic acid is inhaled or ingested, so respirators and skin covering personal protective equipment are recommended to protect against applicator contact.

Discussion

Formic acid is found in nature. Synthetic formic acid is a relatively benign substance when used to treat Varroa mites, an important pest of honeybees. Because of its low environmental impact and GRAS status, the Livestock Subcommittee recommends retaining it on the National List.

Questions to our Stakeholders

1. Are the options for controlling Varroa mites in beehives sufficient or redundant?
2. Are there natural ways to combat mites that could reduce the dependency on parasiticides?

Sucrose octanoate esters

Reference: §205.603(b) As topical treatment, external parasiticide or local anesthetic as applicable
(10) Sucrose octanoate esters (CAS #s-42922-74-7; 58064-47-4)—in accordance with approved labeling
Technical Report: 2005 TR; 2025 Limited Scope TR
Petition(s): 2004 petition; 05/2004 petition amendment; 09/2004 petition amendment
Past NOSB Actions: 08/2005 NOSB recommendation; 10/2010 sunset recommendation; 10/2018 sunset recommendation to remove
Recent Regulatory Background: Sunset renewal notice published 06/06/12 (77 FR 33290); Sunset renewal notice published 03/21/17 (82 FR 14420); Sunset renewal notice published 02/28/2022 (87 FR 10930)
Sunset Date: 3/15/2027

Subcommittee Review
Sucrose octanoate esters (SOEs) belong to the organic chemical family sucrose fatty acid esters (SFAEs) (2005 TR, lines 23-24). SOEs are manufactured from sucrose (table sugar) and an octanoic acid ester commonly found in plants and animals (2005 TR, lines 27-28). SOEs, marketed as biopesticides, are synthetic analogs of the naturally occurring sugar ester isolates of *Nicotiana* plant species (2024 TR, lines 57-58) that mimic the pest control properties of the natural forms of the compound in wild tobacco and other plants in the *Nicotiana* genus. *gossei* Domin (wild tobacco) and other *Nicotiana* species, including wild tomato and wild potato species and the petunia plant (2005 TR, lines 35-38).

Use
Sucrose octanoate esters are listed at §205.603(b)(10) in organic livestock production as a topical treatment, external parasiticide or local anesthetic as applicable, in accordance with approved labeling (2024 TR, lines 34-35). The product is used in controlling Varroa mites in honeybees.

Manufacture
Commercial synthesis of SOEs involves the use of materials such as alcohols, several catalysts, solvents, and sucrose octanoate acid (2024 TR, lines 60-62. Steps in the production include (1) Esterification of fatty acids, (2) Neutralization and separation of catalyst, (3) Second esterification with sugar, (4) Vacuum distillation and emulsification, (5) Separation of emulsified product, and (6) Purification and recovery of sugar ester product (2024 TR, lines 66, 140, 154, 178, 183, and 188). The raw materials are derived from various sources: octanoic acid from both synthetic and nonsynthetic sources, alcohol (methanol or alcohol) from synthetic and nonsynthetic sources, and sucrose that is usually obtained from nonsynthetic sources (2024 TR, lines 197-200). The petitioned substance is a soap derived from coconut oil fatty acids or palm kernel oil fatty acids. Producers use SOEs to control soft-bodied pest organisms including mites, aphids, and whiteflies (2024 TR, line 56). The EPA has registered SOEs as a biopesticide for foliar spray on greenhouse, nursery, and field crops; for *Sciarid* fly control in mushroom-growing media; and for Varroa mite control on honeybees (2005 TR, lines 70-72).

International Acceptance
Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Strychnine is not explicitly mentioned in the regulations.

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165
- Strychnine is not explicitly mentioned in the regulations.

CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)
- Strychnine is not explicitly mentioned in the regulations.

International Federation of Organic Agriculture Movements (IFOAM)
- Strychnine is not explicitly mentioned in the regulations.

Japan Agricultural Standard (JAS) for Organic Production
- Strychnine is not explicitly mentioned in the regulations.

Ancillary Substances
None

Human Health and Environmental Issues

Effect on the Environment
The chemical structure of SOEs, consisting of sucrose and octanoic acid, renders the material readily biodegradable (2024 TR, line 215). Naturally occurring microorganisms in soil and water can break down these compounds. The compound biodegrades within approximately five days at temperatures ranging from 68°F to 80°F in both aerobic and anaerobic conditions. Typical degradation products are carbon dioxide and water, both of which are harmless. In addition to the fact that these degradation products are harmless, some are incorporated as microbial biomass (2024 TR, lines 216-220).

Impact on Non-Target Organisms
The EPA's evaluation report on the potential impact of SOEs on non-target insects and other organisms, such as fish, stated that the use of the compound had minimal potential for exposure and toxicity to these organisms as well as soil and water (2024 TR, lines 223-225). According to the EPA, the fact that the mode of action of the compound is via physical effects as opposed to biochemical toxicity gives the compound a minimal toxicity profile. The petitioned substance primarily targets soft-bodied insects by physically disrupting the lipid layer of their cuticle, thereby causing dehydration and death. Insects with thicker and/or more robust exoskeletons are not affected by the petitioned substance (2024 TR, lines 231-233).

The physical mode of action enables the compound to target soft-bodied insects without producing general toxic metabolites, thereby decreasing the likelihood of adverse effects on mammals and birds (2024 TR, lines 225-229). Soft-bodied organisms targeted include mites and insects such as thrips, aphids, and whiteflies. The fact that SOEs do not exert their pesticidal effects via a biochemical pathway common to all insects renders it selective, resulting in minimal effects on non-target organisms such as pollinators (e.g., bees), predators (ladybugs), earthworms, and other soil organisms (2024 TR, lines 233-236). Some non-synthetic pesticides are known to have adverse effects on beneficial organisms such as predators and parasitoids. An assessment of the effect of SOEs on multiple beneficial insects from different insect orders in citrus ecosystems revealed a high survival rate of ladybeetles (Coccinellidae), lacewings (Chrysopidae), and parasitoids of red scale insects (Anthocoridae) even when exposed to 8,000 ppm (i.e., parts per million) which represents twice the recommended field application rate (2024 TR, lines 238-242). Soil organisms and non-target insects may be exposed to SOEs during and after applications until the compounds

biodegrade in ~5 days. Direct and specific detrimental effects from SOEs on soil organisms have not been studied extensively. Available literature does not show detrimental physiological effects of SOEs on soil organisms, soil microbiome, or non-target insects (2024 TR, lines 257-260). Current literature states that SOEs have low toxicity and biodegrade rapidly. When SOEs are applied according to EPA-approved label directions, no direct exposure of birds or aquatic organisms to SOEs is expected (2005 TR, lines 201-202).

Effect on Human Health:
SOEs have low toxicity to humans and are produced in a closed system. The 2005 technical report (TR) states that no sub-chronic, chronic, immune, or endocrine issues have been identified (2005 TR, lines 303-304). An ocular risk exists but it is unlikely if the product is used according to label (2005 TR, lines 309-311).

Comparison with natural (Nonsynthetic alternatives)
The 2024 TR did not list any natural alternatives to sucrose octanoate esters for use in the management of Varroa mites in honeybee hives. In the absence of research studies that compare SOEs to nonsynthetic alternatives, the 2024 TR covered the performance and characteristics of nonsynthetic pesticides used in managing pests in crop production. Alternatives listed include neem extract, Pyrethrins, *Bacillus thuringiensis* (Bt), Spinosad, miscellaneous botanicals such as essential oils derived from thyme and eucalyptus, garlic extracts and biological control agents. Even though neem extracts were reported to be effective against listed insect pests, cases of neem oil poisoning in humans were reported (2024 TR, lines 299-300). Pyrethrins can harm beneficial insects such as bees and aquatic organisms if used improperly (2024 TR, lines 312-314). *Bacillus thuringiensis* affects a broader range of organisms than SOEs (2024 TR, line 332). There are reports of non-targeted adverse effects on several groups of insects that are closely related or have an affinity to targeted insects (2024 TR, lines 337-339). At regular field application rates, Bt has been reported to impair the growth and developmental time of non-target true flies such as *Drosophila melanogaster* (common fruit fly) larvae (2024 TR, lines 341-344). There are also reports of insect pest resistance to Bt products (2024 TR, line 352). Spinosad breaks down quickly in the environment and is considered safe for humans and most beneficial insects. It can, however, be toxic to bees if applied directly to flowering plants. Spinosad application has also been demonstrated to have adverse effects on genes associated with energy production in honeybees (2024 TR, lines 367-368).

Discussion

Public Comments
There were no substantive comments from beekeepers during the Spring 2018 public comment period on the continued listing of SOEs at §205.603(b); nevertheless, there were comments from other livestock producers who stated that they were aware that SOEs are an important tool for beekeepers in controlling Varroa mites in honeybees.

In 2018, a public health advocacy organization commented that in view of the restrictive use of SOEs and the difficulty that beekeepers are experiencing in maintaining the health of honeybee colonies, they supported keeping SOEs on the National List.

Rationale for Previous NOSB Recommendation
During the sunset review of sucrose octanoate esters (SOEs) in 2018, information at the time indicated that there were no EPA registered products formulated using SOEs as an ingredient. There were also no public comments received from beekeepers stating the need for this material. Alternatives that are more effective have become available since SOEs were first placed on the National List. Based on the information at the time, the NOSB determined that SOEs were not essential. Additional clarification was provided during a

Subcommittee meeting in January 2025. The absence of public comments from organic beekeepers on SOEs was explained to be because organic honey is sourced mainly from outside the United States. The views of these international organic honey producers were not captured because they do not participate in NOSB meetings.

Questions to our Stakeholders

1. Is there current information on the use of SOE formulations by farmers? Is there a large demand for SOE formulations by livestock producers?

EPA List 4 Inerts

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; 10/2020 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 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

Subcommittee Review
As explained below, the LS expects this listing to be fully replaced before its next sunset review.

Use
Inert ingredients in pesticide formulations are added to enhance functionality and efficacy. Any of the pesticides approved for organic use may contain inert ingredients. For example, surfactants may improve the solubility and half-life of active pesticide ingredients. As described in Shistar (Shistar, T. “Inert” Ingredients Used in Organic Production, Beyond Pesticides, Washington, D.C., 2017), “The relatively few registered pesticides allowed in organic production are contained in product formulations with so-called “inert” ingredients that are not disclosed on the product label. The “inerts” make up the powder, liquid, granule, or spreader/sticking agents in pesticide formulations. The “inerts” are typically included in products with natural or synthetic active pesticide ingredients recommended by the National Organic Standards Board (NOSB) and listed by the National Organic Program (NOP) on the National List of Allowed and Prohibited Substances.”

Manufacture
Since this listing covers many different materials, the manufacture of these substances cannot be specifically stated.

International Acceptance
Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Formulants used in crop production aids may only be used with substances listed in Column 2 of this table. Only formulants classified as List 4A or 4B by the Pest Management Regulatory Agency (PMRA) or derived from biological or mineral sources may be used with substances in Table 4.2 (Column 2). Formulants classified as List 3 by PMRA may be used with passive pheromone

dispensers. Formulants classified as List 4A, 4B or 3 by PMRA are not subject to 1.4 or 1.5 of CAN/CGSB-32.310. Formulants classified as List 1 or 2 by PMRA are prohibited (Table 4.2 – Substances for crop production, CAN/CGSB-32.311-2020).

- Formulants (inerts, excipients) shall be used in conjunction with substances listed in Table 5.3. Formulants are not subject to 1.4 or 1.5 of CAN/CGSB-32.310 or 5.1.2 of this standard (Table 5.3 – Health care products and production aids, CAN/CGSB-32.311-2020).
- Formulants may only be used with substances listed in Table 8.2. Only formulants classified as List 4A or 4B by the Pest Management Regulatory Agency (PMRA) or derived from biological or mineral sources may be used with substances in Table 8.2. Formulants classified as List 3 by PMRA may be used with passive pheromone dispensers. Formulants classified as List 4A, 4B or 3 by PMRA are not subject to 1.4 or 1.5 of CAN/CGSB-32.310. Formulants classified as List 1 or 2 by PMRA are prohibited (Table 8.2 – Facility pest management substances, CAN/CGSB-32.311-2020).
- Formulants may only be used with substances listed in Table 8.3. Only formulants classified as List 4A or 4B by the Pest Management Regulatory Agency (PMRA) or are non-synthetic may be used with substances in Table 8.3. Formulants classified as List 3 by PMRA may be used with passive pheromone dispensers. Formulants classified as List 4A, 4B or 3 by PMRA are not subject to 1.4 or 1.5 of CAN/CGSB-32.310. Formulants classified as List 1 or 2 by PMRA are prohibited (Table 8.3 – Post-harvest substances, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- The following products and substances referred to in Article 2(3) of Regulation (EC) No 1107/2009 shall be allowed for use in organic production, provided that they are authorised pursuant to that Regulation: (a) safeners, synergists, and co-formulants as components of plant protection products; (b) adjuvants that are to be mixed with plant protection products (General production rules, EC No. 2018/848).
- In accordance with Article 9(3) of Regulation (EU) 2018/848, safeners, synergists, and co-formulants as components of plant protection products, and adjuvants that are to be mixed with plant protection products shall be allowed for use in organic production, provided that they are authorised pursuant to Regulation (EC) No 1107/2009. The substances in this Annex may only be used for the control of pests as defined in Article 3(24) of Regulation (EU) 2018/848 (Annex I: Active substances contained in plant protection products authorised for use in organic production, EC No. 2021/1165).

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

- Inerts are not explicitly mentioned in the regulations.

International Federation of Organic Agriculture Movements (IFOAM)

- Organic crop production ensures that co-formulants (e.g. inerts and synergists) in formulated farm input products are not carcinogens, mutagens, teratogens or neurotoxins (Crop Production, IFOAM NORMS 2014).
- Recommendation: In case operators need to use commercial formulated inputs, preference should be given to formulations approved for use in organic agriculture by a specialized organic material review organization/program (Pest, Disease, and Weed Management, IFOAM NORMS 2014).
- Any formulated input shall have only active ingredients listed in Appendix 3. All other ingredients shall not be carcinogens, teratogens, mutagens, or neurotoxins (Pest, Disease, and Weed Management, IFOAM NORMS 2014).

Japan Agricultural Standard (JAS) for Organic Production

- Inerts are not explicitly mentioned in the regulations.

Human Health and Environmental Issues
As noted below, some of the materials listed on EPA 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
Inerts are not necessarily biologically or chemically inert. They may be relatively benign or may be documented as harmful to the environment or human health. Without a way to individually evaluate each substance listed on EPA List 4 or to evaluate substances as a group, it is difficult to discern the acceptability of each substance for use in organic agriculture.

Presently, the National List, under §205.601(m), references the EPA List 4 – Inerts of Minimal Concern, as acceptable in organically approved pesticide formulations. List 4, however, is outdated and no longer maintained by EPA. The list of inerts that is referenced for review of products for organic certification was last updated in August 2004 (EPA website https://www.epa.gov/pesticide-registration/epas-national-organic-program-guidance) and may include materials that some stakeholders believe are inappropriate for organic agriculture. For example, nonylphenol ethoxylates (NPEs) are included on List 4. These materials are endocrine disruptors, may adversely impact fauna and flora, and have been identified by the California Department of Toxic Substances Safer Consumer Products program as a likely high priority chemical that should be formally phased out https://www.ams.usda.gov/sites/default/files/media/NPE%20Technical%20Evaluation%20Report%20%282015%29.pdf. If evaluated on an individual basis, NPEs would likely not meet OFPA criteria for acceptability.

The NOSB and NOP have struggled with how to evaluate the EPA List 4 – Inerts of Minimal Concern during sunset review. OFPA has specific criteria for inerts which states: "*(ii) … contains synthetic inert ingredients that are not classified by the Administrator of the Environmental Protection Agency as inerts of toxicological concern"* (§6517 C.1.B.ii). Due to EPA changes in its categorization of inerts and discontinued support for List 4, the NOSB (starting in 2010) adopted a series of recommendations to revise this sunset listing.

Most recently, the Agricultural Marketing Service (AMS) published an Advance Notice of Proposed Rulemaking (ANPR) incorporating several of these recommendations on September 2, 2022, which received extensive stakeholder feedback on updated references for inert ingredients in organic production. Subsequently, based on that feedback, the NOP requested that the NOSB evaluate four options for updating the National List. The NOSB has recommended two of them, plus "hybrid" versions of those two, at the Fall 2024 meeting. At the time of this review, the NOP is moving forward with the rule-making process based on this recommendation.

National List Motion, approved by NOSB, Fall 2024 (shown with changes from current language)**:**

> Motion to add individual substances identified in Appendix A] at 205.601(m)
>
> (m) As synthetic inert ingredients as classified by the Environmental Protection Agency (EPA), for use with nonsynthetic 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~~

~~(2) EPA List 3-Inerts of unknown toxicity-for use only in passive pheromone dispensers~~
(1) 1,2,3-Octadecenoate (CAS 9007-48-1)
(2) 12-Hydroxystearic acid-polyethylene glycol copolymer (CAS 70142-34-6)
(3) …

Motion to add individual substances identified in Appendix A] at 205.603(e)

(e) As synthetic inert ingredients as classified by the Environmental Protection Agency (EPA), for use with nonsynthetic 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~~
~~(2) EPA List 3-Inerts of unknown toxicity-for use only in passive pheromone dispensers~~
(1) 1,2,3-Octadecenoate (CAS 9007-48-1)
(2) 12-Hydroxystearic acid-polyethylene glycol copolymer (CAS 70142-34-6)
(3) …

OR

Motion to amend 205.601(m)

(m) ~~As s~~Synthetic inert ingredients as classified by the Environmental Protection Agency (EPA) and exempted from the requirement of a tolerance, for use with nonsynthetic 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, except for:
~~(1) EPA List 4-Inerts of Minimal Concern~~
~~(2) EPA List 3-Inerts of unknown toxicity-for use only in passive pheromone dispensers~~
(1) Alkylphenol ethoxylate substances
(2) Per- and polyfluoroalkyl substances

Motion to amend 205.603(e)

(e) ~~As s~~Synthetic inert ingredients as classified by the Environmental Protection Agency (EPA) and exempted from the requirement of a tolerance, for use with nonsynthetic 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, except for:
~~(1) EPA List 4-Inerts of Minimal Concern~~
~~(2) EPA List 3-Inerts of unknown toxicity-for use only in passive pheromone dispensers~~
(1) Alkylphenol ethoxylate substances
(2) Per- and polyfluoroalkyl substances
(3) …

The Crops Subcommittee expects an improved listing to be implemented by the NOP in the next two years, replacing the reference to List 4. In the meantime, in order to maintain continuity in pesticide formulations used by organic farmers, we recommend that List 4 Inerts be relisted in this review at 205.601(m) on the National list.

Questions to our Stakeholders

1. Do stakeholders agree that List 4 Inerts should be relisted until they are replaced with a new listing via the rulemaking process currently underway?

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; 10/2020 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 renewal notice published 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

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 (2015 TR, lines 38-41).

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 (2015 TR, lines 75-77). "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 (2015 TR, lines 46-50).

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 (2015 TR, lines 51-55).

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 (2015 TR, lines 60-64).

International Acceptance

Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Formulants used in crop production aids may only be used with substances listed in Column 2 of this table. Only formulants classified as List 4A or 4B by the Pest Management Regulatory Agency (PMRA) or derived from biological or mineral sources may be used with substances in Table 4.2 (Column 2). Formulants classified as List 3 by PMRA may be used with passive pheromone dispensers. Formulants classified as List 4A, 4B or 3 by PMRA are not subject to 1.4 or 1.5 of CAN/CGSB-32.310. Formulants classified as List 1 or 2 by PMRA are prohibited (Table 4.2 – Substances for crop production, CAN/CGSB-32.311-2020).
- Formulants (inerts, excipients) shall be used in conjunction with substances listed in Table 5.3. Formulants are not subject to 1.4 or 1.5 of CAN/CGSB-32.310 or 5.1.2 of this standard (Table 5.3 – Health care products and production aids, CAN/CGSB-32.311-2020).
- Formulants may only be used with substances listed in Table 8.2. Only formulants classified as List 4A or 4B by the Pest Management Regulatory Agency (PMRA) or derived from biological or mineral sources may be used with substances in Table 8.2. Formulants classified as List 3 by PMRA may be used with passive pheromone dispensers. Formulants classified as List 4A, 4B or 3 by PMRA are not subject to 1.4 or 1.5 of CAN/CGSB-32.310. Formulants classified as List 1 or 2 by PMRA are prohibited (Table 8.2 – Facility pest management substances, CAN/CGSB-32.311-2020).
- Formulants may only be used with substances listed in Table 8.3. Only formulants classified as List 4A or 4B by the Pest Management Regulatory Agency (PMRA) or are non-synthetic may be used with substances in Table 8.3. Formulants classified as List 3 by PMRA may be used with passive pheromone dispensers. Formulants classified as List 4A, 4B or 3 by PMRA are not subject to 1.4 or 1.5 of CAN/CGSB-32.310. Formulants classified as List 1 or 2 by PMRA are prohibited (Table 8.3 – Post-harvest substances, CAN/CGSB-32.311-2020).

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Excipients are not explicitly mentioned in the regulations.

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

- Excipients are not explicitly mentioned in the regulations.

International Federation of Organic Agriculture Movements (IFOAM)

- Excipients are not explicitly mentioned in the regulations.

Japan Agricultural Standard (JAS) for Organic Production

- Excipients are not explicitly mentioned in the regulations.

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 (2015 TR, lines 542-552).

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 recommending that the pharmaceutical industry 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. (2015 TR, lines 554-563).

Health Issues

There is no literature to indicate specific human health effects through the use of excipients in livestock healthcare 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 (2015 TR, lines 571-573). 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 includes 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 (2015 TR, lines 581-586).

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 on traces of antibiotics, but formulations specifically allowed in §205.603 can also appear in milk and meat (2015 TR, lines 589-592). 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 (2015 TR, lines 594-595). 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 (2015 TR, lines 608-613, 615-617).

Discussion

In the previous sunset review, 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 did not recommend removal from the National List.

Questions remain as to how excipients are reviewed. Parts 3) and 4) of the annotation allow for myriad excipients to be used in livestock products subject to APHIS and FDA approval, without necessarily complying with OFPA criteria. While this could present a problem, most livestock veterinary treatments are administered in small doses, and there is a significant withdrawal period. This minimizes any effect that the active ingredients or excipients can have on the consumer or the environment. Compared to review and possible disallowance of hundreds or thousands of needed veterinary treatments, the current approach may be optimal in the real world.

Questions to our Stakeholders

1. Is the current annotation sufficient for effective use by certifiers?
2. Is the current review process sufficient to ensure that excipients meet OFPA criteria? If not, are there alternative methods, lists, or classifications that could comply?

Strychnine

Reference: §205.604 Nonsynthetic substances prohibited for use 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; 10/2020 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 08/03/2021 (86 FR 41699)
Sunset Date: 3/15/2027

Subcommittee Review

Use
Strychnine is a toxic alkaloid that is a transparent crystal or white, crystalline powder. It is colorless, odorless, and has a bitter taste. 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.

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 quickly to produce 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.

Manufacture
The main natural source of the alkaloid is extraction from the strychnine tree (*Strychnos nux-vomica*). This plant is found in southern Asia (India, Sri Lanka, and East Indies) and Australia.

International Acceptance

Canadian General Standards Board Allowed Substances List (CAN/CGSB 32.311-2020)

- Strychnine is not explicitly mentioned in the regulations.

European Economic Community (EEC) Council Regulation, EC No. 2018/848 and 2021/1165

- Strychnine is not explicitly mentioned in the regulations.

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

- Strychnine is not explicitly mentioned in the regulations.

International Federation of Organic Agriculture Movements (IFOAM)

- Strychnine is not explicitly mentioned in the regulations.

Japan Agricultural Standard (JAS) for Organic Production

- Strychnine is not explicitly mentioned in the regulations.

Human Health and Environmental Issues

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

Mammalian studies indicate that strychnine is 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 indicates that strychnine is moderately toxic to aquatic invertebrates.

Discussion

In 2017, the Crops Subcommittee determined that strychnine did not meet 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 at §205.604.

Questions to our Stakeholders

None