United States Department of Agriculture
Agricultural Marketing Service | National Organic Program
Document Cover Sheet
https://www.ams.usda.gov/rules-regulations/organic/petitioned-substances

Document Type:

☐ **National List Petition or Petition Update**

A petition is a request to amend the USDA National Organic Program's National List of Allowed and Prohibited Substances (National List).

Any person may submit a petition to have a substance evaluated by the National Organic Standards Board (7 CFR 205.607(a)).

Guidelines for submitting a petition are available in the NOP Handbook as NOP 3011, National List Petition Guidelines.

Petitions are posted for the public on the NOP website for Petitioned Substances.

☒ **Technical Report**

A technical report is developed in response to a petition to amend the National List. Reports are also developed to assist in the review of substances that are already on the National List.

Technical reports are completed by third-party contractors and are available to the public on the NOP website for Petitioned Substances.

Contractor names and dates completed are available in the report.

Poloxalene

Livestock

Identification of Petitioned Substance

Chemical Names:
Polyethylene-polypropylene glycol (USP); Polyoxyethylene-polyoxypropylene block copolymer

Other Names:
Poloxalene; Poloxamer; POP/POE condensate

Trade Names:
Bloat Guard, Bloat-Pac, Prolox Bloat Gel, Therabloat

CAS Numbers:
9003-11-6

Other Codes:
ACX no. X1017331-2

Summary of Petitioned Use

This limited scope technical report provides information to the National Organic Standards Board (NOSB) to support the sunset review of poloxalene, listed at 7 CFR 205.603(a)(26). This report focuses on how poloxalene, used in organic livestock production as an emergency treatment for bloat (per the substance's annotation), is manufactured.

Poloxalene was included on the National List of Allowed and Prohibited Substances (hereafter referred to as the "National List") with the first publication of the National Organic Program (NOP) Final Rule (65 FR 80548, December 21, 2000). The NOSB has continued to recommend its renewal in 2010, 2015, and 2020 (NOSB, 2010, 2015, 2020).

As poloxalene is listed at § 205.603, synthetic forms are allowed. The annotation for poloxalene specifies that it "only be used for the emergency treatment of bloat."

Evaluation Questions for Substances to be used in Organic Livestock Production

Evaluation Question #1(A): Describe if the substance is extracted from naturally occurring plant, animal, or mineral sources.

Poloxalene is a synthetic, nonionic surfactant used primarily as an antifoaming agent to prevent bloat in ruminants, such as cattle and sheep (Constable, 2022; Fubini & Divers, 2008). Poloxalene is not extracted from natural sources. Instead, it is a synthetic compound created through a chemical reaction that polymerizes ethylene oxide (EO) and propylene oxide (PO) (Carrà, Santacesaria, Morbidelli, & Cavalli, 1979; Carrà, Santacesaria, Morbidelli, Schwarz, et al., 1979a, 1979b; Feng et al., 2017; Huang et al., 2002).

Evaluation Question #1(B): Describe the most prevalent processes used to manufacture or formulate the petitioned substance. Include any chemical changes that may occur during manufacture or formulation of the substance.

Poloxalene is synthesized as a polyoxyethylene-polyoxypropylene block copolymer.[1] The manufacturing process involves the polymerization of ethylene oxide (EO) and propylene oxide (PO) to create a copolymer. Poloxalene has a hydrophobic core of polyoxypropylene (POP) and hydrophilic tails of polyoxyethylene (POE). This structure allows poloxalene to act as a surfactant, reducing the surface

[1] A copolymer is a polymer made from two or more different types of monomers that are chemically bonded together in a repeating sequence or pattern within the molecular chain. These different monomers can combine in various arrangements, giving the copolymer specific properties that may differ from those of homopolymers, which are made from only one type of monomer.

A block copolymer is a specific type of copolymer where two or more distinct types of monomers are grouped together in contiguous "blocks" along the polymer chain. Each block consists of repeating units of the same monomer.

tension of gas bubbles. Poloxalene destabilizes foam and allows gas to release from the rumen (Huang et al., 2002; Pandit et al., 2000).

The generalized chemical formula for poloxalene is:

$$HO(C_2H_4O)_a(C_3H_6O)_x(C_2H_4O)_aH$$

(C_2H_4O represents the EO unit, C_3H_6O represents the PO unit, a and x denote the number of repeating ethylene oxide and propylene oxide units)

The number of repeating EO units are typically 11 to 13, whereas the number of repeating PO units is typically 32 to 36. The molecular weight range of poloxalene is ~ 2800 to 3150 Da (21 CFR 573.760).[2]

The process for synthesizing poloxalene always involves the polymerization of ethylene oxide and propylene oxide to form a block copolymer. However, the process manufacturers use to produce the monomers can vary. Below, we discuss propylene oxide and ethylene oxide manufacturing first, followed by the steps involved in the polymerization reaction used to synthesize poloxalene.

Poloxalene precursor manufacturing process: propylene oxide

Hydroperoxide process

In this process, propylene is oxidized with an organic hydroperoxide, such as tert-butyl hydroperoxide (TBHP), using a molybdenum catalyst (Vaishali & Naren, 2016). The molybdenum catalyst facilitates the transfer of oxygen from the hydroperoxide to the propylene.

The reaction mixture contains propylene oxide, tert-butanol, unreacted hydroperoxide, and by-products. The mixture is separated and purified, typically via distillation, to isolate propylene oxide (Russo et al., 2013).

According to Yang, et al. (2024), the hydroperoxide process is the most commonly used method for propylene oxide production.

Chlorohydrin process

The chlorohydrin process is a well-established method for producing propylene oxide. It involves the reaction of propylene with chlorine and water to form propylene chlorohydrin, followed by dehydrochlorination using caustic soda or lime to produce propylene oxide (Carrà, Santacesaria, Morbidelli, & Cavalli, 1979; Carrà, Santacesaria, Morbidelli, Schwarz, et al., 1979a, 1979b; Nijhuis et al., 2006). However, this method is being phased out due to the large amounts of unwanted co-products that are created (Everchem Specialty Chemicals, 2023; Tsuji et al., 2006; Yamamoto & Tsuji, 2007).

Direct oxidation

In this process (see *Equation 1*), propylene is oxidized using a catalyst in the presence of oxygen (air) and sometimes a co-reductant, such as hydrogen, to form propylene oxide. Various catalytic systems may be utilized, including silver-based catalysts (Khatib & Oyama, 2015).

$$CH_3CHCH_2 + \frac{1}{2}O_2 \rightarrow CH_3CHCH_2O$$

(propylene) + (oxygen) → (propylene oxide)

Equation 1

The process is efficient for producing propylene oxide due to the use of selective catalysts, the reduced production of unwanted by-products, and the efficient use of oxygen (Allard, 2023; Feng et al., 2017). Since the process uses oxygen as the oxidant, it is considered more environmentally friendly as compared

[2] One Da (or dalton) is equivalent to 1 atomic mass unit, or 1/12th the mass of a carbon-12 atom.

to other methods that may involve chlorinated compounds or other hazardous materials (Khatib & Oyama, 2015).

Cumene process

Due to unwanted co-products produced in the chlorhydrin process, Sumitomo Chemical developed a new process that went into production in 2003 (Tsuji et al., 2006; Yamamoto & Tsuji, 2007). In this process, cumene (a benzene derivative, typically from petroleum sources) is reacted with atmospheric air to produce cumene hydroperoxide. This is then reacted with propylene to form propylene oxide, using a special catalyst. Cumene itself acts as a recyclable catalyst, and is reformed in the final step (Tsuji et al., 2006; Yamamoto & Tsuji, 2007).

Poloxalene precursor manufacturing process: ethylene oxide

Direct oxidation

In this process (see *Equation 2*), ethylene is reacted with oxygen in the presence of a silver catalyst to produce ethylene oxide (Pu et al., 2019; Rebsdat & Mayer, 2001).

$$C_2H_4 + \frac{1}{2}O_2 \rightarrow C_2H_4O$$

(ethylene) + (oxygen) → (ethylene oxide)

Equation 2

Poloxalene precursor manufacturing process: bifunctional alcohol

Bifunctional alcohols are organic compounds that contain two hydroxyl groups (-OH) attached to different carbon atoms within the molecule. Due to their reactive properties, these compounds are commonly used for initiating polymerization reactions for the preparation of poloxalene or other polymers (Herzberger et al., 2016). Common bifunctional alcohols used for poloxalene synthesis include ethylene glycol (Yue et al., 2012), and propylene glycol (Herzberger et al., 2016).

Poloxalene manufacturing process

Once both monomers (propylene oxide and ethylene oxide) are available, they are copolymerized to form poloxalene (Bar-ilan & Zilkha, A., 1970; Herzberger et al., 2016; Steiner et al., 1964; Vollhardt & Schore, 1987). Manufacturers typically do this in the presence of an initiator or catalyst, such as potassium hydroxide (KOH), which facilitates the polymerization reaction. The manufacturing process consists of three steps:

1) initiation
2) propagation
3) termination

Initiation

The reaction begins with a bifunctional alcohol, which acts as the initiator and forms the polyoxyethylene block by reacting with ethylene oxide (see *Equation 3*) poloxalene (Bar-ilan & Zilkha, A., 1970; Herzberger et al., 2016; Steiner et al., 1964; Vollhardt & Schore, 1987).

$$ROH + CH_2CH_2O \rightarrow RO(CH_2CH_2O)_nH$$

(bifunctional alcohol) + (ethylene oxide) → (polyoxyethylene block)

Equation 3

Propagation

Next, propylene oxide is added to extend the polymer chain, forming the polyoxypropylene block (see *Equation 4*) poloxalene (Bar-ilan & Zilkha, A., 1970; Herzberger et al., 2016; Steiner et al., 1964; Vollhardt & Schore, 1987).

$$RO(CH_2CH_2O)_nH + CH_3CHCH_2O + KOH \rightarrow RO(CH_2CH_2O)_n(CH(CH_3)CH_2O)_mHK^+ + OH^-$$

(polyoxyethylene block) + (propylene oxide) + (potassium hydroxide catalyst) → (polyoxypropylene block) + hydroxide ion

Equation 4

Termination

The reaction is terminated once the appropriate molecular weight (2800-3150 Da) and block composition are achieved (Feng et al., 2017; Vaishali & Naren, 2016). Manufacturers monitor these parameters through various sensors and analytical techniques, as described by Liu et al. (2024). Once the desired molecular weight and block structure are achieved, the reaction is stopped by adding a terminating agent or by quenching the reaction.

Manufacturers typically use alcohols, such as methanol or ethanol to terminate the polymerization reaction, but acids may also be effective (Feng et al., 2017). These agents react with the potassium catalyst (see *Equation 5*). The alcohols convert the polymer chain ends into inert species and neutralize the potassium ion. In some cases, acids, such as acetic acid, can be used to neutralize the basic catalyst and terminate the polymerization (Feng et al., 2017).

$$ROK^+ + CH_3OH \rightarrow ROH + CH_3OK^+$$

(polyoxypropylene with potassium catalyst) + (methanol) → (polyoxypropylene) + (potassium methoxide)

Equation 5

In some cases, acids, such as acetic acid, can be used to neutralize the basic catalyst and terminate the polymerization (see *Equation 6*).

$$ROK^+ + CH_3COOH \rightarrow ROH + CH_3COOK^+$$

(polyoxypropylene with potassium catalyst) + (acetic acid) → (polyoxypropylene) + (potassium acetate)

Equation 6

To terminate the reaction by quenching, manufactures use two different techniques (Feng et al., 2017):

- Rapidly cooling the reaction mixture can effectively stop the polymerization by reducing the reactivity of the monomer and the catalyst.
- Adding a large volume of an inert solvent can dilute the reactants and catalysts, decreasing their effective concentration and halting the reaction.

Evaluation Question #1(C): Based on the manufacturing process description, discuss if the substance is classified as synthetic or nonsynthetic. [7 U.S.C. 6502(21), NOP 5033-1]

Below, we evaluate poloxalene against Guidance NOP 5033-1 *Decision Tree for Classification of Materials as Synthetic or Nonsynthetic* (NOP, 2016).

1. *Is the substance manufactured, produced, or extracted from a natural source?*

No. Poloxalene is not manufactured, produced or extracted from a natural source. It is a synthetic compound, created through a chemical reaction that polymerizes ethylene oxide and propylene oxide, materials which themselves are also synthetic.

Thus, the material is synthetic according to the decision tree.

Evaluation Question #1(D): Does the substance in its raw or formulated forms contain nanoparticles?
We did not find literature that specifically describes the use of poloxalene-based nanoparticles for bloat prevention in livestock. As a surfactant, poloxalene can be used in its original polymer form to treat bloat and does not require nanoparticle formulation (Bartley et al., 1975).

However, other poloxamers, such as polaxamer 407, can be formulated as nanoparticles (Allotey-Babington et al., 2018; Giuliano et al., 2018; Johnston et al., 1992; Li et al., 2023; Pec et al., 1992; Zhang et al., 2016).

Evaluation Question #1(E): Is the substance created using Excluded Methods?
Poloxalene is not created using any of the excluded methods described by NOSB.

Poloxalene is not manufactured from agricultural raw materials or from other biological raw materials, such as those produced by fermentation or enzymatic action, but originates from petrochemical derivatives (Nijhuis et al., 2006; Rebsdat & Mayer, 2001; Tsuji et al., 2006).

Report Authorship

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