Fatty Alcohols (Octanol and Decanol)

Crops

Identification of Petitioned Substance: Fatty Alcohols

Chemical Names:

Fatty Alcohols (54.5% Decanol, 45.1% Octanol, 0.4% Hexanol); octan-1-ol; decan-1-ol

Other Name: Octyl-Decyl Alcohol, 1-Octanol, 1 Octanol, Alcohol, n-Octyl, n Octanol, n Octyl Alcohol, n-Octanol, n-Octyl Alcohol, 1-decanol; n-decanol; n-decyl alcohol; n-decyl alcohol, aluminum salt; n-decyl alcohol, magnesium salt; n-decyl alcohol, sodium salt; n-decyl alcohol, titanium salt

Trade Names:

Kleen-tac 85, O-Tac, Green Tac, Ten-Tac, Sucker-Plucker, Alfol 80, and others.

CAS Numbers:

68603-15-6; 112-30-1; 66455-17-2; 85566-12-7

Other Codes:

Octanol: InChI=1S/C8H18O/c1-2-3-4-5-6-7-8-9/h9H,2-8H2,1H3; InChI Key=KBPLFHHGFOOTCA-UHFFFAOYSA-N; Canonical SMILES=CCCCCCCCO; EC Number= 203-917-6, 271-642-9, 606-925-1; ICSC Number=1030, 1170; RTECS Number=RH6550000, RH795000; UNII=NV1779205D;

Decanol: InChI= 1S/C10H22O/c1-2-3-4-5-6-7-8-9-10-11/h11H,2-10H2,1H3; InChI Key= MWKFXSUHUHTGQN-UHFFFAOYSA-N; Canonical SMILES= CCCCCCCCCCO; EC Number= 203-956-9, 266-367-6, 253-173-1, 287-621-2, 613-644-8; ICSC Number=1490; RTECS Number=HE4375000; UN Number=3082, 1987; UNII=89V4LX79

Summary of Petitioned Use

A petition was received by the National Organic Program to add Fatty alcohols, a mixture of aliphatic alcohols, hexanol, octanol and decanol to the National list 7 CFR 205.601 (k) under the heading plant growth regulator. The petitioned use for a mixture of fatty alcohols, consisting mainly of octanol and decanol, is topping and sucker control on organic crops.

Characterization of Petitioned Substance

Composition of the Substance:

Monohydric aliphatic alcohols containing six to ten carbons are called lower alcohols. Those containing twelve to twenty carbons are called higher alcohols (Atwood, 1963). Historically, lower and higher alcohols were derived from natural fats, oils and waxes hence the name fatty alcohols. Now a similar mixture of fatty alcohols that is synthetically produced from petrochemical feedstocks, is widely available (NPCS Board of Consultants & Engineers, 2010). The C_6-C_{12} linear alcohols are used for plasticizers, surfactants, tobacco sucker control, mining chemicals and in the manufacture of fatty amines.

ALFOL 810 Alcohol, a product containing C_6-C_{12} linear alcohols was the first mixed fatty alcohol product registered with the Environmental Protection Agency as a tobacco topping and suckering agent. It was registered by the Continental Oil Company under EPA reg. no. 39496-1. ALFOL 810 has the same composition as Mascol-80 which is referenced in the petition with EPA registration number 63896-1 (Table 1).

The Alfol process to produce fatty alcohols combines aluminum, ethylene, hydrogen and air to synthetically produce a mixture of lower and higher alcohols (Atwood, 1963). However, sufficient quantities of plant derived raw materials (e.g. palm kernel oil) for this product are available. The Davy process is used to produce fatty alcohol from vegetable oils. Fair products, Inc., mentioned in this petition, and the Drexel Chemical Company currently market fatty alcohols for tobacco sucker control. Drexel's tobacco sucker control agent is called "Sucker-Plucker." It contains 85% active ingredients (fatty alcohols) and 15% non-active ingredients. The non-active label ingredient polysorbate-80 (tween-20) is a surfactant essential to the effectiveness of the fatty alcohols (Tso et al., 1975). The EPA registration number for this product is 19713-35 (Table 1). It is derived from a fatty alcohol mixture typically containing C_6 0.5%, C_8 42.0%, C_{10} 56% and C_{12} 1.5% linear alcohols (EPA, 1993, 2004, 2011). A similar product to "Sucker-Plucker" from Fair products, Inc. is cited in this petition as O-TAC Plant contact agent (EPA reg. no. 51873-18) containing 36.2% Octanol, 48.2% decanol and 0.3% dodecanol (Table 1). O-TAC is currently described as a plant control agent for organic, purity residue clean (PRC) and maleic hydrazide free tobacco. Table 1 provides information about several fatty alcohol products for tobacco topping and suckering.

Table 1 Fatty Alcohol Products for Tobacco Topping and Suckering

Fatty Alcohol Product Name	Composition on EPA registered Label (percent)				EPA Registration Number
	C_6	C_8	C_{10}	C_{12}	
ALFOL 810	≤ 1	39-47	51-59	≤ 1	39496-1
Mascol-80	-	45.1	54.5	-	63896-1
Sucker-Plucker	0.5	42.0	48.2	0.3	19713-35
O-TAC	-	36.2	48.2	-	51873-18
N-TAC		45	55		51873-18

Source or Origin of the Substance:

Petroleum derived feedstocks are the primary source material for synthetically produced medium chain length lower and higher alcohols. However, palm, palm kernel and coconut oils are also available sources for producing fatty alcohols in the C_8-C_{14} chain lengths (Reck, 1985). Because of the importance of fatty alcohols in many industries, there is significant ongoing research in producing medium chain length fatty alcohols via fermentation in yeast or bacteria, i.e. enzymatic reduction of fatty acids. Although reports have shown positive findings, this production route is not yet available commercially. Therefore, naturally produced fatty alcohols are not yet available in sufficient quantities for commercial use as topping and suckering agents (Wang, 2016).

Properties of the Substance:

Fatty alcohols produced from palm oil, palm kernel oil and coconut oil by the Davy process for use as tobacco suckering agents are aliphatic alcohols with six to twelve carbons; however the most abundantly produced fatty alcohols in this mixture are caproic alcohol, caprylic alcohol, and capric alcohol (Tables 2, 3, Fig. 1). The primary alcohols exhibit some trends. For example, for each additional –CH_2- unit the normal boiling point increases about 20°C, the specific gravity increases 0.003 units and the melting point increases about 10°C in the lower range and about 4°C in the higher range. Water solubility decreases and oil solubility increases with increasing molecular weight. The fatty alcohols are all liquid with light natural fruity odors (NPCS, 2010). Both the density and viscosity of fatty alcohols increase with increasing molecular weight (Rauf et al., 1983).

Specific Uses of the Substance:

Fatty alcohols, octanol and decanol are used to chemically remove flower buds and suckers from tobacco plants. Removal of the flower tops and the suckers encourages the growth of larger leaves. The use of fatty alcohols is an alternative to two laborious hand operations in tobacco production. Topping or removal of buds or flowers and subsequent removal of suckers (lower leaves) by hand requires ten or more hours per acre. A course spray of 5% decanol or a combination of decanol and octanol applied before bud formation inhibits the formation of the bud. Fatty alcohol dripping down the stem of the plant inhibits sucker formation. Yields are also increased with the use of this treatment (USDA-ARS, 1970).

Table 2 Physical properties of the low molecular weight fatty alcohols*

IUPAC name	Common name	CAS registry number	Molecular formula	MW	Hydroxyl number	Melting point, °C	Boiling point,°C (p.kPa)
1-Hexanol	Caproic alcohol	111-27-3	$C_6H_{14}O$	102.2	548	-52	157
1-Heptanol	Enanthic alcohol	111-70-6	$C_7H_{16}O$	116.2	482	-30	176
1-Octanol	Caprylic alcohol	111-87-5	$C_8H_{18}O$	130.2	430	-16	195
1-Nonanol	Pelargonic alcohol	143-08-8	$C_9H_{20}O$	144.3	388	-4	213
1-Decanol	Capric alcohol	112-30-1	$C_{10}H_{22}O$	158.3	354	7	230
1-Undecanol	-	112-42-5	$C_{11}H_{24}O$	172.3	326	16	245
1-Dodecanol	Lauryl alcohol	112-53-8	$C_{12}H_{26}O$	186.3	300	23	260

from (Condea, 2000)

Approved Legal Uses of the Substance:

Fatty (aliphatic) alcohols containing a mixture of six, eight, ten and twelve carbons are approved by the US Environmental Protection Agency as the active ingredients for use as plant regulators for tobacco sucker control. Synthetic hexyl-, octyl- and decyl-alcohol maybe safely used in food and in the synthesis of food components provided that the alcohol's purity of the alcohol is 99% or greater. Synthetic fatty alcohols may only be used as substitutes for and to the extent that naturally derived fatty alcohols are found in foods (US FDA, 21 CFR §172.864). The US Department of Agriculture does not regulate the use of fatty alcohols for tobacco sucker control.

Action of the Substance:

Tobacco grades are based on the manufacturer's use for cured leaf. Grades are determined by certain physical and chemical properties. These properties are to a great extent determined by the position of the leaf on the plant. Usually leaves on the lowest part of the plant are not considered useful and removed in the suckering process (Calvert, 1956a). Tso (1964) first reported that alkyl esters of C_9 to C_{12} fatty acids inhibited the growth of axillary buds when applied to tobacco plants that had been topped (Tso et al., 1965). It was later reported that both lower alkyl esters of the C_8 to C_{12} fatty acids and the C_8 to C_{10} fatty alcohols in aqueous emulsions selectively killed the terminal meristems of a wide variety of plants without damaging the axillary meristems, foliage, or stem tissues of the plants (Cathey et al., 1966). Fatty alcohols depress the surface tension along chloroplast and mitochondrial membranes reducing phosphorylation by allowing water to leak into a hydrophobic lipid-protein environment inhibiting nicotinamide adenine dinucleotide dependent respiration (Thore and Baltscheffsky, 1965). The leakiness causes desiccation producing a burned appearance on the leaf tissue surface (Wheeler et al., 1991). Fatty alcohols with chain lengths of C_9, C_{10}, and C_{11} are better on a molar basis in selectively killing or inhibiting axillary and terminal bud growth of tobacco than the corresponding alkyl esters. Pure 1-decanol is reportedly the most effective topping and suckering agent (Steffens and McKee, 1969).

Without an appropriate surfactant both the C_9 to C_{11} methyl esters and the C_8 to C_{10} fatty alcohols exhibited nonselective tissue kill. At a concentration as low as $1.4x10^{-1}$ Molar, fatty alcohols cause immediate swelling of plant cell nuclei and a general cessation of cell division. Cells can become poly-nuclear as a result of exposure. At high concentrations fatty alcohols cause discolorization of root tips (Tso and Burk, 1969). However, with a surfactant the fatty alcohol emulsions are phytotoxic only to young meristematic tissue but caused little or no visible injury to more mature tissue (Steffens et al., 1967).

Topping and desuckering influence the yield and the quality of tobacco topping at the elongated bud stage with 16 leaves producing good yield and quality (Rao et al., 2003). The use of a 4% solution of 1-decanol applied by brushing 10 days after topping to the ten top axils of tobacco improved yield 67% over hand topping or treatments with Neem oil (Singh et al., 1998) The value of topped and suckered tobacco is higher. The use of 7.5% fatty alcohols with a surfactant improves both the price and the yield of burley tobacco. The alkaloid content in topped tobacco is higher than untopped, although total nitrogen was unchanged (Mylonas and Pangos, 1977).

If manual topping is performed on tobacco immediately after flower bud formation, manual suckering must be done frequently and regularly for the following three months as the axillary growth continues. Applying fatty alcohols as a topping agent and/or after topping can reduce the intensive labor required for topping and/or suckering (Bhat et al., 1994). Production lots of fatty alcohols contain a distribution of C_6-C_{12} chain length alcohols. The C_6 alcohols are not active suckercides. Whereas, C_8 chain length alcohol is about 50% effective. C_9, C_{10} and C_{11} chain length alcohols are 100% effective and C_{12} length alcohol is less effective. Higher chain lengths are not effective (Steffens et al., 1967). Suckering with fatty alcohols (C_6-C_{12}) generally produced a higher yield than manual suckering and does not alter USDA grading characteristics (Bruns, 1987).

Combinations of the Substance:

Fatty alcohols are combined with the surfactant polyoxyethylene (20) sorbitan monooleate, i.e. polysorbate 80, (tween 20). The surfactant permits an aqueous emulsion to be formed in the fatty alcohol solution, providing an even distribution of the active substance. There is clear evidence that the use of fatty alcohols for tobacco topping and suckering without a surfactant causes damage to the plant (Tso, 1964). Polysorbate 80 is a mixture of polyoxyethylene ethers of mixed partial oleic esters of sorbitol anhydrides and related compounds. It is approved by the FDA for safe use as an additive in many food applications (21 CFR §172.840).

Status

Historic Use:

Topping and suckering have been used in tobacco production for many years. Benefits include improved tobacco quality and a significant increase in tobacco yield (Hunter, 1954). Hand topping tobacco plants in late summer promotes full development of upper leaves adjacent to the terminal (flower) buds. Two weeks after topping, suckers that have subsequently developed along the stalk are also removed by hand. Suckers interfere with harvesting and curing operations. As much as ten or more hours per acre are spent on hand topping and suckering (USDA-ARS, 1970). Fatty alcohols were introduced in conventional tobacco production as chemical topping and suckering agents in the late 1960s. The use of fatty alcohols for topping and suckering also significantly increases yield (USDA-ARS, 1970).

Organic Foods Production Act, USDA Final Rule:

There is no reference in the National List for fatty alcohols. The proposal to add fatty alcohols to the National List specifies 7 CFR 205.601 (k) under the heading plant growth regulator. This section of the National List currently describes the use of the synthetic substance ethylene in organic crop production as a plant growth regulator for regulation of pineapple flowering. Fatty alcohols as aqueous emulsions inhibit terminal or axillary bud growth of tobacco plants. Contact with meristematic tissue affects plant development by preventing the growth flower buds and suckers (Tso et al., 1965; Steffens and Barer, 1984).

International

Canada - Canadian General Standards Board Permitted Substances List (CAN/CGSB-32.311-2015)

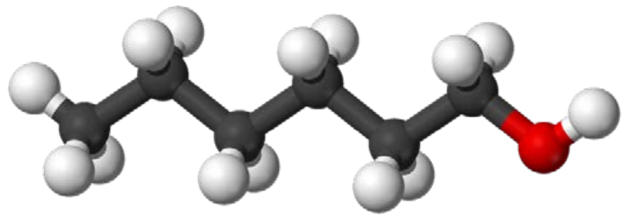
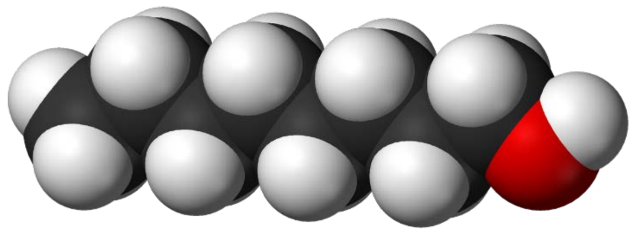
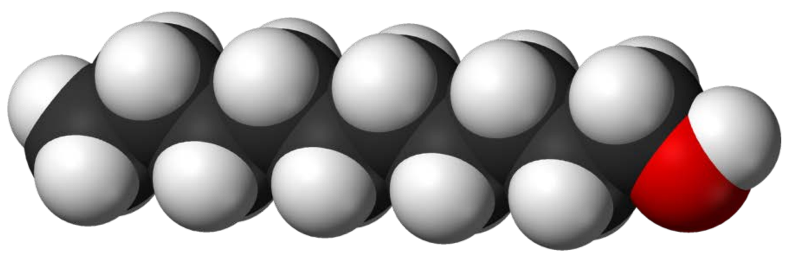
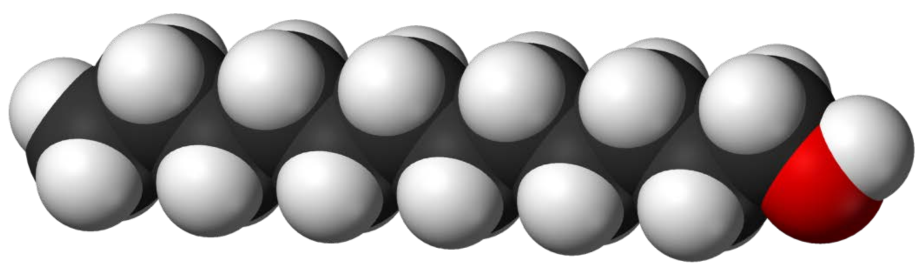
Fatty alcohols were not found in the Canadian standard (CAN/CGSB 2015).

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

Fatty alcohols were not found in the Codex Organic guidelines (GL 32-1999).

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

Fatty alcohols were not found in the EEC organic standards, EC No. 834/2007 and 889/2008.

Table 3 Space Filling Structure Renditions of Lower Fatty Alcohols*	
1-Hexanol	
1-Octanol	
1-Decanol	
1-Dodecanol	
*carbon=black, hydrogen=white, oxygen=red	

Japan Agricultural Standard (JAS) for Organic Production—

Fatty alcohols were not found in the MAFF organic standard.

International Federation of Organic Agriculture Movements (IFOAM) –

Fatty alcohols were not found in the IFOAM guidelines.

Evaluation Questions for Substances to be used in Organic Crop or Livestock Production

<u>Evaluation Question #1: Indicate which category in OFPA that the substance falls under:</u> (A) Does the substance contain an active ingredient in any of the following categories: copper and sulfur compounds, toxins derived from bacteria; pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals; livestock parasiticides and medicines and production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleansers? (B) Is the substance a synthetic inert ingredient that is not classified by the EPA as inerts of toxicological

concern (i.e., EPA List 4 inerts) (7 U.S.C. § 6517(c)(1)(B)(ii))? Is the synthetic substance an inert ingredient which is not on EPA List 4, but is exempt from a requirement of a tolerance, per 40 CFR part 180?

Fatty alcohols do not fall into any of the OFPA categories. Fatty alcohols produced as a mixture of four aliphatic alcohols are not considered inert by the Environmental Protection Agency nor are they included in List 4. Fatty alcohols may be registered with the EPA only for tobacco sucker control. N-decyl alcohol (decanol) and n-octyl alcohol (octanol) are individually approved by the US Food and Drug Administration (FDA) for food and non-food use as solvents or co-solvents (7 CFR §172.864 Synthetic fatty alcohols).

Evaluation Question #2: Describe the most prevalent processes used to manufacture or formulate the petitioned substance. Further, describe any chemical change that may occur during manufacture or formulation of the petitioned substance when this substance is extracted from naturally occurring plant, animal, or mineral sources (7 U.S.C. § 6502 (21)).

Fats and oils from animal and vegetable sources (oleochemical) are the primary feedstocks for manufacturing naturally sourced fatty alcohols. These feedstocks contain triglycerides composed of three fatty acids and glycerol. Alcohols are produced by esterification and/or reducing the fatty acid functional groups. Any triglyceride or fatty acid may be used as a raw material for fatty alcohol production (NCPS, 2010). The common sources are coconut oil, palm kernel oil, lard, tallow, rapeseed oil, soybean oil and corn oil. Producers of natural fatty alcohols typically make a broad range of fatty alcohol products having various carbon chain lengths. They vary feedstocks to meet market needs for particular alcohols and to take advantage of changes in the relative costs of the various feedstock material (NCPS, 2010; Reck, 1985).

There are a number of production processes for producing natural fatty alcohols. These have evolved since the 1930's to improve safety and efficiency. The earliest production began with the sodium reduction of the methyl esters from natural fats and oils. In this process molten sodium was mixed with dried ester and alcohol which acts as a hydrogen donor. Many safety precautions were necessary due to the large amount of metallic sodium used. A safer hydrogenolysis process was developed to replace the sodium reduction process. Triglycerides need to be refined to remove free fatty acids, phosphatides, sterols, and oxidation products as well as debris. This step is followed by esterification to produce fatty acid methyl esters and/or hydrogenolysis of methyl esters or fatty acids in the presence of a catalyst at high pressure and temperature to produce methanol and fatty alcohol. The final products are refined or distilled (Kreutzer, 1984).

In the Lurgi process fatty acids are first converted to wax esters and then hydrogenated over a fixed bed reactor. This differs from the Davy process since there is no conversion to methyl esters and fatty alcohols come directly from wax esters. The Lurgi process has been in commercial use since 2004. The Davy Process is used primarily for detergent alcohols with greater than 12 carbons; however, it can also be used for the production of plasticizer alcohols containing between 6 and 12 carbons. The Davy process provides an improved process for production of fatty alcohols by hydrogenation of lower alkyl esters, particularly methyl esters of fatty acids derived from natural triglycerides under conditions that minimize formation of byproduct alkanes and ethers followed by refining of the resulting ester containing product (Wilmott et al., 1992). Many production plants throughout the world have been licensed to produce fatty alcohols using the Davy process (Fig. 1).

Fatty alcohols are also produced synthetically from petroleum. Alkylaluminum derivatives are produced by adding hydrogen and ethylene to an aluminum slurry. Alkylaluminum reacts with ethylene to increase carbon chain length. Higher trialkylaluminum species produced by reacting ethylene with alkylaluminums under pressure at about $120^{o}C$ can be further reacted with ethylene at higher temperatures to give straight chain alcohols with up to 22 carbons (alfene process). Reaction of the higher trialkylaluminums with air and sulfuric acid yields higher n-alcohols: alfol process (Atwood, 1963; Continental Oil, 1962; 1973). The choice of catalyst and reaction conditions significantly affect the process (Miller, 1969). For fatty alcohol production, it is difficult to practice an esterification on a continuous basis, thus it is convenient to adopt batch processing.

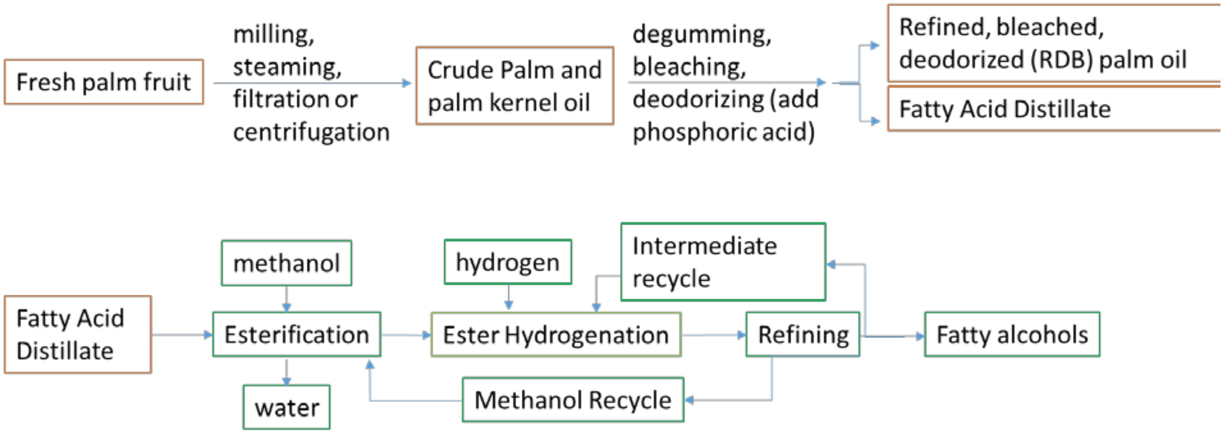


Fig. 1 Davy process for Fatty Alcohols production from olefins (Palm Oil)

<u>Evaluation Question #3:</u> Discuss whether the petitioned substance is formulated or manufactured by a chemical process, or created by naturally occurring biological processes (7 U.S.C. § 6502 (21)).

The present world capacity of plant derived and petroleum derived fatty alcohols is greater than two million metric tons/year. Much of this production goes in to making detergents or plastics. Petroleum derived fatty alcohols production is estimated to be just 23% of total global capacity, whereas plant derived fatty alcohols production is currently 77% of total global capacity (Oleoline, 2015). In the USA the bulk of fatty alcohols is of petrochemical origin, whereas in Europe more than 60% of the total volume is made from natural fats and oils (Kreutzer, 1984).

Fatty alcohols occur in free and esterified form in many animal and vegetable waxes. Although these waxes are normally composed of long carbon chains, 1-octanol and 1-decanol have also been found naturally in various food items (Mahadevan, 1978). The aliphatic alcohols are natural components of apples and oranges, and have been reported as a component of edible seeds, oils and fermented beverages (EPA, 2007). Aliphatic hydrocarbons can be converted to fatty alcohols by many organisms including bacteria with enzymes in the family of fatty acyl-CoA reductases (Roessler et al., 2014). Because fatty alcohols have important industrial uses as medicines, cosmetics, skin care products, detergents, fuels and plasticizers in addition to their role in tobacco production, extensive research to develop fermentation systems producing fatty alcohols has been undertaken over the past few years with the intention of industrial production in the near future (McCoy et al., 2010; Kallio et al., 2014). Naturally found strains of bacteria including *Escherichia coli*, *Salmonella spp*., *Klebsiella spp*., and *Enterobacter spp*. are known to excrete 1-octanol, 1-decanol and 1-dodecanol. Several, *E. coli* strains being examined for commercial scale production of 1-octanol and 1-decanol respectively produced as much as 508 and 740 nanograms/milliliter of culture (Hamilton-Kemp et al., 2005).

Mutations introduced into *Escherichia coli* strains have resulted in a number of commercially viable fermentation approaches to produce n-alcohols (Dellomonaco et al., 2011). By favoring chain elongation in an anaerobic bacterial growth rescue cycle, enzymes for the production of n-hexanol and n-octanol can be enriched increasing the production of fatty alcohols (Machado et al., 2012). High levels of fatty alcohols (> 350 milligrams/liter of culture) can be produced in *E. coli* from a class of enzymes called carboxylic acid reductases (CAR). These enzymes catalyze the reduction of aromatic and short chain carboxylic acids to their respective aldehydes in the presence of adenosine triphosphate (ATP) and nicotinamide adenine dinucleotide phosphate (Akhtar et al., 2013). Mutated *E. coli* strains that produce upwards of 6.33 grams of fatty alcohol per liter of culture support future alternative industrial fermentation methods for the production of fatty alcohols (Liu et al., 2016).

<u>Evaluation Question #4:</u> Describe the persistence or concentration of the petitioned substance and/or its by-products in the environment (7 U.S.C. § 6518 (m) (2)).

Alcohols with chain lengths up to C_{18} including hexanol, octanol, decanol, dodecanol, tetradecanol, hexadecanol and octadecanol are readily biodegradable within ten days. Production plant effluents often appear to only contain naturally occurring products, in spite of fatty alcohols introduced into their influents. This is because microbial action has rapidly altered the influent alcohols to naturally occurring products in the effluent (Mudge et al., 2014; Stahl and Pessen, 1953). Fatty alcohols are relatively stable with respect to abiotic degradation in water. Photo-oxidation in aqueous systems is not significant. Alcohols have no hydrolysable groups and are therefore not susceptible to hydrolysis. Fatty alcohol oxidation is expected under normal environmental conditions. The fatty alcohols are susceptible to atmospheric degradation by hydroxyl radicals, with half-lives ranging between approximately 10-30 hours. Longer chain lengths have shorter estimated half-lives within this range (OECD, 2006). Fatty alcohols are used in the manufacture of surfactants for detergents and personal care products. These products are mostly disposed of down the drain at a rate of about 185,000 metric tons per year. Most use is as laundry detergent totaling about 532,000 metric tons per year. Fatty alcohols used for detergent production are mostly sourced from petroleum products in the US. By comparison, the contribution of fatty alcohols to the environment from tobacco topping and suckering is very small (Mudge and DeLeo, 2014).

Evaluation Question #5: Describe the toxicity and mode of action of the substance and of its breakdown products and any contaminants. Describe the persistence and areas of concentration in the environment of the substance and its breakdown products (7 U.S.C. § 6518 (m) (2)).

The octanol-water partition (Log K_{OW}) coefficient is a laboratory measurement of the hydrophilic-lipophilic balance of a substance. It measures the tendency of a substance in the environment to prefer an organic or oily phase, e.g., fish (fat) and muscle or sediment, rather than an aqueous phase. The compound is first dissolved in water to a known concentration and placed in an octanol-water system and allowed to equilibrate. The concentration in the aqueous phase is re-determined using UV-visible light spectroscopy (Dalyrimple, 2005). The K_{OW} represents the membrane lipid-water barrier because octanol ($C_7H_{15}CH_2OH$) represents lipids in living organisms. Lipids and octanol have a similar carbon to oxygen ratio. Thus, it is used as an indicator of bioconcentration and bioaccumulation in the environment. The density, solubility and K_{ow} values for some fatty alcohols are given in Table 4. K_{ow} values are generally low for the C_6-C_{12} alcohols and increase with increasing molecular weight.

Table 4 Fatty Alcohol Density and Solubility

Name	Carbon Number	Molecular Weight, daltons	Density(d^{20}) grams/ml	Solubility @25°C-grams/liter	Log K_{ow}
Octanol	8	130.2	0.827	0.5	3.15*
Nonanol	9	144.3	0.828	0.1	3.77
Decanol	10	158.3	0.830	0.04	4.57
Undecanol	11	172.3	0.832	0.008	4.72
Dodecanol	12	186.3	0.831@24°C	0.00019	5.36

from Mudge, 2005; Fisk et al., 2009

*octanol-water partition coefficient used to measure K_{ow}

Evaluation Question #6: Describe any environmental contamination that could result from the petitioned substance's manufacture, use, misuse, or disposal (7 U.S.C. § 6518 (m) (3)).

The Safer Chemical Ingredients List (SCIL) lists chemical ingredients that EPA's Safer Choice Program has evaluated and determined to be safer than traditional chemical ingredients. This list was designed to help manufacturers find safer chemical alternatives to meet the criteria of the Safer Choice Program. Safer Choice decides to include a chemical on the SCIL based on the hazard information from a broad set of resources, including the identification and evaluation of all available toxicological and environmental fate data. According to the Safer Choice determination of the EPA, 1-decanol, 1-octanol, 1-dodecanol and the C_6-C_{12} alcohols are expected to be of low concern based on experimental and modeled data.

Linear fatty alcohols in general are easily biodegradable. The solubility of fatty alcohols in water decreases with an increasing C-chain length. Fatty alcohols possess only moderate acute toxicity for aquatic organisms. In general, in their range of water solubility no toxic effects are observed. However, a number of studies were performed with concentrations that are considerably above the water solubility. Available data for fatty alcohols chronic toxicity do not indicate a special toxicological potential (Condea, 2000).

Fatty alcohols are recognized as High Production Volume (HPV) chemicals. Global production volume is estimated at over 1.9 million metric tons. Linear to slightly branched log chain alcohols ranging from 6 to 22 alkyl carbons (C) biodegrade exceptionally rapidly in the environment (half-lives on the order of minutes); however, due to continuous use and distribution to waste water treatment systems, partitioning properties, biodegradation of alcohol based surfactants and natural alcohol sources, linear chain alcohols are universally detected in waste water effluents. A large fraction of environmentally detected alcohols are naturally derived alcohol from animal, plant and microbiologically mediated biotransformations. The fatty alcohols from both natural and manufactured sources represent a low risk for environmental contamination (Belanger et al., 2009).

C_6-C_{12} fatty alcohols are likely to volatize quickly, however, longer chain alcohols (C>12) reaching water supplies are not expected to be hydrolytically degraded (EPA, 2007). The shorter chain fatty alcohols (C<12) are degraded by oxidation and hydrolysis (Patterson et al., 1970). In the atmosphere all C-H containing organic substances react with photochemically generated hydroxyl radicals. The half live for photodegradation of the fatty alcohols varies between 12 and 30 hours (measured for 1-hexanol). Fatty alcohols are biodegradable, and those above C_{11} may be considered potentially bioaccumulative. Alcohols act by non-polar narcosis. Any toxicity produced by the fatty alcohols with chain lengths less than 12 is considered sub-acute with a fifty percent effective concentration (EC_{50}) ranging from 2.0 to 25 milligrams/liter (Fisk et al., 2009). The category comprises a homologous series of linear and essentially linear C_6 - C_{22} alcohols. In addition catalysts such as sulfuric acid present an environmental issue (Condea, 2000).

Increasing carbon chain length leads to a predictable pattern in physico-chemical properties that drives a distinct range of fate behaviors in the environment. Fatty alcohols all have the same mode of ecotoxicological action. In addition, they are all rapidly biodegradable especially at environmentally relevant concentrations. Alcohols are metabolized/bio-transformed in living organisms suggesting that bioaccumulation potentials based on octanol-water partition coefficients are likely to be overestimated. Measured biological concentration factor (BCF) data on fatty alcohols supports the concept that the bioaccumulation potential of these substances will be lower than estimated from log K_{ow}. 1-hexanol and 1-octanol present a hazard for the environment (acute toxicity to fish, daphnids and algae in the range 1 - 100 mg/l). However, both of these substances are readily biodegradable. 1-decanol and 1-undecanol present a greater hazard for the environment (high acute toxicity to fish, daphnids and algae, in the range 0.1 - 1 mg/l, and/or high chronic toxicity). The substances in this subgroup biodegrade rapidly and environmental monitoring data from seven countries indicates exposures to the environment is anticipated to be low (OECD, 2006).

Available toxicity data indicate that aliphatic alcohols are “practically non-toxic” to honey bees (acute contact LD50 > 25 µg/bee). However, given that aliphatic alcohols can be used as Lepidopteran sex inhibitors, there is a potential for sublethal (e.g., reproductive) effects on non-target Lepidopterans, such as butterflies. This potential effect cannot be quantified at this time (EPA, 2007).

<u>Evaluation Question #7:</u> Describe any known chemical interactions between the petitioned substance and other substances used in organic crop or livestock production or handling. Describe any environmental or human health effects from these chemical interactions (7 U.S.C. § 6518 (m) (1)).

Manual topping and suckering is labor intensive, but does not involve the use of any chemical substance. Mineral oil, cooking oil or paraffin oil are currently the only topping and suckering substances used by organic crop producers (Little et al., 2008). Fatty alcohols are used independently of other topping and suckering chemicals. There is no known interaction between the fatty alcohols that might be used for topping and suckering (Calvert, 1953).

<u>Evaluation Question #8:</u> Describe any effects of the petitioned substance on biological or chemical interactions in the agro-ecosystem, including physiological effects on soil organisms (including the salt index and solubility of the soil), crops, and livestock (7 U.S.C. § 6518 (m) (5)).

When fatty alcohols are applied to tobacco plants for suckering with a surfactant such as tween 20, an average residue of 1.6 parts per million (ppm) of the applied fatty alcohols and 1.0 ppm of the surfactant remain on the cured leaves. Over 7000 ppm of naturally occurring fatty alcohols are also present in and on the cured leaves (Tso et al., 1975). Fatty alcohols induce a low incidence of polynucleate root tip cells or root tip cells with fragmented nuclei (Tso and Burk, 1969). The fatty alcohols are produced naturally, in all living organisms, from bacteria to man, and thus, are widely present throughout the natural world. In any agro-ecosystem, fatty alcohols will be present from natural sources. The introduction of C_6-C_{12} fatty alcohols for topping and suckering may produce short term toxicity to many organisms in the range of 1-100 milligrams/liter, however; because the application rate is intermittent and biodegradability and removal rate are high for this substance no readily observable effects occur in the agroeosytem (OECD, 2006).

<u>Evaluation Question #9:</u> Discuss and summarize findings on whether the use of the petitioned substance may be harmful to the environment (7 U.S.C. § 6517 (c) (1) (A) (i) and 7 U.S.C. § 6517 (c) (2) (A) (i)).

The fatty alcohols are of ecological interest because of their widespread use as surfactants, detergents and personal care products. They are "down the drain products." In addition fatty alcohols are chemicals that naturally occur in all plants and animals. In general, fatty alcohols with carbon chains longer than C_{12} are found in the environment. Industrially derived fatty alcohols constitute less than 1% of the total amount of fatty alcohols present in the environment, based primarily on stable radioisotope labelling studies (Mudge et al., 2014).

Fatty alcohol products have been assessed for their chronic ecotoxicity in North America and Europe (Belanger et al., 2006). Statistical modelling of distributions and toxicities to algae, fish, daphnids and various controlled experimental systems has been performed and evaluated with the results refined to toxic units based model. The model indicates that the overall fatty alcohol products as a result of their high level of biodegradability and low toxic units, 0.015 to 0.212, were considered a very low risk for environmental contamination (Sanderson et al., 2013). Fatty alcohols are known for their high level of biodegradability in the environments. Their derivative products are additionally designed to rapidly degrade after use (Atkinson et al., 2009). Fatty alcohols are not considered endocrine disrupters.

Long chain alcohols (LCOH) with a carbon chain length range of C_6–C_{22} covering 30 substances, and 41.5 million metric tons/year consumed globally, were evaluated under the Organization for Economic Cooperation and Development (OECD) high production volume chemicals program in 2006. The main findings of the assessment include: (1) no unacceptable human or environmental risks were identified; (2) these materials are rapidly and readily biodegradable; (3) a parabolic relationship was demonstrated between carbon chain length and acute and chronic aquatic toxicity; (4) category-specific (quantitative) structure-activity relationships were developed enabling prediction of properties across the entire category; (5) LCOH occur naturally in the environment in an equilibrium between synthesis and degradation; (6) industry coming together and sharing resources results in minimizing the need for additional animal tests, produces cost savings, and increases scientific quality of the assessment (Sanderson et al., 2008). Daphnia, a standardized environmental test crustacean, is effected by 1-decanol at a concentration of approximately 1 milligram per liter (Schafers et al., 2009).

Fatty alcohols have a moderate tendency to bind to soils. The portion of applied chemical binding to the soil, rather than volatilizing, will be subject to biodegradation, with estimated half-lives for 1-octanol and 1-decanol of 2.3 days. The portion of applied chemical that does volatilize is estimated to degrade in the air by reaction with hydroxyl radicals with half-lives of about 10 hours (EPA, 2007).

<u>Evaluation Question #10:</u> Describe and summarize any reported effects upon human health from use of the petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (i), 7 U.S.C. § 6517 (c) (2) (A) (i)) and 7 U.S.C. § 6518 (m) (4)).

Toxicity data for the aliphatic alcohols consisting of acute toxicity, irritation, and sensitization studies, developmental rat (oral and inhalation) toxicity studies and a 90-day rat (dermal) study were evaluated for the Environmental Protection Agency (EPA) health risk determination. The available mutagenicity studies included the Ames, micronucleus, and gene mutation assays. Acute inhalation studies with the rat resulted in estimates of the median lethal dose (LD_{50}) above the limit concentration of 2 milligrams/Liter. However, eye irritation studies resulted in severe and sometimes non-reversible eye irritation. Dermal irritation studies revealed slight to moderate irritation in rabbits, and the aliphatic alcohols generally did not produce sensitization in tests with guinea pigs. There is no evidence to suggest that the aliphatic alcohols cause increased susceptibility in infants and children. Based on the results of the available studies, no endpoints of toxicological concern have been identified for human health risk assessment purposes. The EPA concluded that there are no human health risks of concern for aliphatic alcohols. Currently, there is no known mode of toxicological action for the aliphatic alcohols. Based on the low hazard concern via the oral, dermal, and inhalation routes of exposure, a quantitative risk assessment for the aliphatic alcohols was not found necessary (EPA, 2007).

EPA is updating the Restricted Entry Interval (REI) and Personal Protective Equipment (PPE) requirements for aliphatic alcohols. 1-Decanol, which is a component of all the tobacco sucker control products in this case, is an acute Toxicity Category I eye irritant; therefore, pursuant to the Worker Protection Standard (WPS) and according to the EPA Office of Pollution Prevention and Toxics (OPPTS) Label Review Manual 3rd Edition, products with agricultural uses must require a 48 hour REI and the following personal protective equipment (PPE) for early entry: coveralls, chemical-resistant gloves made of any water proof material, shoes plus socks, and protective eyewear (EPA, 2007).

Fatty alcohol products used for tobacco topping and suckering are of not very toxic following acute and repeated exposures. Although, skin and eye irritation are commonly observed. The mammalian metabolism of fatty alcohols used in tobacco topping and suckering is highly efficient. (Veenstra et al., 2009; OECD, 2006). Aliphatic alcohols are absorbed by all common routes of exposure, widely distributed within the body and efficiently eliminated. There is a limited potential for retention or bioaccumulation for the parent alcohols and their biotransformation products. Overall, toxicology databases show an inverse relationship between chain length and toxicity. The shorter chain alcohols tend to induce more pronounced effects when compared to materials with a longer chain length. This is illustrated most clearly by the degree of irritation in skin and eye irritation studies in laboratory animal studies. For the aliphatic alcohols in the range C_6 – C_{11} a potential for skin and eye irritation exists, without concerns for tissue destruction or irreversible changes. Aliphatic alcohols in the range C_{12} – C_{16} have a low degree of skin irritation potential. The eye irritation potential for alcohols with a chain length of C_{12} and above has been shown to be minimal. Aliphatic alcohols have no skin sensitization potential. Repeated exposure to aliphatic alcohols is generally without significant systemic toxicological findings and regarded to be of a low order of toxicity upon repeated exposure. C_6-C_{12} can induce local irritation at the site of first contact. There is a suggestion of mild change consistent with low-grade liver effects. Typical findings include: slightly increased liver weight, in some cases accompanied by clinical chemical changes but generally without concurrent histopathological effects. Aliphatic alcohols do not have a potential for producing peroxisome proliferation. Central nervous system (CNS) effects were absent upon inhalation or dietary administration, however 1-hexanol and 1-octanol showed a potential for CNS depression upon repeated administration of a bolus dose. Similarly, 1-hexanol and 1-octanol induced respiratory distress upon repeated administration of a bolus dose. Aliphatic alcohols do not have a potential for peripheral neuropathy. Typical no observable adverse effects level (NOAEL) for aliphatic alcohols range from 200 mg/kg/day to 1000 mg/kg/day in the rat upon sub-chronic administration via the diet. There has not been evidence of a carcinogenic potential for aliphatic alcohols. They do not contain structural elements of concern for potential interaction with DNA and have been shown to be without mutagenic activity, primarily on the basis of Ames assays and mouse micronucleus assays (Nelson et al., 1990a; OECD, 2006).

On the basis of the lack of adverse findings in the reproductive organs in repeated dose toxicity studies and in screening studies for reproductive effects aliphatic alcohols are considered without a potential for adverse effects on fertility and reproductive toxicity. Similarly, developmental toxicity studies with aliphatic alcohols have confirmed the lack of potential adverse effects on the developing fetus. As a rule aliphatic alcohols are manufactured and processed in established chemical complexes in closed installations; these are usually operated at high temperature and pressure. At these sites standard personal protective equipment is routinely applied to prevent direct skin and eye contact. Generally, aliphatic alcohols are of a low volatility and as a rule engineering controls are available preventing the need for respiratory protection. For non-routine operations involving a break in enclosed systems a higher level of protection is applied. Operations with a potential for significant exposure require a permit to work system and a case-by-case assessment is made for appropriate protective measures. Exposure through the use of products in industry and commerce is mitigated by applying measures aimed to prevent direct skin and eye contact by following the recommendations in the material safety data sheet (MSDS). Aliphatic alcohols are formulated in consumer laundry, cleaning and personal care products. Product labels reflect the hazard potential of the chemical ingredients in these products and include first aid instructions in case of non-intentional exposure (Nelson et al., 1990b; OECD, 2006).

<u>Evaluation Question #11:</u> Describe all natural (non-synthetic) substances or products which may be used in place of a petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (ii)). Provide a list of allowed substances that may be used in place of the petitioned substance (7 U.S.C. § 6518 (m) (6)).

Tobacco is apically dominant. The growing point via plant hormones exerts an influence throughout the vegetative and most of the reproductive phases, preventing the development of the axillary buds. Topping causes the axillary buds of the upper leaves to develop rapidly into suckers that must be removed at regular intervals until the final harvest. The suckers provide a harbor for insects and plant diseases. The use of a chemical for suckering and/or for topping results in a saving of labor, reduced infestations of insect pests, reduced spread of plant diseases, for example mosaic. There would also be less damage to the crop as a result of less travel through it. Indoleacetic acid at 10,000 ppm applied in lanolin will prevent sucker growth. Mineral oil daubed on the stem after topping also prevents sucker growth (Calvert, 1953).

Ten percent neem oil, 20% mohua oil, 25% groundnut oil and mineral oil applied to each plant after topping were evaluated against hand topping and suckering. All of these treatments improved sucker control and yield (Bangaryya et al., 1982).

Methyl caprate has been used effectively for topping and suckering. Although this fatty acid is an oleochemical, it may also be possible to produce it by fermentation (Tso, 1964).

Mineral oil, properly used can produce results in chemical suckering that are similar to hand suckering. However, some mineral oils may be too dangerous to use or must be diluted (emulsified) otherwise the oil may not only remove the suckers, but also burn the leaves. Mineral oil treatment is affected by rain. The use of mineral oil saves labor costs and exposure of personnel to nicotine and potentially green tobacco syndrome. Labor savings can be significant and as much 50% (Salmon, 1959; Wilson et al., 1952).

Apical dominance in tobacco can be controlled with plant growth hormones. However the removal of the tobacco inflorescence, topping acts as an immediate stimulus for the growth of suckers. The use of mineral and vegetable oil for suckering has the potential to cause or exacerbate soft rot. The cause may be too much oil and it running down the plant to contact roots. Highly refined mineral oil with very low aromatic content should be used. Liquid paraffin, white oil and light medicinal oil have been successfully used for suckering. Although it takes about twice as long to apply the oil as it does to hand sucker, subsequent manual suckering sessions are eliminate saving time and labor (Calvert, 1956b).

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<u>Evaluation Question #12:</u> Describe any alternative practices that would make the use of the petitioned substance unnecessary (7 U.S.C. § 6518 (m) (6)).

When the tobacco crop is about half-grown, flower buds begin to appear. These flower heads are removed or "topped" to prevent seed formation, forcing the plant to focus on leaf production. The result is larger, thicker, darker leaves that mature more uniformly and contain more nicotine. Topping may be done by hand or with special machines that cut the flower heads and sacrifice a few leaves. Topping requires two or three trips over the field to catch all the plants. Topping of plants also stimulates the growth of secondary stems from the base and/or leaf axils. These "suckers" must also be removed to assure uniformity and quality. While chemicals are available to suppress suckering, these may not be allowable under organic certification standards. The alternative is removal by hand every seven to ten days. Suckering is one of the most labor-intensive activities in tobacco production, as many plants sucker two or three times before harvest (Kuepper and Thomas, 2008).

The aim of sucker control is to focus the plant's energy into filling the leaves rather than growing the flower. Because tobacco sells by weight, heavier leaves are favored economically. In organic tobacco production, early topping to improve yield and quality is usually done by hand. Suckers can be removed by hand as well as stunted by carefully applying approved soybean oil or mineral oil to the top of the plant. Topping and suckering are the most time consuming tasks associated with growing organic tobacco, and may be necessary every week for 10 weeks. It can take one person per acre per day to do the job. Plants may not be permitted to flower, instead, they are topped at 15 leaves. In organic tobacco production, controlling insects without insecticides and weeds without herbicides is not as big a big problem as controlling suckers. Application of mineral or cooking oil to prevent the suckers from coming back has to be done mostly by hand. Initial topping and suckering is done by hand. Vegetable oil or mineral oil is poured from gallon jugs over each plant, allowing the oil to run into each leaf axil to the way to the bottom of the plant. Topping early keeps the aphid off tobacco plants. Soybean cooking oil and mineral oil applied to the heads of plants prevents flowering. Eighteen hours can be spent per acre removing suckers (Little et al., 2008). There are currently 314 certified organic tobacco production operations. All of them are located in the United States of America (Organic Integrity Database).

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