	Processing Steps affecting contaminants						
	CO1 Process Steps affecting contaminants		RBD Process Steps affecting contaminants				
	Neutralization	Acidification	Degumming	Caustic Refining	Water Wash	Bleaching	Deodorization
Processing Aids	Ethanol, Sodium Hydroxide, RO water	Sulfuric Acid or Citric Acid Solution	Phosphoric Acid, Citric Acid Solution	11% NaOH solution	5-8 w% Water	0.5% Bleaching earth, 0.2% DE	0.5-2% steam
Temperature, °C	70	73	150	73	90	120	260
Retention Time, mins	550	17	35	10	10	45	20
Aflatoxin	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	Near 100% Adsorbed	Inactivated
Deoxynivalenol (DON)	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	Partially Adsorbed	Inactivated
Fumonisin	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	Partially Adsorbed	Inactivated
Virginiamycin	100:0 Water: Oil Fractionation	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	50:50 Water: Oil Fractionation	Partially Adsorbed	Inactivated
Penicilin	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	Partially Adsorbed	Inactivated
Erythromycin	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	Partially Adsorbed	Inactivated
Tylosin	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	Partially Adsorbed	Inactivated
Tetracycline	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	100:0 Water: Oil Fractionation	Partially Adsorbed	Inactivated

Physical and chemical properties

		Stability		Solubility		
		Temperature	pH condition	Water (mg/L @ 25°C)	Ethanol (mg/L @ 25°C)	Adsorption Potential
Mycotoxins	Aflatoxin	Unstable >250°C	Unstable < 2pH	233-994	More soluble than in water	Bentonite: Near complete Adsorption
	Deoxynivalenol (DON)	Unstable>150°C	Unstable >10pH	36000	8890	Bentonite: 20% Adsorption
	Fumonisir	Unstable >150°C	Unsatble <4pH	20000	Soluble	Adsoption range is 30% to 100%
Antibiotics	Virginiamycin	Inactivated >100°C	Inactivated pH<3	45	More soluble than in water	Adsorps in soil at approx. Koc = 980
	Penicilin	Inactivated >35°C	Inactivated pH<4 and >8	18704	9352	Adsorps in soil at approx Koc = 570
	Erythromycin	Inactivated >120°C	Inactivated <2pH	2000	Soluble	
	Tylosin	Inactivated >100°C	Inactivated <3pH and >9pH	5000	Soluble	Adsorps in sandy loam at approx. Koc = 79880, 5664, 553 and 771, and silty clay, clay, sand soils Koc = 1350-95532
	Tetracycline	Inactivated >100°C	Inactivated <2pH	231	20000	

Low water solubility:	<10 mg/l	25:75 Water: Oil
Moderate water solubility:	10-1,000 mg/l	50:50 Water: Oil
High water solubility:	>1,000 mg/l	100:0 Water: Oil

Solubility Literature Cited:

Virginiamycin	US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Jan, 2010. Available from, as of May 8, 2012: http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm Lactrol- Virginiamycin and Dextrose, Product Data Sheet, Phibro Ethanol Performance, https://www.pahc.com/wp-content/uploads/ProductDataSheets/EPG/Antibiotics/phibro-lactrol-4-4-16.pdf O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006.
	US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Jan, 2010. Available from, as of May 8, 2012: http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm Lactrol- Virginiamycin and Dextrose, Product Data Sheet, Phibro Ethanol Performance, https://www.pahc.com/wp-content/uploads/ProductDataSheets/EPG/Antibiotics/phibro-lactrol-4-4-16.pdf O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006.
Penicillin	Weiss P.J.; Andrew, M.L.; Wright, W.W. Antibiotics and Chemotherapy 1957,7, 374. David J. Maggs, Chapter 3 - Ocular Pharmacology and Therapeutics, Slatter's Fundamentals of Veterinary Ophthalmology (Fourth Edition), 2008 Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 178 E. Tomlinson, A. Regosz, Solubility data series, Antibiotics: 1, beta-lactam antibiotics, Pergamon Press, Vol 16/17 1985
Erythromycin	https://www.chemicalbook.com/ChemicalProductProperty_US_CB8300078.aspx Lide, D.R. CRC Handbook of Chemistry and Physics 88TH Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-230 Photo-Degradation of Amoxicillin, Streptomycin, Erythromycin and Ciprofloxacin by UV and UV/TiO2 Processes. Evaluation of Toxicity Changes Using a Respirometric Biosensor, Palmisano, Campanella, Ambrosetti, J Environ Anal Chem 2015, 2:3
Tylosin	O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1823
Tetracyclin	Yalkowsky SH, Dannenfelser RM; The AQUASOL database of Aqueous Solubility. Fifth ed, Tucson, AZ: Univ AZ, College of Pharmacy (1992) Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1143
Aflatoxin	NTP, US National Toxicology Program (2000) NTP technical report on the toxicology and carcinogenesis studies of fumonisin B1 (CAS No 116355–83-0) in F344/N Rats and B6C3F1 Mice (Feed Studies) (TR 496; NIH Publication No 99–3955). Research Triangle Park, NC
Fumonisin	NTP, US National Toxicology Program (2000) NTP technical report on the toxicology and carcinogenesis studies of fumonisin B1 (CAS No 116355–83-0) in F344/N Rats and B6C3F1 Mice (Feed Studies) (TR 496; NIH Publication No 99–3955). Research Triangle Park, NC Lawrence, James & Niedzwiadek, Barbara & Scott, Peter. (2000). Effect of Temperature and Solvent Composition on Extraction of Fumonisins B1 and B2 from Corn Products. Journal of AOAC International. 83. 604-11. 10.1093/jaoac/83.3.604.
DON	Impact of food processing and detoxification treatments on mycotoxin contamination, Karlovsky, Suman, Berthiller, Meester, Eisenbrand, Perrin, Oswald, Speijers, Chiodini, Recker, Dussort; Mycotoxin Res (2016) 32:179–205 https://www.tocris.com/products/deoxynivalenol_3976#ds_datasheets

Stability Literature Cited

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Karlovsky etc al, Impact of food processing and detoxification treatmentson mycotoxin contamination, Mycotoxin Res (2016) 32:179–205
CHARLENE E. WOLF AND LLOYD B. BULLERMAN*, Heat and pH Alter the Concentration of Deoxynivalenolin an Aqueous Enviromentt, Journal of Food Protection, Vol. 61, No.3, 1998, Pages 365-367

								Processing Steps													
								CO1 Process Steps						RBD Process Steps							
								Neutralization	Acidification	Oil Drying	Oil Stripper	Crystallization	Wax Separation	Degumming	Dryer	Caustic Refining	Water Wash	Bleaching	Winterization	Deodorization
							Processing Aids	Ethanol, Sodium Hydroxide, RO water	Sulfuric Acid or Citric Acid					Phosphoric Acid, Citric Acid		11% NaOH solution	5-8 wt% Water	0.5% Bleaching earth, 0.2% DE		0.5-2% steam
							Temperature, °F	160	163	230	260	45	75	140-150	185-190	165	190-195	230-250		480-500
			Thermo-physical and Chemical Characteristics				Pressure, mmHg	755	755	206	206	755	755		50			<36		3 to 6
			Stability			Solubility	Retention Time, mins	552	17	54	9	1332	10	30-40		8-12	8-10	30-45		20-30
			Decomposition Temperature (°F, unless noted)	Acidic	Alkaline	Water (mg/L @ 25°C)	Ethanol (mg/L @ 25°C)	State @ STP													
Mycotoxins	Aflatoxin		Ellis, Milani, Karlovsky, Doyle	Wagan, Milani, Karlovsky, Doyle	Wagan, Milani, Karlovsky, Doyle	White, Karlovsky	Hron		50:50 Fractionation by Mass Fraction; Unstable	Unstable	Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction	Unstable	Will not Vaporize	Unstable	50:50 Fractionation by Mass Fraction	Near 100% Adsorbed	No Effect	
	Deoxynivalenol (DON)		Numanoglu, Milani		Karlovsky	Karlovsky	Tocris		50:50 Fractionation by Mass Fraction	Stable	Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction	Stable	Will not Vaporize	Stable	0:100, Oil:H2O Fractionation	Near 20% Adsorbed	No Effect	
	Fumonisin		Jackson	Jackson	Jackson, Karlovsky	Karlovsky	Caymnchem		0:100, Oil:H2O/ETOH Fractionation; Unstable	Jackson	Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction	Jackson	Will not Vaporize		0:100, Oil:H2O Fractionation	30% Adsoption		
Antibiotics	Virginiamycin			Islam		Fish Chem	Fish Chem		0:100, Oil:H2O/ETOH Fractionation; Unstable	Islam	Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction		Will not Vaporize	Unstable	0:100, Oil:H20 Fractionation			100% Will vaporize
	Penicillin		Pub Chem	Islam		Budwani	Budwani		0:100, Oil:H2O/ETOH Fractionation; Unstable	Unstable	Chem Spider	Chem Spider	No Effect	50:50 Fractionation by Mass Fraction	Unstable		Unstable	0:100, Oil:H20 Fractionation			
	Erythromycin			Fiese	Fiesen	Fishmanly			0:100, Oil:H2O/ETOH Fractionation		Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction		Will not Vaporize		0:100, Oil:H20 Fractionation			
	Tylosin								0:100, Oil:H2O/ETOH Fractionation; Unstable	Unstable	Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction		Will not Vaporize	Unstable	0:100, Oil:H20 Fractionation			
	Tetracycline								0:100, Oil:H2O/ETOH Fractionation; Unstable	Unstable	Will not Vaporize	Will not Vaporize	No Effect	50:50 Fractionation by Mass Fraction			Unstable	0:100, Oil:H20 Fractionation			

Toxicology Questions

Q1. Please provide details about the original literature search strategy, such as the search terms and the timeframe (month/year to month/year), and please update the literature search to include the most recent possible references.

Response:

Literature searches were conducted in April 2020 using PubMed, with supplemental searches performed in GoogleScholar to identify studies containing information pertinent to the safety of corn oil. The following search terms were used with the search field restricted to titles, and with no other limitations:

> Corn oil OR 8001-30-7 OR corn oils OR oil, corn OR maize oil OR maize oils OR oil, maize OR oils, maize OR lipomul

Titles of 882 citations were returned and reviewed, followed by review of abstracts in cases where the title did not provide sufficient information to judge the relevance of a publication. Based on this initial titles and abstracts review, a large number of citations were not safety relevant and were excluded from further review. Publications that were excluded from further consideration were:

- Mechanistic studies, *in vitro*, mode of action, and mixture studies (258, e.g. gene expression, protein expression, and biochemical pathway analyses; experimentation on genetically modified animals; evaluations on additive, synergistic, or antagonistic effects; initiation and promotion effects involving other compounds, such as carcinogens)
- Behavioral studies (18, e.g. reinforcement behavior, palatability, food preference, orosensory, feeding motivation, conditioning, and grooming)
- Agriculture, animal feed, and non-relevant mammalian species studies (122)
- Composition, chemical properties, analytical methods/techniques, and technical applications (322)
- Pre-clinical toxicity studies using non-relevant routes of exposure (4, e.g. subcutaneous, percutaneous and intraperitoneal routes of exposure)
- Efficacy studies (25)
- Dated publications (pre-1980, reviews, and commentaries (81))
- Unrelated articles (28, e.g. environmental-related study, social science, study concerns a compound/substance that is not relevant to corn oil)

All pre-clinical studies related to ADME and toxicity and clinical studies and case reports (potentially containing safety outcomes reporting) were retained for further review. A total of 24 citations were determined to be potentially relevant and the full publications (3 with abstracts

only) were obtained and screened for information related to the toxicity and ADME of corn oil. The publications were categorized according to the primary physiological, toxicological, and/or biochemical effects that were observed, including ADME, cardiac effects; liver, kidney, pancreas, GI effects; lipid and metabolic effects; DART; and cancer. The citations for these publications are summarized in Table 1. Additional literature search was conducted for ADME publications and is described in response to question 3 (below).

Table 1. Safety Relevant Citations

Types of Effect	Author, year	Citation
ADME	Degrace et al., 1996	Degrace P, Caselli C, Rayo JM, Bernard A.Intestinal lymph absorption of butter, corn oil, cod liver oil, menhaden oil, and eicosapentaenoic and docosahexaenoic acid ethyl esters in rats.Lipids. 1996 Apr;31(4):405-14.
	Mitchell et al., 1989	Mitchell DC, McMahon KE, Shively CA, Apgar JL, Kris-Etherton PM.Digestibility of cocoa butter and corn oil in human subjects: a preliminary study.Am J Clin Nutr. 1989 Nov;50(5):983-6.
	Apgar et al., 1987	Apgar JL, Shively CA, Tarka SM Jr.Digestibility of cocoa butter and corn oil and their influence on fatty acid distribution in rats.J Nutr. 1987 Apr;117(4):660-5.
Cardiac	Eid et al., 2019a	Eid RA, Alkhateeb MA, El-Kott AF, Eleawa SM, Zaki MSA, Alaboodi SA, Salem Al-Shudiefat AA, Aldera H, Alnamar NM, Alassiri M, Khalil MA.A high-fat diet rich in corn oil induces cardiac fibrosis in rats by activating JAK2/STAT3 and subsequent activation of ANG II/TGF-1Î²/Smad3 pathway: The role of ROS and IL-6 trans-signaling.J Food Biochem. 2019 Aug;43(8):e12952. doi: 10.1111/jfbc.12952. Epub 2019 Jun 20.
	Eid et al., 2019b	Eid RA, Eleawa SM, Alkhateeb MA, Aldera H, Zaki MSA, Al-Shraim M, Saeed MA, El-Kott AF, Alaa Eldeen M, Alassiri M, Alshehri MM, Salem Al-Shudiefat AA, Khalil MA.Chronic consumption of a high-fat diet rich in corn oil activates intrinsic cell death pathway and induces several ultrastructural changes in the atria of healthy and type 1 diabetic rat.Clin Exp Pharmacol Physiol. 2019 Dec;46(12):1111-1123. doi: 10.1111/1440-1681.13158. Epub 2019 Sep 10.
	Das et al., 2017	Das S, Hamsi MA, Kamisah Y, Qodriyah HMS, Othman F, Emran A, Zakaria Z, Jaarin K.Changes in blood pressure, vascular reactivity and inflammatory biomarkers following consumption of heated corn oil.Pak J Pharm Sci. 2017 Sep;30(5):1609-1615.
Liver, kidney,	Milin et al., 2000	Milin C, DomitroviÄ‡ R, Tota M, Giacometti J, Cuk M, RadoseviÄ‡-StasiÄ‡ B, Ciganj Z.Effect of olive oil- and corn

Types of Effect	Author, year	Citation
pancreas, GI		oil-enriched diets on the tissue mineral content in mice.Biol Trace Elem Res. 2001 Summer;82(1-3):201-10.
	Sato et al., 2000	Sato M, Wada K, Marumo H, Nagao T, Imai K, Ono H.Influence of corn oil and diet on reproduction and the kidney in female Sprague-Dawley rats.Toxicol Sci. 2000 Jul;56(1):156-64.
	Nwanguma et al., 1998	Nwanguma BC, Achebe AC, Ezeanyika LU, Eze LC.Toxicity of oxidized fats II: tissue levels of lipid peroxides in rats fed a thermally oxidized corn oil diet.Food Chem Toxicol. 1999 Apr;37(4):413-6.
	Anderson, 1987	Anderson RL.Intestinal responses in the male rat to gavaged corn oil.Cancer Lett. 1987 Jul;36(1):55-63.
	Alexander et al., 1987 (abstract only)	Alexander JC, Valli VE, Chanin BE.Biological observations from feeding heated corn oil and heated peanut oil to rats.J Toxicol Environ Health. 1987;21(3):295-309.
	Eustis and Boorman, 1985	Eustis SL, Boorman GA.Proliferative lesions of the exocrine pancreas: relationship to corn oil gavage in the National Toxicology Program.J Natl Cancer Inst. 1985 Dec;75(6):1067-73.
Lipids and metabolic	Pavlisova et al., 2016	Pavlisova J, Bardova K, Stankova B, Tvrzicka E, Kopecky J, Rossmeisl M.Corn oil versus lard: Metabolic effects of omega-3 fatty acids in mice fed obesogenic diets with different fatty acid composition.Biochimie. 2016 May;124:150-162. doi: 10.1016/j.biochi.2015.07.001. Epub 2015 Jul 4.
	Wong et al., 2015	Wong CK, Botta A, Pither J, Dai C, Gibson WT, Ghosh S.A high-fat diet rich in corn oil reduces spontaneous locomotor activity and induces insulin resistance in mice.J Nutr Biochem. 2015 Apr;26(4):319-26. doi: 10.1016/j.jnutbio.2014.11.004. Epub 2014 Dec 15.
	Boyle et al., 1996 (abstract only)	Boyle FG, Yuhas RJ, Lien EL.Red blood cell and tissue phospholipid fatty acid profiles of weanling rats fed infant formula fat blends containing soy and/or corn oil.Ann Nutr Metab. 1996;40(4):234-42.
	Apgar et al., 1987	Apgar JL, Shively CA, Tarka SM Jr.Digestibility of cocoa butter and corn oil and their influence on fatty acid distribution in rats.J Nutr. 1987 Apr;117(4):660-5.
	Deshaies, 1986 (abstract only)	Deshaies Y.Plasma lipoprotein cholesterol and triglycerides and lipoprotein lipase activity in epididymal white adipose tissue of rats fed high sucrose or high corn oil diets.Can J Physiol Pharmacol. 1986 Jul;64(7):885-91.
DART	Guerra et al., 2019	Guerra LHA, Tamarindo GH, de Campos SGP, Taboga SR, Vilamaior PSL.Do mineral and corn oil serve as potential

Types of Effect	Author, year	Citation
		endocrine disruptors in the gerbil prostate?Reprod Toxicol. 2019 Dec;90:141-149. doi: 10.1016/j.reprotox.2019.09.004. Epub 2019 Sep 27.
	Moral et al., 2011	Moral R, Escrich R, Solanas M, Vela E, Costa I, de Villa MC, Escrich E.Diets high in corn oil or extra-virgin olive oil provided from weaning advance sexual maturation and differentially modify susceptibility to mammary carcinogenesis in female rats.Nutr Cancer. 2011;63(3):410-20. doi: 10.1080/01635581.2011.535956.
	Sato et al., 2000s	Sato M, Wada K, Marumo H, Nagao T, Imai K, Ono H.Influence of corn oil and diet on reproduction and the kidney in female Sprague-Dawley rats.Toxicol Sci. 2000 Jul;56(1):156-64.
Cancer	NTP, 1994	National Toxicology Program. NTP Comparative Toxicology Studies of Corn Oil, Safflower Oil, and Tricaprylin (CAS Nos. 8001-30-7, 8001-23-8, and 538-23-8) in Male F344/N Rats as Vehicles for Gavage.Natl Toxicol Program Tech Rep Ser. 1994 Apr;426:1-314.
	Rao and Haseman, 1993	Rao GN, Haseman JK.Influence of corn oil and diet on body weight, survival, and tumor incidences in F344/N rats.Nutr Cancer. 1993;19(1):21-30.
	Haseman and Rao, 1992	Haseman JK, Rao GN.Effects of corn oil, time-related changes, and inter-laboratory variability on tumor occurrence in control Fischer 344 (F344/N) rats.Toxicol Pathol. 1992;20(1):52-60.
	Haseman et al., 1985	Haseman JK, Huff JE, Rao GN, Arnold JE, Boorman GA, McConnell EE.Neoplasms observed in untreated and corn oil gavage control groups of F344/N rats and (C57BL/6N X C3H/HeN)F1 (B6C3F1) mice.J Natl Cancer Inst. 1985 Nov;75(5):975-84.

Q2. Further, FDA's literature search revealed reports of adverse effects from orally administered corn oil on the following organs/systems or physiological effects associated with the dysregulation of these organs/systems in rodents (rats or mice); some examples are listed below:

I. **Kidney**, such as proximal tubular as well as glomerular lesions.
II. **Pancreas**, such as hyperplasia of acinar cells of the exocrine pancreas.
III. **Heart**, such as cardiac fibrosis, myocardial damage.
IV. **Metabolic effects,** such as insulin resistance and type 2 diabetes.
V. **Maternal effects**, such as abnormal clinical signs after parturition, reduced pup viability.
Please address why chronic consumption of COZ corn oil wouldn't be associated with adverse effect(s) as described in the published references.

Response:

Findings in the literature searches as described under Q1 are summarized below. For all of the responses provided to Q2, the dose conversion is based on the following reference: EFSA Scientific Committee; Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579. [32 pp.] doi:10.2903/j.efsa.2012.2579.

Cardiac effects

Three studies that were identified from the literature search containing cardiovascular-related endpoints are summarized in Table 2. Each study describes a single dose of corn oil that was administered to rats in the diet. Eid et al. (2019a,b) showed that rats fed a high-fat diet enriched in corn oil (HFD-CO, 40% fat; equivalent to 36 g/kg bw/day[1])for 8 weeks exhibited traits of type 2 diabetes, along with increased left ventricular collagen synthesis; disrupted systolic and diastolic function; and increased oxidative stress, cell death activation, and ultrastructural changes. In a study comparing diets fortified with 15% (w/w; weight ratio of rat chow to oil is 100:15; equivalent to 7.5 g/kg bw/day[2]) of either fresh, once-heated, five-times heated, or ten-times heated corn oil administered to rats in the diet for 16 weeks, the overall results showed that all of the heated oils caused a significant increase in blood pressure (Das et al., 2017).

[1] 40% high fat diet-corn oil was converted to 40 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 400,000 mg/kg diet = 40%; 1 mg/kg in rat feed for a subchronic duration study is equivalent to 0.09 mg/kg bw/day; therefore, 400,000 mg/kg diet is equivalent to 36 g/kg bw/day (i.e. (400,000 X 0.09)/1000).

[2] 15% w/w of corn oil was converted to 7.5 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 150,000 mg/kg diet = 15%; 1 mg/kg in rat feed for a chronic duration study is equivalent to 0.050 mg/kg bw/day; therefore, 150,000 mg/kg diet is equivalent to 7.5 g/kg bw/day (i.e. (150,000 X 0.050)/1000).

Collectively, these studies demonstrate that repeated, subchronic exposure to dietary corn oil in very high amount >=7.5 g/kg bw/day in rats can adversely affect cardiac ultrastructure and function as well as induce traits consistent with type 2 diabetes.

Table 2. Studies with cardiac effects in rats

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
Eid et al., 2019a	Left ventricular (LV) fibrosis was evaluated in rats fed a low-fat diet or high-fat diet enriched in corn oil (HFD-CO, 40% fat; equivalent to 36 g/kg bw/day[1]) for 8 weeks	HFD-CO induced type 2 diabetes phenotype and increased LV collagen synthesis in rats that were fed a HFD-CO (40% fat) diet.
Eid et al., 2019b	Atrial cells ultrastructure, antioxidant levels and markers of intrinsic cell death in adult male Wistar healthy control and T1DM-induced rats fed control or HFD-CO (40% fat; equivalent to 36 g/kg bw/day[1]) for 60 days	Healthy rats that received a HFD-CO (40% fat) displayed T2DM phenotype; systolic and diastolic function were impeded; increased oxidative stress, cell death activation, and ultrastructural changes
Das et al., 2017	Blood pressure changes in male Sprague-Dawley rats (200-280 g in body weight) that were fed control diet, or basal diet fortified with 15% (w/w; weight ratio of rat chow to oil is 100:15; equivalent dose 7.5 g/kg bw/day[2]) of either fresh, once-heated, five-times heated, or ten-times heated corn oil for 16 weeks	Significant increase in the blood pressure in groups fed the basal diet with 7.5 g/kg bw/day of once-heated, five- and ten-times heated corn oil compared to the control diet; overall results suggest that repeatedly heated corn oil increases blood pressure and vascular inflammation

Liver, Kidney, Pancreas and GI Effects

Six studies that were identified from the literature search containing liver, kidney, pancreas, or gastrointestinal (GI) effects are summarized in Table 3. Two separate, 21-day, single dose dietary studies are described whereby mice and rats were fed corn oil at 5% (w/w; equivalent to 10 g/kg bw/day[3]) and 12% in the diet, respectively (Milin et al., 2000; Nwanguma et al., 1998). Compared to mice that received a control diet, corn oil-exposed mice had increases in spleen iron and calcium concentrations, liver and thymus calcium. Rats that were fed corn oil (12% in the

[3] 5% w/w corn oil was converted to 10 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 50,000 mg/kg diet = 5%; 1 mg/kg in mouse feed for a subacute duration study is equivalent to 0.2 mg/kg bw/day; therefore, 50,000 mg/kg diet is equivalent to 0.2 g/kg bw/day (i.e. (50,000 X 0.2)/1000).

diet; equivalent to 14.4 g/kg bw/day[4]) exhibited significantly increased liver and kidney lipid peroxides, decreased body weight gains, and increased relative liver weights compared to controls. In a separate dietary study from Alexander et al. (1987; abstract only) in weanling rats that received diets containing 15% (by weight; equivalent to 18 g/kg bw/day[5]) of fresh or laboratory-heated corn oil (FCO, HCO), total weight gain, feed consumption, feed efficiency, liver and kidney weights were increased in FOC-exposed rats, while in HCO-exposed rats, reported clinical signs included diarrhea, dermatitis, seborrhea, and hair loss as well as thymus and liver injury.

In a gavage study, female Sprague-Dawley rats were administered 0, 2, or 10 ml corn oil/kg body weight/day (equivalent to 0, 1.8, or 9 g/kg bw/day, respectively, based on the corn oil density of 0.9 g/ml) via gavage during pre-mating (2 weeks), mating, gestation, and until day 3 of lactation (Sato et al., 2000). Overall results showed that the kidneys of dams fed an animal protein diet combined with corn oil providing intake of 9 g/kg bw/day of corn oil had severe lesions in the proximal tubular epithelium, which was reported as necrosis and fatty degeneration (Sato et al., 2000). The study authors concluded that the animal protein diet may have enhanced the corn oil toxicity (Sato et al., 2000). In a separate oral gavage study in male Fischer-344 rats that were administered 5 ml/kg bw/day corn oil (equivalent to 4.5 g/kg bw/day based on the corn oil density of 0.9 g/ml) for 5 weeks (5 days/week), results revealed small intestinal mucosal tissue mass, and increased DNA and protein content, along with increased DNA/dry mass ratio that was suggestive of rapid cell division (Anderson, 1987). Finally, Eustis and Boorman (1985) reviewed pancreata data from corn oil vehicle control and untreated control F344/N male rats in 37, 2-year carcinogenicity studies to assess the extent and strength of the association of proliferative exocrine pancreatic lesions with corn oil gavage. The study authors concluded that "there was no relationship between incidences of proliferative acinar lesions and the animal laboratory, the animal source, and the brand, lot, or peroxide level of the corn oil. The incidences of focal acinar hyperplasia and acinar adenoma were related to maximum mean body weights attained by the groups during the course of the study."

[4] 12% w/w of corn oil was converted to 14.4 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 120,000 mg/kg diet = 12%; 1 mg/kg in rat feed for a subacute duration study is equivalent to 0.12 mg/kg bw/day; therefore, 120,000 mg/kg diet is equivalent to 14.4 g/kg bw/day (i.e. (120,000 X 0.12)/1000).

[5] 15% w/w of corn oil was converted to 18 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 150,000 mg/kg diet = 15%; 1 mg/kg in weanling rat feed is equivalent to 0.12 mg/kg bw/day; therefore, 150,000 mg/kg diet is equivalent to 18 g/kg bw/day (i.e. (150,000 X 0.12)/1000).

Taken together, corn oil administered in the diet and via gavage at doses ranging from 4.5 -18 g/kg bw/day have been shown to cause adverse effects in the liver, kidney, and GI, while pancreatic effects observed in rat 2-yr carcinogenicity studies are not attributed to corn oil.

Table 3. Studies with liver, kidney, pancreas, GI effects in rats and mice

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
Milin et al., 2000	Mineral content changes in the liver, spleen, and thymus were examined in male Balb/c mice (2-3 mo old) that were fed diets enriched with 5% corn oil added to the standard pellet diet, w/w (equivalent to 10 g/kg bw/day[3]) for 21 days	Compared to the control diet, diet enriched with corn oil (5%) caused an increase in spleen iron and calcium concentrations; increased liver calcium; and increased thymus calcium
Sato et al., 2000	Kidney histopath evaluations in female Sprague-Dawley rats divided into two (CA-1 and CE-2) groups* that were administered 0, 2, or 10 ml corn oil/kg body weight/day (equivalent to 0, 1.8 or 9 g/kg bw/day, respectively) via oral gavage during pre-mating (2 wk), mating, gestation, and until day 3 of lactation *CA-1 dietary protein is primarily from animal protein while CE-2 is primarily from plant protein	Kidneys of dams fed the CA-1 diet combined with 9 g/kg bw/day of corn oil exhibited severe lesions in the proximal tubular epithelium reported as necrosis and fatty degeneration; CA-1 diet was suggested to enhance the corn oil toxicity
Nwanguma et al., 1998	Tissue levels of lipid peroxides in organs, organ and body weights of male Wistar albino rats that were administered thermally oxidized corn oil (12% fat in the diet; equivalent to 14.4 g/kg bw/day[4]) in the diet for 21 days	At the 14.4 g/kg bw/day dose, significantly increased lipid peroxides were observed in the liver and kidney; body weight gains were significantly decreased; relative liver weights were significantly increased compared to controls
Anderson, 1987	Intestinal responses in male Fischer-344 rats that were administered 5 ml/kg bw/day corn oil (equivalent to 4.5 g/kg bw/day) via oral gavage for 5 weeks (5 days/week)	At the 4.5 g/kg bw/day dose, small intestinal mucosal tissue mass, DNA and protein content were increased along with increased DNA/dry mass ratio that was suggestive of rapid cell division
Alexander et al., 1987 (abstract only)	Organ, tissue, and biochemical effects were evaluated in 5 groups of male weanling rats that received diets containing 15% (by weight; equivalent to 18 g/kg bw/day[5]) of	In FCO-exposed rats (18 g/kg bw/day corn oil), total weight gain, feed consumption, feed efficiency, liver and kidney weights were increased.

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
	fresh or laboratory-heated corn oil (FCO, HCO)	In HCO-exposed rats (18 g/kg bw/day corn oil), clinical signs included diarrhea, dermatitis, seborrhea, and hair loss as well as thymus and liver injury
Eustis and Boorman, 1985 (abstract only)	Microscopic review of pancreata from corn oil vehicle control and untreated control F344/N male rats in 37, 2-year carcinogenicity studies to assess the extent and strength of the association of proliferative exocrine pancreatic lesions with corn oil gavage	"There was no relationship between incidences of proliferative acinar lesions and the animal laboratory, the animal source, and the brand, lot, or peroxide level of the corn oil. The incidences of focal acinar hyperplasia and acinar adenoma were related to maximum mean body weights attained by the groups during the course of the study."

Metabolic Effects

Five studies that were identified from the literature search containing lipid and metabolic effects are summarized in Table 4. Recent single-dose dietary studies performed in mice that received 32% (w/w ; equivalent to 64 g/kg bw/day[6]) corn oil for 8 weeks (Pavlisova et al., 2016) or 19% (w/w; equivalent to 38 g/kg bw/day[7]) corn oil for 6 weeks (Wong et al., 2015) revealed that corn oil-exposed mice gained weight, had impaired insulin sensitivity, decreased locomotor activity, lower respiratory ratio, hyperinsulinemia, and impaired glucose disposal. These results suggest that repeated exposure to dietary corn oil at high doses in mice can cause metabolic impairment.

In a separate dietary study from Deshaies (1986; abstract only), rats fed diets high in corn oil (65% of calories as sucrose or corn oil, equivalent to 58.5 g/kg bw/day[8]) for 4 weeks had higher HDL to total cholesterol ratio compared to rats that consumed sucrose; plasma total triglyceride levels were also 73% higher in the sucrose-treated animals compared to corn oil. Corn oil-

[6] 32% w/w corn oil was converted to 64 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 320,000 mg/kg diet = 5%; 1 mg/kg in mouse feed for a subchronic duration study is equivalent to 0.2 mg/kg bw/day; therefore, 320,000 mg/kg diet is equivalent to 64 g/kg bw/day (i.e. (320,000 X 0.2)/1000).

[7] 19% w/w corn oil was converted to 38 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 190,000 mg/kg diet = 19%; 1 mg/kg in mouse feed for a subchronic duration study is equivalent to 0.2 mg/kg bw/day; therefore, 28,500 mg/kg diet is equivalent to 38 g/kg bw/day (i.e. (190,000 X 0.2)/1000).

[8] 65% corn oil in the diet was converted to 58.5 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 650,000 mg/kg diet = 65%; 1 mg/kg in rat feed for a subchronic duration study is equivalent to 0.09 mg/kg bw/day; therefore, 650,000 mg/kg diet is equivalent to 58.5 g/kg bw/day (i.e. (650,000 X 0.09)/1000).

treated rats accumulated large amounts of liver triglycerides; however, due to limited study details, the implications for this finding are unclear. Boyle et al. (1996; abstract only) concluded that corn oil is inappropriate for use in infant formulas based on large changes in liver long-chain polyunsaturated fatty acid profiles. Lastly, Apgar et al. (1987) determined that rats fed up 0, 5, 10, or 20% (equivalent to 0, 6, 12, or 24 g/kg bw/day, respectively[9]) corn oil in the diet for 2 weeks had an overall fecal fatty acid profile of 27-34% palmitic acid (16:0), 22-32% stearic acid (18:0) and 25-37% oleic acid (18:1).

Collectively, these studies reveal that repeated dietary corn oil exposure at high doses ranging from 28.5 – 58.5 g/kg bw/day in rats and mice leads to phenotypes associated with metabolic dysfunction.

Table 4. Studies with lipid and metabolic effects in rats and mice

Reference	**Relevant endpoint(s) specific to corn oil**	**Primary results/conclusion specific to corn oil**
Pavlisova et al., 2016	Male C57BL/6N mice fed a corn oil (32% w/w; equivalent to 64 g/kg bw/day[6]) diet for 8 weeks	At the 64 g/kg bw/day dose, weight gain induction and impaired insulin sensitivity were observed
Wong et al., 2015	Estimation of spontaneous locomotor activity, body composition and in vivo metabolic outcomes in female C57/Bl6 mice fed either high-fat (HF) diets [40% energy corn oil (CO; 19% w/w; equivalent to 38 g/kg bw/day[7]) or isocaloric olive oil (OO; 19% w/w) or chow for 6 weeks	Mice fed a HF diet containing 38 g/kg bw/day of corn oil demonstrated reduced spontaneous locomotor activity, lower respiratory ratio, hyperinsulinemia and impaired glucose disposal; skeletal muscle failed to up-regulate fat oxidation genes, indicating metabolic insufficiencies
Boyle et al., 1996 (abstract only)	Omega 3 long-chain polyunsaturated fatty acid (LCP) accretion in red blood cells, liver, and brain phospholipids were evaluated in rats fed diets containing infant formula fat blends with essential fatty acids provided from soy and/or corn oil.	Large changes in liver LCP profiles; substantial tissues differences b/w the oils (no further details provided in the abstract); authors state that corn oil is inappropriate for use in infant formulas
Apgar et al., 1987	Study to evaluate fecal fatty acid profile and fecal lipid elimination in male Sprague-Dawley rats fed 0, 5,	Overall fecal fatty acid profiles in rats fed up to 24 g/kg bw/day corn oil diets consisted primarily of 27-34% palmitic

[9] 5, 10, and 20% corn oil in the diet was converted to 6, 12, and 24 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 50,000, 100,000, 200,000 mg/kg diet = 5, 10, and 20%, respectively; 1 mg/kg in rat feed for a subacute duration study is equivalent to 0.12 mg/kg bw/day; therefore, 50,000, 100,000, 200,000 mg/kg diet is equivalent to 6, 12, and 24 g/kg bw/day, respectively (e.g. (50,000 X 0.12)/1000).

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
	10, or 20% corn oil (equivalent to 0, 6, 12, or 24 g/kg bw/day, respectively[9]) for 2 weeks	acid (16:0), 22-32% stearic acid (18:0) and 25-37% oleic acid (18:1)
Deshaies, 1986 (abstract only)	Plasma lipoprotein lipid composition and white adipose tissue lipoprotein lipase activity in rats fed diets high in either sucrose or corn oil (65% of calories as sucrose or corn oil, equivalent to 58.5 g/kg bw/day[8]) for 4 weeks; reference diet group was also included	HDL to total cholesterol ratio was higher in the animals fed 58.5 g/kg bw/day corn oil compared to the sucrose-treated group, which had 73% higher plasma total triglyceride levels compared to the corn oil group; oil-fed rats accumulated large amounts of liver triglycerides; however, due to limited study details, the implications for this finding are unclear

DART-related effects

Three studies that were identified from the literature search containing DART-related effects are summarized in Table 5. In a single-dose study, Guerra et al. (2019) evaluated the effects of corn oil on the prostate of male Mongolian gerbils that received corn oil at 0.1 ml/day (equivalent to 1.286 g/kg bw/day, based on the corn oil density of 0.9 g/ml and the reported average animal weight of 70 g) via gavage for 25 days. Overall results from the study showed reduced body weight, an increased incidence of atrophic acini, decreased epithelial and stromal androgen receptor as well as increased epithelial levels of ERalpha and ERbeta. In another single-dose study, Moral et al. (2011) showed that female Sprague-Dawley rats fed a high corn oil (20% corn oil w/w, equivalent to 20 g/kg bw/day[10] diet from weaning through puberty exhibited increased body weight around puberty, increased corpora lutea, and earlier sexual maturation compared to low-fat diet fed animals.

In a separate dietary study, female Sprague-Dawley rats were administered 0, 2, or 10 ml corn oil/kg body weight/day (equivalent to 0, 1.8, or 9 g/kg bw/day, respectively, based on the corn oil density of 0.9 g/ml) via oral gavage during pre-mating (2 weeks), mating, gestation, and until day 3 of lactation (Sato et al., 2000). No effects on mating or fertility indices were reported and no clinical signs observed during gestation. However, at the highest tested dose of 9 g/kg bw/day, decreased food consumption and decreased body weight gain from lactation days 0-4 (only when combined with an animal protein diet) were observed. Additionally, mortality and

[10] 20% corn oil in the diet was converted to 18 g/kg bw/day based on EFSA guidelines (2012): 1 mg/kg diet = 0.0001%; 200,000 mg/kg diet = 20%; 1 mg/kg in rat feed for a subchronic duration study is equivalent to 0.09 mg/kg bw/day; therefore, 200,000 mg/kg diet is equivalent to 18 g/kg bw/day (i.e. (200,000 X 0.09)/1000).

clinical signs were observed post-parturition as well as reduced pup viability when combined with an animal protein diet. Thus, adverse effects from corn oil were primarily observed when combined with an animal protein diet.

Taken together, these studies reveal differential effects of corn oil exposure in Mongolian gerbils and rats based on the corn oil dosage and route of administration. In male Mongolian gerbils that were administered 1.286 g/kg bw/day of corn oil via gavage for 25 days, body weights were decreased and effects on the prostate were observed. Separately, in female rats that received 0, 1.8, or 9 g/kg bw/day of corn oil via gavage combined with an animal protein diet during pre-mating (2 wk), mating, gestation, and until day 3 of lactation, rats from the highest dose group had decreased body weight, mortality, exhibited clinical signs, and reduced pup viability; however, the study authors note these observed effects occurred when combined with an animal protein diet. In a separate non-gavage rat study, females that that received an 18 g/kg bw/day high corn oil diet from weaning through puberty exhibited earlier sexual maturation and increased body weight. Although the Sato et al. (2000) study is the only multiple-dose study among the three that were identified for DART, the dose range is inadequate for determining dose-dependent effects. The collective data from the three studies suggest reproductive toxicity below 1.286 g/kg bw/day based on the effects that were observed in male Mongolian gerbils, and developmental toxicity at less than 18 g/kg bw/day based on the observed effects in female Sprague-Dawley rats fed an 18 g/kg bw/day corn oil diet from weaning through puberty.

Table 5. Studies with DART effects

Reference	**Relevant endpoint(s) specific to corn oil**	**Primary results/conclusion specific to corn oil**
Guerra et al., 2019	Effects of corn oil on the prostate were evaluated in male Mongolian gerbils that received corn oil at 0.1 ml/day (equivalent to 1.286 g/kg bw/day, based on the corn oil density of 0.9 g/ml and the reported average animal weight of 70 g) via oral gavage for 25 days	At a dose of 1.286 g/kg bw/day of corn oil, the following were observed: atrophic acini, reduced body weight, decreased androgen receptor in the epithelium and stroma, and increased epithelial levels of ERalpha and ERbeta
Moral et al., 2011	Effects of a high corn oil diet (20% corn oil w/w, equivalent to 18 g/kg bw/day[10]) on puberty and mammary gland development in female Sprague-Dawley rats fed high corn oil diet from weaning through puberty	At a corn oil dose of 18 g/kg bw/day, increased body weight nearing puberty, increased corpora lutea, and earlier sexual maturation were observed compared to low-fat diet fed animals
Sato et al., 2000	Corn oil effects on gestation, parturition, and lactation in female Sprague-Dawley rats divided into 2 (CA-1 and CE-2) groups* that were administered 0, 2, or 10 ml corn	-No effects on mating or fertility indices; No clinical signs observed during gestation Effects observed at the highest tested dose of 9 g/kg bw/day:

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
	oil/kg body weight/day (equivalent to 0, 1.8, or 9 g/kg bw/day, respectively, based on the corn oil density of 0.9 g/ml) via oral gavage during pre-mating (2 wk), mating, gestation, and until day 3 of lactation *CA-1 dietary protein is primarily from animal protein while CE-2 is primarily from plant protein	-Decreased food consumption (both diets) -Decreased body weight gain from lactation days 0-4 on CA-1 diet -Clinical signs observed post-parturition and mortality on CA-1 diet -Reduced pup viability from dams on CA-1 diet

Cancer Effects

Three studies that were identified containing cancer-related information along with an NTP study are summarized in Table 6. In the NTP study, control male rats that received a corn oil vehicle were shown to have a higher incidence of pancreatic proliferative lesions and a lower incidence of mononuclear cell leukemia compared to untreated control males (NTP, 1994). Additionally, corn oil is not mutagenic in Salmonella typhimurium strains TA97, TA98, TA100, or TA1535, with or without S9 (NTP, 1994). Based on a study comparing the effects of various concentrations of safflower (very high in polyunsaturated fat), corn oil (high levels of polyunsaturated and monounsaturated fats), and tricaprylin (high in saturated medium-chain fatty acids) (tricaprylin) on the incidence and pattern of neoplasms in the F344/N rat, it was concluded that safflower oil and tricaprylin do not offer significant advantages over corn oil as a gavage vehicle in long-term rodent studies (NTP, 1994).

The primary objective of each of the remaining three studies was to comprehensively evaluate corn oil gavage data obtained from carcinogenicity studies in order to determine tumor incidence. Overall conclusions from the study authors are in general agreement with the NTP (1994) regarding the higher incidence of pancreatic proliferative lesions and a lower incidence of mononuclear cell leukemia in corn oil vehicle-treated control male rats compared to untreated control males. The study authors further suggest that the pancreatic acinar cell tumor incidence is due to a combination of fat intake and body weight (Rao and Haseman, 1993).

Table 6. Studies on cancer in rats and mice

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
NTP, 1994	Studies conducted to evaluate the effects of various concentrations of safflower oil, corn oil, and tricaprylin on the incidence and pattern of neoplasms in the F344/N rat; safflower oil and	• Corn oil-treated, control male rats exhibited a higher incidence of pancreatic proliferative lesions and a lower incidence of mononuclear cell leukemia compared to untreated control males

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
	tricaprylin were also evaluated as replacements for the corn oil vehicle.	• Corn oil was not determined to be mutagenic in Salmonella typhimurium strains TA97, TA98, TA100, or TA1535, +/- S9 • Safflower oil and tricaprylin do not offer significant advantages over corn oil as a gavage vehicle in long-term rodent studies
Rao and Haseman, 1993	Summary of the influence of corn oil gavage and different nonpurified diets on spontaneous tumor incidences in 64 dietary groups and 59 corn oil gavage control groups in 2-yr studies on ~6100 Fischer 344 rats of each sex	• Corn oil gavage significantly increased the body weight and pancreatic tumor incidences but decreased the incidence of leukemia, which resulted in higher survival in male rats. • Corn oil gavage significantly lowered the body weight and anterior pituitary tumor incidence in female rats. • Pancreatic acinar cell tumor incidence was suggested by the study authors to be due to a combination of fat intake and body weight.
Haseman and Rao, 1992	Survival, body weight, and site-specific tumor rates in untreated, corn oil gavage, and water gavage control Fischer 344 (F344/N) rats from 88 National Toxicology Program (NTP) long term carcinogenicity studies were evaluated to determine which factors were primarily responsible for inter-study variability.	• Corn oil increases pancreatic acinar cell tumor rates and reduces leukemia rates in male F344/N rats but has no significant effect on tumors in female rats • Corn oil increases body weight and survival in male rats • The gavage technique per se does not appear to affect tumor rates
Haseman et al., 1985	Control data on F344/N rats and (CS7BL/6N X C3H/HeN)F1 (B6C3F1) mammary tumor virus-free mice from the NTP were evaluated to compare tumor incidence between untreated controls versus animals that were administered corn oil via gavage	• Corn oil-treated male F344/N control rats showed a higher incidence of pancreatic acinar cell adenoma and a lower incidence of leukemia (primarily mononuclear cell leukemia) than did the corresponding untreated controls. • The increased incidences of pancreatic acinar cell adenoma observed in corn oil-treated male rats were associated with elevated body weights compared to untreated controls. • Female F344 rats and male and female B6C3F1 mice showed little or no evidence of a difference in tumor incidence between corn oil gavage-treated and untreated controls. • A review of ~300 carcinogenesis studies conducted by the National Cancer Institute (NCI) and the NTP revealed that there were no corn oil gavage studies in which

Reference	Relevant endpoint(s) specific to corn oil	Primary results/conclusion specific to corn oil
		increased incidences of pancreatic acinar cell tumors or leukemia in male F344/N rats were the sole evidence of the carcinogenicity of a test chemical. • Corn oil appears to have little impact on the interpretation of NCI-NTP carcinogenicity studies

Overall, the pre-clinical evidence showed that exposure to very high amount of corn oil could result in various target organ effects, including:

- Subchronic dietary exposure corn oil in amount >=7.5 g/kg bw/day in rats can adversely affect cardiac ultrastructure and function as well as induce traits consistent with type 2 diabetes.
- Corn oil administered in the diet and via gavage at doses ranging from 4.5 -18 g/kg bw/day have been shown to cause adverse effects in the liver, kidney, and GI; however, pancreatic effects observed in rat 2-yr carcinogenicity studies are not attributed to corn oil.
- Repeated dietary corn oil exposure at high doses ranging from 28.5 – 58.5 g/kg bw/day in rats and mice leads to phenotypes associated with metabolic dysfunction.
- The collective data from DART studies suggest reproductive toxicity below 1.286 g/kg bw/day, and developmental toxicity at less than 18 g/kg bw/day

Assuming a default 60 kg body weight, these effects were observed with very high intake in the range of 77 g to 3,516 g of corn oil per day. These intakes are much higher than the EDI of 6 g of corn oil per day based on US consumption data (see appendix H of GRN). Corn oil is a food with a long history of use in the U.S. food supply. The principal food uses of corn oil include salad and cooking oil, margarine, blends of butter, mayonnaise and emulsion type salad dressings. Corn oil is used as an oil ingredient in a variety of packaged and restaurant foods, including spaghetti sauce, potato chips and snack foods, French fries and breaded foods, baking mixtures, frosting and whipped toppings, crumb coating for meat and poultry, and baked goods. The published literature also indicates that corn oil was commonly used in infant formulas in the U.S. as recently as the late 1990s (LSRO, 1998[11]; Ponder et al. 1992[12]; Green Corkins and

[11] Life Sciences Research Office (LSRO) Expert Panel Report. Raiten DJ, Talbot JM, Waters JH, Eds. Assessment of nutrient requirements for infant formulas. J Nutr. 1998 Nov;128(11 Suppl):i-iv, 2059S-2293S. Review. No abstract available. Erratum in: J Nutr 1999 May;129(5):1090.

[12] Ponder DL, Innis SM, Benson JD, Siegman JS. Docosahexaenoic acid status of term infants fed breast milk or infant formula containing soy oil or corn oil. Pediatr Res. 1992 Dec;32(6):683-8

Shurley, 2016[13]). Further, due to its beneficial effect of significantly lowering elevated blood pressure, a qualified health claim petition – Corn Oil and Corn Oil-Containing Products and a Reduced Risk of Heart Diseases (Docket No. 2006P-0243) was filed and FDA concluded that there is sufficient scientific support for a qualified health claim for corn oil (FDA, 2007[14]). Thus, chronic consumption of COZ corn oil, which is the same as conventional edible corn oil, would not be expected to be associated with the effects observed in animals at very high doses that well exceed dietary exposure to corn oil among the US population.

Q3. Please discuss what is known about the absorption, distribution, metabolism and excretion (ADME) profile of corn oil, which informs the safety of COZ corn oil.

Response:

Literature searches were conducted in April 2020 using PubMed, with supplemental searches performed in GoogleScholar to identify studies containing information related to the pharmacokinetics (i.e. absorption, distribution, metabolism, and excretion; ADME) of corn oil. The following search terms were used with the search field restricted to titles, and with no other limitations:

> Corn oil OR 8001-30-7 OR corn oils OR oil, corn OR maize oil OR maize oils OR oil, maize OR oils, maize OR lipomul AND (metabolism OR metabolic OR absorption OR bioavailability OR pharmacokinetics OR oral OR pharmacodynamics)

Titles of 73 citations were returned and reviewed, followed by review of abstracts in cases where the title did not provide sufficient information to judge the relevance of a publication. Based on this initial titles and abstracts review, only a single study was identified that contained relevant information on the pharmacokinetics of corn oil. Although this single study is limited in scope, it was included for comprehensiveness. Publications that were excluded from further consideration were:

- Mechanistic studies, mode of action, mixture studies, studies on an unrelated compound (44, e.g. biochemical pathway analyses; evaluations on additive, synergistic, or antagonistic effects; initiation and promotion effects involving other compounds, such as carcinogens)
- Behavioral grooming study (1)

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[13] Green Corkins K, Shurley T. What's in the Bottle? A Review of Infant Formulas. Nutr Clin Pract. 2016 Dec;31(6):723-729. doi: 10.1177/0884533616669362.

[14] Food and Drug Administration (FDA). Qualified Health Claims: Letter of Enforcement Discretion – Corn Oil and Corn Oil- Containing Products and a Reduced Risk of Heart Disease (Docket No. 2006P-0243). March 25, 2007.

- Agriculture, animal feed, and non-relevant mammalian species studies (7)
- Chemical properties, analytical methods/techniques, and technical applications (6)
- Dated publications (pre-1980 with no available abstract (13))
- A study from Pavlisova et al., 2016 that was previously captured for lipid and metabolic effects that is described in Table 4

Two studies that were not captured in the 73 citations from the ADME literature search but were identified in the first literature search (i.e. 882 citations) as well as five separate reviews were included for supporting information.

Relevant ADME Citations:

Author, year	**Citation**
Barrera-Arellano, 2019	Daniel Barrera-Arellano, Ana Paula Badan-Ribeiro,Sergio O. Serna-Saldivar. Chapter 21 Corn Oil: Composition, Processing, and Utilization. Corn (Third Edition). Chemistry and Technology. 2019, Pages 593-613.
Wang and White, 2019	Tong Wang and Pamela J. White. Chapter 13 - Lipids of the Kernel. Corn (Third Edition). Chemistry and Technology. 2019, Pages 337-368**.**
Lichtenstein et al., 2012	Lichtenstein A, Jones PJ. Lipids: Absorption and Transport. In: Erdman JWJ, Macdonald IA, Zeisel SH, eds. Present Knowledge in Nutrition. 10th ed: ILSI Wiley-Blackwell; 2012:118-131.
Patterson et al., 2012	Patterson E, Wall R, Fitzgerald GF, Ross RP, Stanton C. Health implications of high dietary omega-6 polyunsaturated Fatty acids. J Nutr Metab. 2012;2012:539426.
Degrace et al., 1996	Degrace P, Caselli C, Rayo JM, Bernard A.Intestinal lymph absorption of butter, corn oil, cod liver oil, menhaden oil, and eicosapentaenoic and docosahexaenoic acid ethyl esters in rats.Lipids. 1996 Apr;31(4):405-14.
Dupont, 1990	Dupont J, White PJ, Carpenter MP, Schaefer EJ, Meydani SN, Elson CE, Woods M, Gorbach SL. Food uses and health effects of corn oil. J Am Coll Nutr. 1990 Oct;9(5):438-70.
Mitchell et al., 1989	Mitchell DC, McMahon KE, Shively CA, Apgar JL, Kris-Etherton PM.Digestibility of cocoa butter and corn oil in human subjects: a preliminary study.Am J Clin Nutr. 1989 Nov;50(5):983-6.
Apgar et al., 1987	Apgar JL, Shively CA, Tarka SM Jr.Digestibility of cocoa butter and corn oil and their influence on fatty acid distribution in rats.J Nutr. 1987 Apr;117(4):660-5.

Corn oil ADME

Corn oil is a highly digestible fat that consists of approximately 60%, 25%, and 15% polyunsaturated, monosaturated, and saturated fatty acids, respectively (Apgar et al., 1987;

Mitchell et al., 1989; Dupont, 1990; Patterson et al., 2012; Wang and White, 2019; Barrera-Arellano, 2019). Therefore, the metabolism and bioavailability of corn oil is expected to be similar to other fatty acids. Following dietary ingestion of fats such as corn oil, the fatty acids are hydrolyzed by pancreatic enzymes and bile salts prior to being absorbed in the small intestine, for eventual distribution to other tissues in the body such as the liver and adipose (Lichtenstein et al., 2012). In the single study that was captured from the ADME literature search, male rats that received an intragastric bolus dose of corn oil comprised of 82.4% oleic and linoleic acids had a peak absorption of 2.0 ± 0.4 mL/h (Degrace et al., 1996). The study authors concluded that intestinal absorption of fatty acids such as corn oil can vary based on fatty acid composition, but the metabolic processes underlying fatty acid metabolism are generally the same (Degrace et al., 1996). Thus, the pharmacokinetic profile of corn oil can be reasonably inferred from the processes underlying fatty acid metabolism.

Q4. In Table 7 on Page 28, the units of the percentage values presented in columns 5 (FCC Specification) and 6 (COZ Corn Oil Mean) are not specified. Please address whether these values reflect a percentage of 100 g oil (as in column 2) or a percentage of 100 g fatty acids (as in column 3).

Response:

The percentage values in column 5 (FCC Specification) reflects a percentage of 100 g oil.
The percentage in column 6 (COZ Corn Oil Mean) reflects a percentage of 100 g oil.

Q5. Please clearly state **in your own words** your OVERALL CONCLUSION that the COZ corn oil (subject of this GRAS notice) is GRAS for its intended use and why the concerns associated with corn oil exposure raised by various studies such as these noted above by FDA are adequately addressed.

Response:

COZ corn oil derived from distillers corn oil by CO1™ and conventional RBD processes is equivalent to conventional corn oil. COZ corn oil meets FCC specifications for color, water, free fatty acids, iodine value, peroxide value, unsaponifiable matter, and fatty acids. In addition to having a fatty acid profile consistent with conventional corn oil, the phytosterol and fat soluble vitamin concentrations are comparable to conventional corn oil. COZ corn oil therefore is nutritionally equivalent to conventional corn oil. The proposed use of COZ corn oil as edible corn oil will be substitutional to other conventional corn oil sources in the US market. As shown in the response to Q2. the dietary exposure to corn oil in the US is well below intake level in animal studies in which adverse effects were observed. Conventional corn oil has had a long history of dietary exposure with recognized health benefits via an approved qualified health

claim. Conventional corn oil is generally recognized as safe (GRAS). As such, COZ corn oil, which is the same as conventional edible corn oil, is also GRAS.

GRN 000890 – Responses to Chemistry Questions (April 24, 2020)

Chemistry questions

Manufacturing and Raw Materials

Q1. In Tables 3 and 4 on pages 17 and 18, you have listed several processing aids and materials with "regulatory status". Some of them do not address the uses described in your notice.[1] For clarity, please provide a statement that any processing aids, materials and components added during manufacture, and any antioxidants added to the final product are commonly used in production of edible oils, food grade, and safe and suitable for their intended use.

Response:
All processing aids used in the CO1™ processing steps have regulatory approvals for use in food, are commonly used in the production of edible oils, and are safe and suitable for their intended use.

Q2. Please provide a statement that the COZ corn oil is produced in accordance with current good manufacturing practices and general requirements for production of human food (21 CFR Part 110).

Response:
Production of COZ corn oil is comprised of two distinct phases, as described in the GRN document. Both production processes are in compliance with current good manufacturing practices and general requirements for production of human food.

Q3. On page 14, the notice states that several components added during ethanol production and fermentation byproducts may be present in the crude oil.

a. Please provide a narrative based on standard industry practices to address removal of the other chemicals (i.e. urea, caustic soda, oil recovery chemicals, enzymes, and pH control agents) and fermentation byproducts that may be present following crude oil production.

Response:
As shown in Appendix C, Table D1, urea, caustic soda, sulfuric acid, enzymes, yeast used in the fermentation process have regulatory approval for use in food. Except for PhibroBreak Corn Oil additive, all substances listed in Table D2 are used for the purpose of boiler and water treatment in the ethanol production process. The active ingredients used in these substances are listed as permissible chemicals as boiler water additives and are listed in 21 CFR 173.310.[1] As a result, these substances are designed to be highly soluble in water and will be separated into the aqueous streams of the fermentation process. In an unlikely scenario where residues of these substances are present in the crude corn oil feedstock, they will be removed in the neutralization step of the Phase 1 CO1 process and refining step of the Phase II RBD process due to their high solubility in water.

PhibroBreak is a processing aid for the separation of crude corn oil from condensed solubles at ethanol production facilities. A major component of this substance is a polymeric surfactant the use of which is GRAS in feed. Further, the manufacturer provided a letter stating that the additive does

[1] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=173.310

not pose any health risk to humans. [2,3] Most of the substance will remain in the rag layer; an extremely low amount of it might be left as a residue in the crude corn oil. Any residue will be removed by the filtration process step during dewaxing in the Phase 1 CO1 process and bleaching in the Phase II RBD process.

	Product Name	**Active Ingredient**	**GRAS status of active Ingredient**
A	VOxOUT 70C CO_2 Scrubber Chemical	Ammonium Bisulfite[4]	Extremely Soluble in water
B	Boiler MP Plus Scale Inhibitor Boiler Chemical	Sodium Hydroxide[5]	Extremely Soluble in water. 21 CFR 184.1763 Sodium hydroxide
C	BWT 200 B Alkalinity Builder Boiler Chemical	Sodium or Potassium Hydroxide is typically used	Extremely Soluble in water. 21 CFR 184.1763 Sodium hydroxide
D	Oxigon 200 Oxygen Scavenger Boiler Chemical	Inorganic sulfite, diethylhydoxylamine are typically used. [6]	Extremely soluble in water
E	RLT 19 Condensate Treatment Boiler Chemical	Amines such as 2-Diethylaminoethanol are typically used. [7]	Extremely soluble in water
F	Bulab 8170GR Evaporator Anti-scalant	Poly acrylic acids, Polyphosphates, Phosphonates are typically used. [8]	Extremely soluble in water
G	FermaSure XL	Chlorine Dioxide[9]	Extremely Soluble in water. 21 CFR 173.300
K	Phibro AC Clean-in-Place Chemical	Nitric Acid, Proprietary Chemical[10]	Extremely Soluble in water. 49 CFR 173.158

b. Please clarify whether active enzymes and red yeast used in ethanol production are expected to remain in the refined oil.

Response:

As shown in Appendix C, Table D1 of the GRN, the enzymes and yeast used in the ethanol production have regulatory approval to be used in the production of food. In addition, due to the amount of water used in the fermentation process, the enzymes and the red yeast used in the ethanol production must be either soluble or dispersible in water. The likelihood of enzymes and yeast residues being present in the crude oil is very low. In the event any of the residues are present in the crude oil, they will be removed in the dewaxing filters during the dewaxing step of the Phase 1 CO1 process.

Q4, In Table D-2 on page 62, the notice lists substances A through L that you state, "do not have

[2] Letters from the manufacturer stating that the additive does not pose human health risk (attached to this response)
[3] PhibroBreak SDS sheet (attached to this response)
[4] VOxOUT SDS sheet (attached to this response)
[5] Boiler MP Plus SDS Sheet (attached to this response)
[6] https://www.suezwatertechnologies.com/handbook/chapter-11-preboiler-and-boiler-corrosion-control
[7] https://www.suezwatertechnologies.com/handbook/chapter-19-condensate-system-corrosion
[8] https://www.sciencedirect.com/topics/engineering/antiscalant
[9] FermaSure XL SDS sheet (attached to this response)
[10] Phibro AC SDS sheet (attached to this response)

the appropriate regulatory status." Please provide additional information to assess the regulatory status of these substances. Consider the following in your response:

a. Please provide a statement addressing if the substances A through K are standard to the corn oil industry or industrial fermentations for food use.
Please see response above in Q3-a

b. Substance L is added directly to the crude oil and therefore would not meet the "food contact substance" definition as you have cited. Please address its regulatory status as a direct ingredient.
Please see response above in Q3-a

c. You have provided a Threshold of Toxicological Concern (TTC) discussion for substances termed "impurities" (p. 35-39, 61-62). We note that FDA has a process for submitting a threshold of regulation (TOR) exemption, and information provided in a GRAS notice cannot serve as a TOR exemption submission. Further, we note that boiler water additives are within the purview of the Division of Food Contact Substances (DFCS) within OFAS, while sanitation chemicals may be within the purview of DFCS or the Environmental Protection Agency. We would not evaluate safety of these materials within the context of a GRAS notice.

Response:
None of the substances in question are being treated as food contact substances for which TOR can be used. Rather, the substances are being treated as residues the safety of which are being addressed through the threshold of toxicological concern (TTC) paradigm. TTC is based on scientific risk assessment principles and can be used to assess the safety of such residues. The lowest TTC value (0.15 microgram/day) was used as the basis to derive an acceptable limit.

GRN 000890 – Responses to Chemistry Questions (April 24, 2020)

Antibiotics Use

The notice suggests that the assurance that antibiotics are not present in COZ corn oil relies on two factors: 1) absence of antibiotics in the crude oil (as determined by monthly random sampling (regular protocol), and 2) removal of any residual antibiotics during the method of manufacture. The information provided in the notice does not sufficiently address this topic. We request that you address the following:

Q1. Antibiotic use in ethanol production varies by country. Please clarify whether the source of the crude corn oil is only domestic or also from outside the U.S. If crude corn oil is obtained from outside the U.S., please specify where it is obtained from.

Response:
Only domestic crude oil is used as feedstock.

Q2. On page 15, the notice cites a report by the U. S. Grain Council that states that the following antibiotics may be used in production of ethanol from distiller's grains: virginiamycin, erythromycin, penicillin G, tetracycline, and tylosin.

a. Will suppliers of crude corn oil provide data on use of antibiotics other than those five?

   Response:
   Yes, the suppliers of crude corn oil will provide data on use of antibiotics other than those five

b. If so, what are the acceptance criteria for crude corn oil for antibiotics other than those five?

   Response:
   Similar to the five antibiotics, the acceptance criteria for the remaining antibiotics will be 'Not Detected (LOD=0.05ppm)'.

Q3. Please comment whether the FDA LIB (4438) method for analysis of antibiotic residues is validated for use in an oil matrix.

Response:
The method was validated for oil matrices. The method is based on FDA LIB 4438. While the extraction procedure is the same, the method uses a different analytical column, mobile phases, and gradient.

Q4. Have specifications been set for limits on the levels of antibiotics in the refined oil product? Please discuss.

Response:
Antibiotics are not expected to be present in the crude oil starting material and that will be verified using methods with low limits of detection. Therefore, antibiotics will not be present in the refined oil.

Q5. Please provide a narrative to explain why antibiotics will not remain in the crude oil after

fermentation, and how the RBD process (pp, 18-19, pp. 66-68) would remove residual antibiotics. Consider the following in your response:

a. Include reference(s) used for the data in Appendix E (pp. 66-68).
Response: please see comprehensive narrative response below; references have been added to the updated Appendix E (enclosed with this response in excel format to facilitate viewing)

b. Consider relevant publications regarding distribution of antibiotic residues between distiller's grains (dry matter) and crude oil.
Response: please see comprehensive narrative response below

c. The information in the tables pp. 66-68 suggests at least a portion of the antibiotics might distribute in oil. Please clarify how the information in this table was used to predict the distribution of antibiotics in water:oil (100:0) to support statements regarding removal of antibiotics during degumming and neutralization (pp. 18-19). Support your assumption with data on fractionation of antibiotics in these matrices (either from DDGS producer data or in a laboratory setting).

Response: Information in the narrative (see below) and updated Appendix E addresses the above question.
Water solubility of a contaminants is measured in mg/l. Solubility is divided into three categories as below[11]:

Low water solubility: <10 mg/l
Moderate water solubility: 10-1,000 mg/l
High water solubility: >1,000 mg/l

Based on the above criteria, the antibiotics and mycotoxins are predicted to be distributed in the solvent (water and ethanol) in various ratios.

Low water solubility: 25:75 Water: Oil
Moderate water solubility: 50:50 Water: Oil
High water solubility: 100:0 Water: Oil

d. Several cells in the Tables pp. 66-68 are blank. Please rectify.

Response:
Appendix E has been updated to reflect parameters used in the mass balance calculation; extraneous data not relied upon have been removed to avoid confusion. The updated Appendix E is enclosed with this response in excel format to facilitate viewing

Response Narrative:
During the corn fermentation process, antibiotics are typically added to minimize bacterial contamination that could result in lower ethanol yield and quality. Virginiamycin and Penicillin are the most widely used antibiotics in the corn fermentation process.[12] FDA's Center for Veterinary Medicine (CVM) conducted a nationwide survey in 2012 for 13 possible antibiotic residues in Distillers Grains. The survey found that out of total 46 samples analyzed, only 3 samples had

[11] Ronald Ney, "Fate and Transport of Organic Chemicals in the Environment" 1995; p. 10
[12] https://grains.org/wp-content/uploads/2018/01/Chapter-9DDGS.pdf

detectable concentrations of erythromycin, penicillin and/or virginiamycin.[13] The first sample contained 0.58 ppm erythromycin, the second sample contained 0.24 ppm penicillin and 0.15 ppm virginiamycin, and the third sample contained 0.16 ppm virginiamycin. Erythromycin had a detection limit of 0.5 ppm, penicillin had a detection limit of 1.0 ppm, and virginiamycin had a detection limit of 0.1 ppm.[14]

Virginiamycin M1: Virginiamycin is a commonly used antibiotic in corn fermentation process added at levels of 0.25 ppm to 2ppm. Virginiamycin is approved by the FDA to be used in treatment of livestock, for example at levels of 5.5 to 110ppm in swine feed. In November 1993, the FDA's Center for Veterinary Medicine issued a "letter of no objection" for the use of virginiamycin at concentrations of between 2 to 6 ppm in the fermentation phase of ethanol and distiller's dried grain with solubles? (DDGS) production, and had no objection to potential virginiamycin residues of 0.2 to 0.5 ppm in DDGS. Virginiamycin concentrations below 0.5 ppm pose no concern to animals consuming the feed, nor to humans consuming food derived from those animals. [15, 16] The FDA also conducted a quantitative risk assessment on virginiamycin and human health in 2004 and concluded that virginiamycin poses no threat to human health.[12,16]
Virginiamycin is significantly inactivated at temperatures of the ethanol distillation process at 100°C.[17] Temperature conditions in the drying step in Phase I CO1 process and deodorization step in the Phase II RBD process can be as high as 260°C - enough to deactivate any Virginiamycin residues if present in the crude corn oil. Virginiamycin has limited solubility in both water (45mg/l)[18] but high solubility in polar organic solvents such as ethanol.[19,20] Aqueous ethanol solutions are used as solvent in the neutralization step of Phase I CO1 process. So, any residues of Virginiamycin that might be present in crude corn oil will be removed in the process.

Penicillin G: Penicillin is often added at concentrations above 1.5 mg/L in fuel ethanol production due to the possibility of induced enzymatic degradation of the antibiotic. This concentration is much lower than concentrations approved for use in food animals. [12]
The stability of penicillin is directly affected by temperature and pH. High temperatures (>35°C) and pH values greater than 8.0 and less than 4.0 cause penicillin to become unstable. [21] It was reported that within 48 hours, penicillin G (0.5 unit/mL) was almost completely? inactivated at 35°C and at pH of 3.8, 4.0, 4.2, and 4.5 during sterile malt glucose yeast extract fermentation. [22]

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[13] FY 2010 Nationwide Survey of Distillers Grains for Antibiotic Residues, 2009. http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/Contaminants/ucm190907.htm
[14] Luther, M. 2012. Report of FY 2010 nationwide survey of distillers products for antibiotic residues, Center for Veterinary Medicine, FDA, Silver Springs, MD.
[15] Benz, S. A. 2007. In: J. A. Miller (ed.). Department of Health & Human Services, Rockville, MD, p.2.
[16] Juranek, P. and P. Duquette. 2007. Antibiotic regulatory considerations for distiller's grains. Distillers Grains Quarterly, 4th Quarter.
[17] Hamdy, M.K. R.T. Tolew, C.J. Shieh, M.A. Fpannenstiel and R. Wang. 1996. Effects of virginiamycin on fermentation rate by yeast. Biomass and Bioenergy 11:1-9.
[18] US EPA; Estimation Program Interface (EPI) Suite. Ver. 4.1. Jan, 2010. Available from, as of May 8, 2012: http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm
[19] Lactrol- Virginiamycin and Dextrose, Product Data Sheet, Phibro Ethanol Performance, https://www.pahc.com/wp-content/uploads/ProductDataSheets/EPG/Antibiotics/phibro-lactrol-4-4-16.pdf
[20] O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006.
[21] Kheirolomoom, A., A. Kazemi-Vaysri, M. Ardjmand, A. Baradar-Khoshfetrat. 1999. The combined effects of pH and temperature on penicillin G decomposition and its stability modeling. Process Biochemistry 35:205-211.
[22] Islam, M., R. Toledo, and M.K. Hamdy. 1999. Stability of virginiamycin and penicillin during

Penicillin is significantly inactivated at temperatures of the ethanol distillation process of 100°C.[23] Temperature conditions in the drying step in Phase I CO1 process and deodorization step in the Phase II RBD process can be as high as 260ºC enough to deactivate any Penicillin residues if they are present in the crude corn oil. Penicillin G has high solubility in both water (>0.056mol/l or 18704mg/l) and ethanol (>0.028mol/l or 9352mg/l).[24,25,26,27] So, in the unlikely event any Penicillin residues are present in crude corn oil the resudues will be removed during contact with aqueous ethanol solutions in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process.

Erythromycin: The stability of erythromycin is pH and temperature dependent, where it is more stable at the pH range from 7.0 to 8.0 and lower temperatures. [28] Erythromycin is likely inactivated by the low pH and high temperatures encountered during fermentation and distillation of ethanol. Temperature conditions in the drying step in Phase I CO1 process and deodorization step in the Phase II RBD process can be as high as 260°C which is enough to deactivate any Erythromycin residues if present in the crude corn oil. Further, Erythromycin is soluble in water (2000mg/l) and polar solvents such as ethanol. [29, 30, 31] So, in the unlikely event any Erythromycin residues are present in the crude corn oil, the residues will be removed during contact with aqueous ethanol solutions in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process.

Tylosin: Tylosin is not a commonly used antibiotic in the corn fermentation process. Tylosin is most stable at about pH of 3.5 to about pH of 9. Outside of those pH ranges, there is significant inactivation of the anitibiotic. In addition, exposure to increased temperatures can lead to inactivation. [32] Temperature conditions in the drying step in Phase I CO1 process and deodorization step in the Phase II RBD process can be as high as 260°C which is enough to deactivate any Tylosin residues if present in the crude corn oil. Tylosin is approved to be fed to livestock.
Further, Tylosin is highly soluble in water at levels of 5000 mg/l and freely soluble in methanol and other lower alcohols. [33] So, in the an unlikely event any Tylosin residues are present in the crude corn oil, the residues will be removed during the contact with aqueous ethanol solutions in the

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alcohol fermentation.Biomass and Bioenergy 17 :369-376.

[23] Hamdy, M.K. R.T. Tolew, C.J. Shieh, M.A. Fpannenstiel and R. Wang. 1996. Effects of virginiamycin on fermentation rate by yeast. Biomass and Bioenergy 11:1-9.

[24] Weiss P.J.; Andrew, M.L.; Wright, W.W. Antibiotics and Chemotherapy 1957,7, 374.

[25] David J. Maggs, Chapter 3 - Ocular Pharmacology and Therapeutics, Slatter's Fundamentals of Veterinary Ophthalmology (Fourth Edition), 2008

[26] Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 178

[27] E. Tomlinson, A. Regosz, Solubility data series, Antibiotics: 1, beta-lactam antibiotics, Pergamon Press, Vol 16/17 1985

[28] Brisaert, M., M. Heylen and J. Plaizier-Vercammen. 1996. Investigation on the chemical stability of erythromycin solution using an optimizing system. Pharm. World Sci. 18:182-186.

[29] https://www.chemicalbook.com/ChemicalProductProperty_US_CB8300078.aspx

[30] Lide, D.R. CRC Handbook of Chemistry and Physics 88TH Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-230

[31] Photo-Degradation of Amoxicillin, Streptomycin, Erythromycin and Ciprofloxacin by UV and UV/TiO2 Processes. Evaluation of Toxicity Changes Using a Respirometric Biosensor, Palmisano, Campanella, Ambrosetti, J Environ Anal Chem 2015, 2:3

[32] Aksenova, I. A., E. M. Ter-Sarkisian, R. D. Soifer, G. Florova, and L. S. Iustratova. 1984. [Effect of the ph of the medium and of temperature on tylosin stability]. Antibiotiki 29:179-182.

[33] O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Cambridge, UK: Royal Society of Chemistry, 2013., p. 1823

neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process.

Tetracycline: Tetracycline is not a commonly used antibiotic in the corn fermentation process. Tetracycline is inactivated in acidic conditions (pH<2) forming anhydroteracyline. [34] Further, Tetracycline has limited solubility in water at levels of 231 mg/l [35] and highly soluble in ethanol at levels of 20,000 mg/ml.[36] So, in the an unlikely event any Tetracycline residues are present in the crude corn oil, the residues will be removed during the contact with aqueous ethanol solutions in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process.

Q6. On pages 66-68, the notice notes 3 of 5 antibiotics are unstable under acidic conditions (C01 process and degumming) and 4 of 5 antibiotics are unstable to caustic refining. Please provide a narrative on the effect of these processes on the removal of antibiotics and/or their degradants including references or data (e.g., spiked samples) in support. Consider the following in your discussion:

a. Discuss the basis for concluding removal of residues of virginiamycin by deodorization (p. 68). Are other antibiotics or their degradants affected by deodorization?

Response:

Antibiotics are inactivated at high temperature conditions. Specifically, virginiamycin is inactivated at temperatures greater than 100°C and penicillin at temperatures greater than 35°C. Temperatures in deodorization process can reach as high as 260°C and will therefore inactivate the antibiotics. However, due the solubility of these virginiamycin and other antibiotics in water and ethanol, they will be removed from the oil in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process. Appendix E is updated accordingly.

b. Address solubility of erythromycin in oil based on the data from one of the crude oil samples (page 69). Other than the single batch analysis, there is no supporting information in the notice.

Response:

Erythromycin is soluble in water (2000mg/l) and polar solvents such as ethanol. [37, 38, 39] So, in the unlikely event any Erythromycin residues are present in the crude corn oil, the residues will be removed during contact with aqueous ethanol solutions in the neutralization

[34] Wang, L., H. Yang, C. Zhang, Y. Mo, and X. Lu. 2008. Determination of oxytetracycline, tetracycline and chloramphenicol antibiotics in animal feeds using subcritical water extraction and high performance liquid chromatography. Anal. Chim. Acta 619: 54-58.

[35] Yalkowsky SH, Dannenfelser RM; The AQUASOL database of Aqueous Solubility. Fifth ed, Tucson, AZ: Univ AZ, College of Pharmacy (1992)

[36] Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1143

[37] https://www.chemicalbook.com/ChemicalProductProperty_US_CB8300078.aspx

[38] Lide, D.R. CRC Handbook of Chemistry and Physics 88TH Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-230

[39] Photo-Degradation of Amoxicillin, Streptomycin, Erythromycin and Ciprofloxacin by UV and UV/TiO2 Processes. Evaluation of Toxicity Changes Using a Respirometric Biosensor, Palmisano, Campanella, Ambrosetti, J Environ Anal Chem 2015, 2:3

step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process.

c. Address the step(s) of the CO1 or RBD process that removes erythromycin.
Response:
As addressed in Q5, temperature conditions in the drying step in Phase I CO1 process and deodorization step in the Phase II RBD process can be as high as 260°C which is enough to deactivate any Erythromycin residues if present in the crude corn oil. Further, Erythromycin is soluble in water (2000mg/l) and polar solvents such as ethanol. [40, 41, 42] So, in the unlikely event any Erythromycin residues are present in the crude corn oil, the residues will be removed during contact with aqueous ethanol solutions in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process.

d. Address the affinity of antibiotics and their degradants in the oil to the bleaching material proposed for use (bentonite).
Response:
There is evidence that some of the antibiotics will be adsorbed by soil.[43,44] The adsorption of the antibiotics depends on the adsorption potential of the clay. [45] However, due to the solubility of these antibiotics in water and ethanol, the antibiotics will be removed from the oil in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process prior to the bleaching step. Appendix E is updated accordingly.

Q7. On page 34, the presumed body weight of 60 kg used in the acceptance criteria rationale for antibiotics would not be appropriate for children. Please discuss how children were considered in the safety evaluation of antibiotic intake.

Response:
The acceptance criteria for antibiotics are **non-detects** based on the limit of detection (LOD) of 0.05 ppm. (FDA LIB 4438). The following assessment was conducted to provide support that a **non-detection** at the LOD 0.05 ppm is safe:

- Based on 21 CFR §556.750, the ADI for **virginiamycin** is 250 µg/kg bw/day.
- JECFA (2006) established an ADI of 0–0.7 µg/kg bw for **erythromycin**
- JECFA (1998) established an ADI of 30 µg/p/d for **penicillin G.**
- Based on 21CFR §556.750, the ADI for **tetracycline** is 25 µg/kg bw/day
- JECFA (2008) established an ADI of 0–30 µg/kg bw for **tylosin.**

Assuming that the daily intake of corn oil of 6g/day (see EDI in **Appendix H of the GRN)** is exposed at the LOD of 0.05 ppm, for a 10 kg bw of a child, the EDI would be 0.03 µg/kg bw/day.

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[40] https://www.chemicalbook.com/ChemicalProductProperty_US_CB8300078.aspx
[41] Lide, D.R. CRC Handbook of Chemistry and Physics 88TH Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-230
[42] Photo-Degradation of Amoxicillin, Streptomycin, Erythromycin and Ciprofloxacin by UV and UV/TiO2 Processes. Evaluation of Toxicity Changes Using a Respirometric Biosensor, Palmisano, Campanella, Ambrosetti, J Environ Anal Chem 2015, 2:3
[43] Meylan WM et al; Environ Sci Technol 26: 1560-67 (1992)
[44] Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000)
[45] Kumar K, Gupta SC, Chander Y, Singh AK (2005) Antibiotic use in agriculture and its impact on the terrestrial environment. Advances in Agronomy 87: 1-54

This is well below the ADIs for these antibiotics. Therefore, there is an ample margin of safety when there is no detection at the LOD of 0.05 ppm in the crude corn oi when considering the children population.

Mycotoxin Levels

Q1. Provide a narrative to address the levels of mycotoxins in COZ corn oil compared to corn oil produced by traditional methods.

Response:
Corn is primarily used in four different applications (1) animal feed production, (2) dry milling to produce ethanol, distillers grains and distillers corn oil. (3) wet milling to produce corn starch, corn flour and corn oil (4) distillers to produce industrial grade ethanol. The corn used in all these applications is sourced from the same corn crop across the US. All grain crops are susceptible to fungal infections when specific weather patterns occur during the growing season. These fungi are capable of producing mycotoxins. The most common mycotoxins that are present in corn are aflatoxins, fumonisin and deoxynivalenol. T2-Toxin and Zearalenone are less commonly found in corn crops. FDA acknowledges that the wet-milling is an effective process for removing mycotoxins like aflatoxin and fumonisin from corn starch, corn derived sweeteners and corn oil.[46] This is due the high solubility of Aflatxin, fumonisin and deoxynivalenol in water and other aqueous solvents such as ethanol. Various studies, as shown in the sections below, have indicated that the mycotoxins are not major concern in the food products derived from corn through wet milling process. [46]

The first step in a wet-milling corn plant is called steeping where all the corn in soaked in 50ºC water for about 30-40 hours. This allows the corn to swell and loosen the gluten bonds. In the next step the germ is mechanically separated. Germ is then processed to extract crude corn oil which is then further refined by standard refining process similar to the Phase II RBD process used to produce COz product. The rest of the corn is further processed to separate starch, fiber and other food grade products. [47]

Aflatoxin: Predicted water solubility of aflatoxins is in the range of 233 to 994mg/l. [51] Due to its high solubility in water, Aflatoxins are primarily recovered in the steep water. For example, it was reported that up to 50% of the aflatoxin present initially was found in the steep water solubles. Corn germ, from which corn oil is extracted contains up to 10% of the aflatoxins present initially. [48,49, 50]

Fumonisin: Water solubility of fumonisin is experimentally tested and is reported at >20,000mg/l. [51] A joint USDA-University of Illinois wet-milling study found that about 40% of fumonisin B1 and B2 were recovered in the gluten and fiber fractions and that of corn germ,

[46] Food Safety Information Papers, Corn Refiners Association, Inc. Mycotoxins prepared by WHITE Technical Research group, Revised by DTB Associates, LLP 217/795-4437
[47] https://corn.org/wp-content/uploads/2009/11/CornRefiningProcess.pdf
[48] Romer, T., Detecting mycotoxins in corn and corn milling products, Feedstuffs, 56 (37): 22-23, 1984
[49] Yahl, K.R., S.A. Watson, R.J. Smith and R. Barabolok, Laboratory wet-milling of corn containing high levels of aflatoxin and a survey of commercial wet-milling products, Cereal Chem., 48: 385-391, 1971.
[50] Bennett, G.A. and R.A. Anderson, Distribution of aflatoxin and/or zearalenone in wet-milled corn products: a review, J. Agri. Food Chem, 26 (5): 1055-1060, 1978.
[51] NTP, US National Toxicology Program (2000) NTP technical report on the toxicology and carcinogenesis studies of fumonisin B1 (CAS No 116355–83-0) in F344/N Rats and B6C3F1 Mice (Feed Studies) (TR 496; NIH Publication No 99–3955). Research Triangle Park, NC

from where corn oil is extracted, contained about 20% of the initial Fumonisin level.[52,53]

Deoxynivalenol: Predicted water solubility of aflatoxin is 36,000mg/l. [54] Due to relatively high water solubility, like fumonisin and aflatoxin, the highest concentration of deoxynivalenol was found in steep water. [55] The lowest levels of deoxynivalenol was found in the germ fraction, where the corn oil is extracted.

Similar to the procedures used in wet milling process, a typical corn ethanol process also starts by grinding the corn followed by soaking the corn in water along with some enzymes at 75-95ºC to allow for the starch, germ and fiber fractions to swell and be released into the water slurry. This slurry is then fermented using yeast. If there are mycotoxins present in the corn, they will preferentially be released into steep water. If the mycotoxins are carried along with the crude corn oil, they will transger into the aqueous phase during the neutralization step in the Phase 1 CO1 process, when the crude corn oil is in mixed with aqueous alcohol solutions at 70ºC for 8-10 hours. Further, in the Phase II RBD process, both in the degumming process and refining process, the corn oil is mixed with water at 70-90ºC for 10-40 min during which mycotoxins will transfer into the aqueous phase.

Q2. Provide a narrative to address the removal of mycotoxin residues, if any, by the CO1 process or subsequent chemical refining and/or bleaching steps[56] Consider the following in a discussion:

a. In Appendix E (p. 66), the notice states near complete adsorption of aflatoxin on bentonite. Indicate if this was determined experimentally or based on a published reference.

Response:
Greater than 99% of aflatoxin was adsorbed on to bentonite clay withing 15 min. [57] Montmorillonite clay, due to its adsorption potential, is also used in animal feed to adsorb aflatoxin residues. [58]

b. On p. 68, the notice states that 20% of DON is removed and 30% of fumonisin is removed by bleaching. We note that the information in the table on p. 68 regarding low affinity of DON (20% absorbed) and fumonisin (30% absorbed) for bentonite contradicts

[52] Saunders, D. F, Meredith, F. I and Voss, K. A, Control of Fumonisin: Effects of processing, Environmental Health Perspectives, 109: 333-6, 2001
[53] Bennett, G. A., J.L. Richard and S.R. Eckhoff, Distribution of fumonisins in food and feed products prepared from contaminated corn, in Fumonisins in Food, L. Jackson et. al. ed., Plenum Press, New York, 317, 1996.
[54] Impact of food processing and detoxification treatments on mycotoxin contamination, Karlovsky, Suman, Berthiller, Meester, Eisenbrand, Perrin, Oswald, Speijers, Chiodini, Recker, Dussort; Mycotoxin Res (2016) 32:179–205
[55] Lauren, D. R and M. A. Ringrose, Determination of the fate of three Fusarium mycotoxins through wet-milling of maize using an improved HPLC analytical technique, Food Additives and Contaminants, 14 (5): 435-443, 1997
[56] Park J et al. 2018. Toxins.10:319; Escobar J et al. 2013. Food and Chemical Toxicology. 62: 514-20
[57] Nuryono, Nuryono & Agus, Ali & Wedhastri, Sri & Maryudhani, Y.M.S & Pranowo, Deni & Yunianto, & Razzazi-Fazeli, Ebrahim. (2012). Adsorption of Aflatoxin B1 in corn on natural zeolite and bentonite. Indonesian Journal of Chemistry. 12. 279-286. 10.22146/ijc.21343.
[58] Q. Desheng, L. Fan, Y. Yanhu, and Z. Niya; Poultry Science, Volume 84, Issue 6, 1 June 2005, Pages 959-961

the statement on
Response: Appendix E has been updated and is enclosed

c. p. 19 that any residual mycotoxins will be absorbed by bleaching clay. Please clarify and state your conclusions (from laboratory data or published information) regarding how these mycotoxins are removed.

Response: There is evidence that some of the mycotoxins will be adsorbed by clay/soil.[57] The adsorption of the mycotoxin depends on the adsorption potential of the clay. However, due to the solubility of these mycotoxins in water and ethanol, the mycotoxins will be removed from the oil in the neutralization step of Phase I CO1 process and the water wash step during the refining step of the Phase II RBD process prior to the bleaching step. Appendix E is updated accordingly.

Q3. On page 34, the notice cites the FDA action level for total aflatoxin and guidance levels for fumonisin and deoxynivalenol. For clarity, do the suppliers of the crude corn oil use corn starting material for the fermentation that meet those acceptance criteria (for use in food and feed)?

Response: Suppliers of crude corn oil will use the acceptance criteria on crude corn oil and not on corn starting material.

Q4. Zearalenone has been reported to be present in corn oil (e.g., Escobar et al., 2013) although there are no FDA guidance levels. Is the level of zearalenone considered in the acceptance criteria for the crude corn oil?

Response: Zearalenone was not considered in the GRN as there are no established FDA guidance levels for zearalenone in corn. The paper FDA cited by Escobar et al does point to the fact that zearalenone can occur in corn oil. The study found zearalenone in 32% of samples at a mean level of 15µg/kg, a level more than an order of magnitude below the European Commission maximum limit of 400 ppb. Therefore, zearalenone levels in refined corn oil are not expected to raise safety concerns.

Other Contaminants

Q1. Do the contaminant analyses include 2- and 3-monochloropropane diols and glycidyl esters? Please clarify if the refining method incorporates strategies to mitigate formation of these contaminants.[59]

Response:

Corn Oil One tested Coz oil samples from three non-consecutive batches for MCPD esters and glycidyl esters. The results are as followed:

	Batch 1	**Batch 3**	**Batch 5**	**Method**
MCPD Esters, mg/kg of COz	0.42	0.32	0.42	A2LA ISO/IEC 17025:2005 2993-01
Glycidyl Esters, mg/kg of COz	11.18	0.72	11.67	A2LA ISO/IEC 17025:2005 2993-01

Assuming the average concentration from three tested samples, the daily intake of corn oil of 6g/day (see EDI in **Appendix H of the GRN)** and a default body weight of 60kg, the following EDI can be estimated and compared to the JECFA limits for these compounds:

	EDI (µg/kg bw/day)	**Exposure Limits –JECFA 83rd report** [60]
MCPD Esters	0.039	4 µg/kg bw/day (PMTDI)→ (TDI = 0.13 µg/kg bw/day)
Glycidyl Esters	0.79	2.4 mg/kg bw/day ($BMDL_{10}$)

The EDI for MCPD esters is below the JECFA TDI. The EDI for glycidyl esters has a margin of exposure (MOE) of 3000 based on the JECFA-BMDL. Therefore, these levels in Coz corn oil are not of safety concern.

Q2. The regulation the notice cites (p.15) to indicate the acceptance limit (40 CFR 180 Tolerances and exemptions for pesticide and chemical residues in food) does not include all the pesticides listed in the batch analyses. Please check.

Response: The list of pesticides tested in the COA is obtained from USDA/FSIS Blue Book. [61] United States National Residue Program (NRP) summarizes the process used by the USDA/FSIS, for sampling and testing of FSIS products for chemical compounds of public health concern and are modified annually in response to emerging chemical residue concerns and

[59] Codex CoP available from: https://www.ofimagazine.com/content-images/news/3MPCDE.GE_CCCF13_May_2019_Report_.pdf
[60] https://apps.who.int/iris/bitstream/handle/10665/254893/9789241210027-eng.pdf;jsessionid=0A327754F5F9418EB2E970854A0FEAB0?sequence=1
[61] https://www.fsis.usda.gov/wps/wcm/connect/0d633930-b5fa-4db1-965c-4f4769827301/2018-Blue-book.pdf?MOD=AJPERES

improved testing methodologies. The 2018 NRP Residue Sampling Plan focuses on chemical residues in domestic meat, poultry, and egg products and the import reinspection of meat, poultry, and egg products.

Q3. Several of the pesticides listed in the Pesticide/PCB screen have action levels listed in CPG 575.100, i.e. chlordane, lindane, aldrin and dieldrin, BHC, DDT/DDE/TDE. Please confirm that the source material does not exceed action levels for pesticides and that is produced in accordance with good agricultural practices.

Response: Levels of the pesticides listed in CPG 575.100 in the source material will not exceed the action levels for the respective pesticides. Also, the levels of the pesticides are non-detects as per the COA's and therefore below any action levels for these contaminants.

SAFETY DATA SHEET

VOxOUT 70

1 PRODUCT AND COMPANY IDENTIFICATION

Product Identifier:	VOxOUT 70
Common Name:	MIXTURE
SDS Number:	3000
Revision Date:	2/15/2017
Version:	1
Internal ID:	200C
Product Use:	VOC Scavenger
Supplier Details:	U.S. Water Services 12270 43rd St. NE St. Michael, MN 55376
Contact:	Non-emergency #: 866-663-7632
Email:	SDS@uswaterservices.com
Web:	www.uswaterservices.com

EMERGENCY RESPONSE: (ChemTel)
US & Canada: 800-255-3924
International: +01-813-248-0585

HAZARDS IDENTIFICATION

Classification of the substance or mixture

GHS Classification in accordance with 29 CFR 1910 (OSHA HCS):

Physical, Corrosive to Metals, 1
Health, Skin corrosion/irritation, 1

GHS Label elements, including precautionary statements

GHS Signal Word: DANGER

GHS Hazard Pictograms:

GHS Hazard Statements:

H290 - May be corrosive to metals
H314 - Causes severe skin burns and eye damage

GHS Precautionary Statements:

P281 - Use personal protective equipment as required.
P302+352 - IF ON SKIN: Wash with soap and water.
P305+351+338 - IF IN EYES: Rinse continuously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing.
P301+330+331 - IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P315 - Get immediate medical advice/attention.
P260 - Do not breathe vapours.

Hazards not otherwise classified (HNOC) or not covered by GHS

COMPOSITION/INFORMATION ON INGREDIENTS

Ingredients:

Cas#	%	Chemical Name
10192-30-0	60-70%	Ammonium bisulfite

FIRST AID MEASURES

Inhalation: Remove to fresh air. If breathing is difficult, administer oxygen. If not breathing, give artificial respiration, preferably mouth-to-mouth. GET MEDICAL ATTENTION IMMEDIATELY.

Skin Contact: Immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention immediately. Do not reuse clothing and shoes until cleaned.

Eye Contact: Immediately flush eyes with plenty of water for at least 15 minutes while holding eyelids open. Tilt head to avoid contaminating unaffected eye. Get immediate medical attention.

Ingestion: If fully conscious, drink a quart of water. DO NOT induce vomiting. CALL A PHYSICIAN IMMEDIATELY. If unconscious or in convulsions, take immediately to a hospital or a physician. NEVER induce vomiting or give anything by mouth to an unconscious victim. If vomiting occurs spontaneously, keep head below hips to prevent aspiration of liquid into the lungs.

Most important symptoms & effects (acute & delayed):
Eye Contact: CORROSIVE-Causes severe irritation and burns. May cause: permanent eye damage.
Skin Contact: CORROSIVE-Causes severe irritation and burns. Contact may cause: redness, blistering, pain, tissue destruction.
Inhalation: Vapors or mists may irritate: nose. throat. respiratory tract. May cause: coughing, difficulty breathing, tightness of the chest, Extreme exposures may cause: severe irritation, pulmonary edema.
Ingestion: May be corrosive to the gastrointestinal tract. Severe irritation and burns may result. May irritate or burn: mouth, throat, digestive tract. May cause: vomiting. Small amounts of liquid aspirated into the lungs during ingestion or from vomiting may cause pulmonary edema
Indication of need for immediate medical attention: Treat symptomatically. Not potential for anaphylactic shock with allergic individuals.
Special treatment needs: No data available

FIRE FIGHTING MEASURES

Flammability:	Nonflammable
Flash Point:	None
Flash Point Method:	Pensky Martens Closed cup
Burning Rate:	No data available
Autoignition Temp:	No data available
LEL:	Not applicable
UEL:	Not applicable

Extinguishing Media:

Suitable: Use extinguishing media suitable for surrounding fire.

Unsuitable: No information available

Hazardous combustion products: Hazardous decomposition products formed under fire conditions- Toxic vapors, sulfur oxides, ammonia.

Unusual Fire or Explosion Hazards: Sulfur dioxide gas will released at a rate increasing with temperature

Special protective equipment/precautions: Wear self-contained breathing apparatus

ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective equipment, emergency procedures: Corrosive material. Avoid contact with the material. See section 8 of SDS for PPE recommendations
Environmental Precautions: Keep runoff from entering drains or waterways
Spill/Leak procedures: Shut off source of leak if safe to do so. Contain spill, place into drums for proper disposal. Soak up residue with inert absorbent material. Place in non-leaking containers for immediate disposal. Flush remaining area with water to remove trace residue and dispose of properly. Prevent entry into basements, low areas, or confined areas. Avoid direct discharge to sewers and surface waters. Notify authorities if entry occurs.
Cleanup: After collection/absorption of splill, flush away remaining traces with large amounts of water.
Regulatory Requirements: Dispose of recovered material in accordance with all applicable state and federal regulations.

HANDLING AND STORAGE

Handling Precautions:	Avoid contact with eyes, skin, and clothing. Use with adequate ventilation. Do not swallow. Avoid breathing vapors, mists, or dust. Do not eat, drink, or smoke in work area. Wash thoroughly after handling. Empty containers retain product residue (vapor, dust, or liquid) and can be dangerous. DO NOT pressurize, cut, weld, braze, solder, drill, grind, or expose such containers to heat, flame, sparks, static electricity, or other source of ignition. They may explode and cause injury or death.
Storage Requirements:	CORROSIVE MATERIAL. Store in a cool, well ventilated area, out of direct sunlight. Store in a dry location away from heat. Keep away from incompatible materials. Keep containers tightly closed. Do not store in unlabeled or mislabeled containers. Prolonged exposure to the atmosphere will slowly oxidize this product, releasing sulfur dioxide gas. Do not freeze. Relieve pressure in drums weekly.

EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls:	Provide local exhaust ventilation as needed to control misting or vapor accumulation.
Personal Protective Equipment:	HMIS PP, C | Safety Glasses, Gloves, Apron Respiratory protection: May be required if ventilation is inadequate. If needed use MSHA/NIOSH approved respirator for dusts, mists, and/or SO2 vapors. Seek professional advice prior to respirator selection and use. Follow all requirements of OSHA respirator regulations (29 CFR 1910.134) Safety Stations: Make emergency eyewash stations, safety/quick-drench showers, and washing facilities available in work area.

General Hygiene: Never eat, drink, or smoke in work areas. Practice good personal hygiene after using this material, especially before eating, drinking, using the toilet, or applying cosmetics.
PPE recommendation is advisory only and based on typical use conditions. An industrial hygienist or safety officer familiar with the specific situation of anticipated use must determine actual PPE required when using this product (29 CFR 1910.132)

Exposure Limits:
Sulfur Dioxide gas may be released. Exposure limit for Sulfur Dioxide are 5ppm TWA (OSHA); 5ppm TWA, 5ppm-STEL (ACGIH)

PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Clear, colorless to light yellow		
Physical State:	Liquid	Odor:	Sulfur dioxide smell
Odor Threshold:	No data available	Solubility:	Soluble in water
Spec Grav./Density:	11.59Lb/Gal @25°C	Percent Volatile:	Not determined
Viscosity:	No data available	Freezing/Melting Pt.:	14°F
Boiling Point:	Not determined	Flash Point:	Does not Flash
Flammability:	Non Flammable	Vapor Density:	Not determined
Partition Coefficient:	No data available	VOC:	0% (w/w)
Vapor Pressure:	Not determined	Auto-Ignition Temp:	Not Determined
pH:	5.4 (as is)	UFL/LFL:	Not determined
Evap. Rate:	Not determined		
Decomp Temp:	Not determined		

STABILITY AND REACTIVITY

Chemical Stability:	Product is stable under normal storage and use conditions.
Conditions to Avoid:	Avoid heat, sparks or open flames. Avoid elevated temperatures
Materials to Avoid:	Acids. Oxidizing agents. Alkalies. Copper, zinc or their alloys (i.e. bronze, brass, galvanized metals, etc.). Oils. Combustible materials. Hypochlorites. Water-reactive materials. Aluminum. Lead diacetate. Mercury chloride. Steel. Corrosive to some metals.
Hazardous Decomposition:	Toxic vapors, Sulfur dioxide gas, Ammonia.
Hazardous Polymerization:	Hazardous polymerization will not occur under normal conditions. Both acidification and heating accelerate the release of Sulfur dioxide fumes. Alkaline materials will accelerate the evolution of ammonia.

TOXICOLOGICAL INFORMATION

Acute Toxicity: No data available
Skin Corrosion/Irritation: Corrosive. Causes severe irritation and burns. Contact may cause redness, blistering, pain, tissue destruction
Serious eye damage/irritation: Corrosive. Causes severe irritation and burns. May cause permanent eye damage.

Respiratory or skin sensitization: Vapors or mists may irritate nose, throat, respiratory tract. May cause coughing, difficulty breathing, tightness of the chest. Extreme exposures may casue severe irritation, pulmonary edema.
Specific target organ toxicity (single exposure): No data available
Specific target organ toxicity (repeated exposure): No data available
Aspiration hazard: No data available
Carcinogenicity: No carcinogenic effects are known for the components of this product
Germ Cell Mutagenicity: No mutagenic effects are known for the components of this product
Teratogenicity: No teratogenic effects are known for the components of this product

ECOLOGICAL INFORMATION

Aquatic Toxicity No data available
Elimination (persistency & degradability): No data available
Bioaccumulative potential: No data available
Mobility in soil: No data available
Other adverse effects: No data available

DISPOSAL CONSIDERATIONS

Dispose of in accordance with local regulations.

This material should be fully characterized for toxicity and possible reactivity prior to disposal (40 CFR 261). Use which results in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials, consult state and local regulations regarding the proper disposal of this material.

Container contents should be completely used and containers should be emptied prior to discard. Container rinsate could be considered a RCRA hazardous waste and must be disposed of with care and in full compliance with federal, state and local regulations. Larger empty containers, such as drums, should be returned to the distributor or to a drum reconditioner. To assure proper disposal of smaller empty containers, consult with state and local regulations and disposal authorities.

14 TRANSPORT INFORMATION

UN2693, Bisulfites, aqueous solutions, n.o.s., 8, PGIII, (Ammonium Bisulfite)

Certain shipping modes or package sizes may have exceptions from the transport regulations. The classification provided may not reflect those exceptions and may not apply to all shipping modes or package sizes.

DOT Transportation data (49 CFR 172.101)

See section 15 for information on Reportable Quantity chemicals (RQ)

REGULATORY INFORMATION

Component (CAS#) [%] - CODES

RQ(5000LBS), Ammonium bisulfite (10192-30-0) [60-70%] CERCLA, CSWHS, MASS, PA, TSCA

Regulatory CODE Descriptions

RQ = Reportable Quantity
CERCLA = Superfund clean up substance
CSWHS = Clean Water Act Hazardous substances
MASS = MA Massachusetts Hazardous Substances List
PA = PA Right-To-Know List of Hazardous Substances
TSCA = Toxic Substances Control Act

SARA TITLE III: Toxic Chemical List (SARA 313): This product does not contain any chemicals subject to routine annual toxic chemical release reporting.
Extremely Hazardous Substance (SARA 302/304): This product does not contain any extremely hazardous substances subject to emergency planning requirements.
SARA 312: Acute
California Proposition 65: May contain the following in trace amounts: Sulfer Dioxide
RCRA: Material as supplied is considered: Corrosive, D002

16 OTHER INFORMATION

HMIS III: Health = 3, Fire = 0, Physical Hazard = 0
HMIS PPE: C - Safety Glasses, Gloves, Apron

Author: U.S. Water Services

Revision Notes: Updated to GHS format

Disclaimer:
Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained herein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequences of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s). The above information is not claiming characteristics of the product in term of legal claims of performance / guarantee. This information only describes safety measures and no liability may arise from the use or application of the product described herein. This information is given in good faith and based on our current knowledge of the product.

Material Safety Data Sheet

DuPont™ FermaSure® XL

Version 3.0

Revision Date 10/01/2012 Ref. 130000043784

This SDS adheres to the standards and regulatory requirements of the United States and may not meet the regulatory requirements in other countries.

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name	:	DuPont™ FermaSure® XL
MSDS Number	:	130000043784
Product Use	:	Formulation Processing aid, Fermentation
Manufacturer	:	DuPont 1007 Market Street Wilmington, DE 19898
Product Information	:	1-800-441-7515 (outside the U.S. 1-302-774-1000)
Medical Emergency	:	1-800-441-3637 (outside the U.S. 1-302-774-1139)
Transport Emergency	:	CHEMTREC: 1-800-424-9300 (outside the U.S. 1-703-527-3887)
Importer/Distributor	:	International Dioxcide, Inc., A DuPont Subsidiary, 40 Whitecap Drive, North Kingstown, RI 02852
Telephone	:	
Other information	:	professional use

SECTION 2. HAZARDS IDENTIFICATION

Potential Health Effects

Skin

Oxychlorine compounds	:	May cause: Corrosion with pain, ulceration or blisters, cracking or peeling of skin.

Eyes

Oxychlorine compounds	:	Corrosive, may cause permanent eye injury if not promptly treated. May cause:, Tearing, pain, redness, swelling, ulceration, visual impairment, or blindness..

Inhalation

Oxychlorine compounds : Causes respiratory tract irritation. May cause:, Cough, sneezing, runny nose, sore throat, or shortness of breath..

Repeated exposure

Oxychlorine compounds : Adverse effects from repeated ingestion may include: Gastrointestinal effects Abnormal decrease in number of red blood cells (anaemia) which could produce tiredness, rapid heartbeat, dizziness, pale skin, leg cramps, shortness of breath. altered blood chemistry

Target Organs

Oxychlorine compounds : Blood

Carcinogenicity

None of the components present in this material at concentrations equal to or greater than 0.1% are listed by IARC, NTP, or OSHA, as a carcinogen.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Component	CAS-No.	Concentration
Oxychlorine compounds		15 - 25 %
Water	7732-18-5	75 - 85 %

SECTION 4. FIRST AID MEASURES

Skin contact : Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water. Call a poison control center or doctor for treatment advice.

Eye contact : Rinse immediately with plenty of water and seek medical advice.

Inhalation	:	Move to fresh air. If not breathing, give artificial respiration. Call a poison control center or doctor for treatment advice.
Ingestion	:	Call a poison control center or doctor for treatment advice. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.
Notes to physician	:	Probable mucosal damage may contraindicate the use of gastric lavage.

SECTION 5. FIREFIGHTING MEASURES

Flammable Properties Flash point	:	does not flash
Fire and Explosion Hazard	:	Drying of this product on clothing or combustible materials may cause fire.
Suitable extinguishing media	:	Water
Firefighting Instructions	:	Wear self-contained breathing apparatus (SCBA). Wear suitable protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

NOTE: Review FIRE FIGHTING MEASURES and HANDLING (PERSONNEL) sections before proceeding with clean-up. Use appropriate PERSONAL PROTECTIVE EQUIPMENT during clean-up.

Safeguards (Personnel)	:	Wear personal protective equipment. Avoid contact with the skin and the eyes.
Spill Cleanup	:	Dilute with water. Pick up and transfer to properly labelled containers. After cleaning, flush away traces with water.
Accidental Release Measures	:	Prevent material from entering sewers, waterways, or low areas. Do not allow to dry.

SECTION 7. HANDLING AND STORAGE

Handling (Personnel)	:	Use only in well-ventilated areas. Avoid contact with skin, eyes and clothing. Wash hands before breaks and at the end of workday.
Handling (Physical Aspects)	:	Avoid letting the product become dry.
Storage	:	Keep tightly closed in a dry, cool and well-ventilated place. Keep away from food, drink and animal feedingstuffs. Avoid heat, freezing and ultraviolet light. Do not allow to dry. Keep away from: Strong acids and oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering controls	:	Ensure adequate ventilation, especially in confined areas.
Personal protective equipment		
Respiratory protection	:	Where there is potential for airborne exposures in excess of applicable limits, wear approved respiratory protection with dust/mist cartridge. Provide adequate ventilation. In case of insufficient ventilation, wear suitable respiratory equipment.
Hand protection	:	Additional protection: Impervious gloves
Hand protection	:	Material: Polyvinyl chloride - PVC
Eye protection	:	Wear coverall chemical splash goggles. Additionally wear a face shield where the possibility exists for face contact due to splashing, spraying or airborne contact with this material.
Skin and body protection	:	Where there is potential for skin contact, have available and wear as appropriate, impervious gloves, apron, pants, jacket, hood and boots.
Protective measures	:	Avoid exposure - obtain special instructions before use. Wear suitable gloves and eye/face protection.

Exposure Guidelines

Exposure Limit Values

None established.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Form	:	liquid
Color	:	light yellow
Odor	:	odourless, slight chlorine
pH	:	9.5 - 9.7
Freezing point	:	ca. -18 °C (0 °F)
Crystallization temperature	:	ca. -12 °C (10 °F)
Boiling point	:	ca. 106 °C (223 °F)
Density	:	ca. 9.9 lb/gal at 20 °C (68 °F)
Specific gravity	:	ca. 1.18 - 1.21
Water solubility	:	miscible

SECTION 10. STABILITY AND REACTIVITY

Stability	:	Stable at normal temperatures and storage conditions. Decomposes on heating.
Conditions to avoid	:	Stable under normal conditions. Decomposes on heating.
Incompatibility	:	Strong acids and oxidizing agents Organic materials, chlorinated compounds, Reducing agents
Hazardous decomposition products	:	Hazardous decomposition products: Chlorine , Chlorine dioxide...%
Hazardous reactions	:	Contact with acids, organic materials, reducing agents and oxidizing agents will release toxic gases of chlorine and/or chlorine dioxide.

SECTION 11. TOXICOLOGICAL INFORMATION

DuPont™ FermaSure® XL

Dermal LD50	:	> 2,000 mg/kg , rat
Oral LD50	:	1,075 mg/kg , rat
Skin irritation	:	Non-corrosive No skin irritation Information given is based on data obtained from similar product.
Eye irritation	:	Risk of serious damage to eyes. Information given is based on data obtained from similar product.

Oxychlorine compounds

Inhalation 4 h LC50	:	0.23 mg/l , rat
Skin sensitization	:	Animal test did not cause sensitization by skin contact., guinea pig
Repeated dose toxicity	:	Oral rat 1 y Target Organs: Blood Gastrointestinal effects, Abnormal decrease in number of red blood cells, Abnormal decrease in red -blood -cell haemoglobin (hemoglobinemia) Oral rat 14 d altered hematology, altered urinalysis results Oral Monkey altered hematology, altered blood chemistry
Carcinogenicity	:	Animal testing did not show any carcinogenic effects.
Mutagenicity	:	Tests on bacterial or mammalian cell cultures did not show mutagenic effects.

Animal testing did not show any mutagenic effects.

Reproductive toxicity	:	Animal testing showed effects on reproduction at levels equal to or above those causing parental toxicity.
Teratogenicity	:	Animal testing showed effects on embryo-fetal development at levels equal to or above those causing maternal toxicity.

SECTION 12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Oxychlorine compounds

96 h LC50	:	Cyprinodon variegatus (sheepshead minnow) 105 mg/l
96 h ErC50	:	Scenedesmus capricornutum (fresh water algae) 1 mg/l
48 h EC50	:	Daphnia magna (Water flea) < 1.0 mg/l
96 h LC50	:	Americamysis bahia (mysid shrimp) 0.65 mg/l

Environmental Fate

Oxychlorine compounds

Biodegradability	:	Readily biodegradable.
Additional ecological information	:	No data is available on the product itself.

SECTION 13. DISPOSAL CONSIDERATIONS

Waste Disposal	:	Treatment, storage, transportation, and disposal must be in accordance with applicable federal, state/provincial, and local regulations.
Environmental Hazards	:	Empty containers should be taken to an approved waste handling site for recycling or disposal. If recycling is not practicable, dispose of in compliance with local regulations.

SECTION 14. TRANSPORT INFORMATION

Not classified as dangerous in the meaning of transport regulations.

SECTION 15. REGULATORY INFORMATION

Other regulations	:	For professional users only.
TSCA	:	On the inventory, or in compliance with the inventory
SARA 313 Regulated Chemical(s)	:	SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.
California Prop. 65	:	Chemicals known to the State of California to cause cancer, birth defects or any other harm: none known
NJ Right to Know Regulated Chemical(s)	:	Substances on the New Jersey Workplace Hazardous Substance List present at a concentration of 1% or more (0.1% for substances identified as carcinogens, mutagens or teratogens): Sodium chlorite

SECTION 16. OTHER INFORMATION

		HMIS
Health	:	2
Flammability	:	1
Reactivity/Physical hazard	:	0
PPE	:	Personal Protection rating to be supplied by user depending on use conditions.

DuPont™ FermaSure® XL

Version 3.0

Revision Date 10/01/2012 Ref. 130000043784

Contact person	:	MSDS Coordinator, DuPont Chemicals and Fluoroproducts, Wilmington, DE 19898, (800) 441-7515

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

Significant change from previous version is denoted with a double bar.

BOILER MP

1 PRODUCT AND COMPANY IDENTIFICATION

Product Identifier: BOILER MP
Common Name: MIXTURE
SDS Number: 0250
Revision Date: 3/27/2015
Version: 2
Internal ID: 200C
Product Use: BOILER WATER TREATMENT

Supplier Details:
U. S. Water Services
12270 43rd St. NE
St. Michael, MN 55376

Contact: Non-emergency #: 866-663-7632
Email: SDS@uswaterservices.com
Web: www.uswaterservices.com

EMERGENCY RESPONSE: (ChemTel)
US & Canada: 800-255-3924
International: +01-813-248-0585

2 HAZARDS IDENTIFICATION

Classification of the substance or mixture

GHS Classification in accordance with 29 CFR 1910 (OSHA HCS):

Health, Acute toxicity, 5 Oral
Health, Acute toxicity, 5 Dermal
Health, Specific target organ toxicity - Single exposure, 3
Health, Serious Eye Damage/Eye Irritation, 2 A
Health, Skin corrosion/irritation, 3

GHS Label elements, including precautionary statements

GHS Signal Word: **WARNING**

GHS Hazard Pictograms:

GHS Hazard Statements:

H303 - May be harmful if swallowed
H313 - May be harmful in contact with skin
H335 - May cause respiratory irritation
H319 - Causes serious eye irritation
H316 - Causes mild skin irritation

GHS Precautionary Statements:

P102 - Keep out of reach of children.
P281 - Use personal protective equipment as required.

P302+352 - IF ON SKIN: Wash with soap and water.
P305+351+338 - IF IN EYES: Rinse continuously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing.

P301+330+331 - IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P304+340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.

Hazards not otherwise classified (HNOC) or not covered by GHS

PPE recommendation is advisory only and based on typical use conditions. An industrial hygienist or safety officer familiar with the specific situation of anticipated use must determine actual PPE required when using this product (29 CFR 1910.132)

3 COMPOSITION/INFORMATION ON INGREDIENTS

Ingredients:

Cas#	%	Chemical Name
1310-73-2	< 5	Sodium hydroxide

4 FIRST AID MEASURES

Inhalation: Remove from contamination. If person has stopped breathing administer artificial respiration. Seek medical attention.

Skin Contact: Wash off with soap and plenty of water. Remove contaminated garments and wash or destroy. Seek medical attention if irritation develops. Consult a physician if irritation develops.

Eye Contact: Flush eyes with plenty of running water for 15 minutes. Seek medical attention.

Ingestion: If conscious, give plenty of water. If discomfort or other symptoms develop, seek medical attention. Do not induce vomiting unless directed to do so by medical personnel.

Most important symptoms & effects (acute & delayed)**:** No data available
Indication of need for immediate medical attention: None
Special treatment needs: None

5 FIRE FIGHTING MEASURES

Flammability: Not flammable
Flash Point: None
Flash Point Method: Pensky Martens Closed cup
Burning Rate: No data available
Autoignition Temp: No data available
LEL: Not applicable
UEL: Not applicable

Extinguishing Media:

Suitable: Use extinguishing media suitable for surrounding fire.

Unsuitable: No information available

Hazardous combustion products: Hazardous decomposition products formed under fire conditions- Carbon oxides, and other hazardous compounds

Unusual Fire or Explosion Hazards: None known

Special protective equipment/precautions: Wear self-contained breathing apparatus

6 ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective equipment, emergency procedures: Avoid contact with the material. See section 8 of SDS for PPE recommendations
Environmental Precautions: Keep runoff from entering drains or waterways
Spill/Leak procedures: Contain spill or leak. Dike area if necessary to prevent spill from spreading or entering sewers and waterways. Recover as much as possible then absorb remainder with inert material. Place into closed container for disposal.
Regulatory Requirements: Dispose of recovered material in accordance with all applicable state and federal regulations.

7 HANDLING AND STORAGE

Handling Precautions: Avoid contact with eyes, skin, or clothing. Do not taste or swallow. Do not inhale vapor or mist. Use with adequate ventilation. For industrial use only!

Storage Requirements: Keep away from children. Store in closed containers away from temperature extremes and incompatible materials.
Store in properly labeled containers in accordance with all local, state and federal guidelines.

8 EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls: Provide local exhaust ventilation as needed to control misting.

Personal Protective Equipment: HMIS PP, C | Safety Glasses, Gloves, Apron

Respiratory protection: If needed use MSHA/NIOSH approved respirator for dusts and mists. Seek professional advice prior to respirator selection and use. Follow all requirements of OSHA respirator regulations (29 CFR 1910.134)
Safety Stations: Make emergency eyewash stations, safety/quick-drench showers, and washing facilities available in work area.
General Hygiene: Never eat, drink, or smoke in work areas. Practice good personal hygiene after using this material, especially before eating, drinking, using the toilet, or applying cosmetics.
PPE recommendation is advisory only and based on typical use conditions. An industrial hygienist or safety officer familiar with the specific situation of anticipated use must determine actual PPE required when using this product (29 CFR 1910.132)

Exposure Limits:
OSHA (TWA)/PEL: Sodium Hydroxide 2 mg/m^3
NIOSH (REL): Sodium Hydroxide 2 mg/m^3

9 PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Clear, yellow		
Physical State:	Liquid	**Odor:**	Mild
Odor Threshold:	Not determined	**Solubility:**	Complete in water
Spec Grav./Density:	9.26 lb/gal	**Freezing/Melting Pt.:**	30°F
Viscosity:	Not determined	**Flash Point:**	None
Boiling Point:	Similar to water	**Vapor Density:**	Not determined
Partition Coefficient:	Not determined	**Auto-Ignition Temp:**	Not determined
Vapor Pressure:	Similar to water	**UFL/LFL:**	Not determined
pH:	12-13		
Evap. Rate:	Not determined		
Decomp Temp:	Not determined		

10 STABILITY AND REACTIVITY

Stability:	Product is stable under normal storage and use conditions.
Conditions to Avoid:	Avoid temperature extremes. Protect from freezing
Materials to Avoid:	Strong Oxidizing Agents may cause exothermic reaction, Strong Acids
Hazardous Decomposition:	Thermal decomposition may produce carbon oxides and other toxic compounds.
Hazardous Polymerization:	Will not occur.

11 TOXICOLOGICAL INFORMATION

Acute Toxicity:
Oral LD_{50} (rat) > 5,000 mg/kg (estimated)
Skin Corrosion/Irritation: No data avaible
Serious eye damage/irritation: No data available
Respiratory or skin sensitization: No data available
Specific target organ toxicity (single exposure): No data available
Specific target organ toxicity (repeated exposure): No data available
Aspiration hazard: No data available
Carcinogenicity: No carcinogenic effects are known for the components of this product
Germ Cell Mutagenicity: No mutagenic effects are known for the components of this product
Teratogenicity: No teratogenic effects are known for the components of this product

12 ECOLOGICAL INFORMATION

Aquatic Toxicity

Ceriodaphnia dubia	LC_{50} (48h) > 1,000 mg/L
Daphnia magna	LC_{50} (48h) > 3,000 mg/L
Fathead minnow	LC_{50} (96h) > 8,000 mg/L

Elimination (persistency & degradability): No data available
Bioaccumulative potential: No data available
Mobility in soil: No data available
Other adverse effects: No data available

13 DISPOSAL CONSIDERATIONS

Dispose of in accordance with local regulations.

This material should be fully characterized for toxicity and possible reactivity prior to disposal (40 CFR 261). Use which results in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials, consult state and local regulations regarding the proper disposal of this material.

Container contents should be completely used and containers should be emptied prior to discard. Container rinsate could be considered a RCRA hazardous waste and must be disposed of with care and in full compliance with federal, state and local regulations. Larger empty containers, such as drums, should be returned to the distributor or to a drum reconditioner. To assure proper disposal of smaller empty containers, consult with state and local regulations and disposal authorities.

14 TRANSPORT INFORMATION

UN1760, Corrosive liquids, n.o.s., 8, PGIII, (Sodium Hydroxide)

DOT Transportation data (49 CFR 172.101)

See section 15 of SDS for information on Reportable Quantity chemicals (RQ)

15 REGULATORY INFORMATION

Component (CAS#) [%] - CODES

RQ(1000LBS), Sodium hydroxide (1310-73-2) [< 5] CERCLA, CSWHS, MASS, OSHAWAC, PA, TSCA, TXAIR

Regulatory CODE Descriptions

RQ = Reportable Quantity
CERCLA = Superfund clean up substance
CSWHS = Clean Water Act Hazardous substances
MASS = MA Massachusetts Hazardous Substances List
OSHAWAC = OSHA Workplace Air Contaminants
PA = PA Right-To-Know List of Hazardous Substances
TSCA = Toxic Substances Control Act
TXAIR = TX Air Contaminants with Health Effects Screening Level

TSCA: All components of this product are listed (or are not required to be listed) in the TSCA inventory
EPA / CERCLA / SARA TITLE III:
Toxic Chemical List (SARA 313): This product does not contain any chemicals subject to routine annual toxic chemical release reporting.
Extremely Hazardous Substance (SARA 302/304): This product does not contain any extremely hazardous substances subject to emergency planning requirements.
SARA 312: Acute
RCRA: Corrosive, D002

16 OTHER INFORMATION

HMIS III: Health = 2, Fire = 0, Physical Hazard = 0
HMIS PPE: C - Safety Glasses, Gloves, Apron

Author: U.S. Water Services

Revision Notes: Updated to GHS format

Disclaimer:
Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained herein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequences of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s). The above information is not claiming characteristics of the product in term of legal claims of performance / guarantee. This information only describes safety measures and no liability may arise from the use or application of the product described herein. This information is given in good faith and based on our current knowledge of the product.

PhibroBreak(TM)

January 19, 2018

Dear Customer,

This letter will serve to addend our April 2016 GRAS (Generally Recognized as Safe) positioning and regulatory acceptability for use of PhibroBreak™, Phibro Animal Health's new product used for distillers oil extraction in the ethanol and beverage alcohol process.

The FDA requires that all process additives fall into one of three regulatory options to be acceptable for use:

1. *Defined by AAFCO (Association of American Feed Control Officials)*
2. *A permitted Food Additive*
3. *GRAS (Generally Recognized as Safe) in animal feeds*

As part of achieving full regulatory compliance, Phibro sought a rigorous safety review by an independent panel of experts with the introduction of PhibroBreak. The PhibroBreak panel members, assembled by Intertek Scientific & Regulatory Consultancy of Somerset NJ, included:

- *Dr. Robert J Nicolosi – Holds a Ph.D from the University of New Hampshire and received subsequent training in nutritional biochemistry at Harvard University. He has held faculty positions at Harvard University (13 years) and the University of Massachusetts (26 years).*
- *Dr. John A. Thomas - Ph.D., F.A.C.T., D. A.T.S. is an Adjunct Professor, Department of Pharmacology & Toxicology, Indiana University School of Medicine. He is the author of numerous publications in the fields of endocrine pharmacology and environmental toxicology.*
- *Dr. David Bechtel - D.A.B.T. is a board certified toxicologist with 40 years' experience in food safety and regulatory matters. He spent the first 20 years in the food industry and for the last 20 years has held a senior industry consulting position.*

The panel conducted an extensive review of available data and scientific literature on PhibroBreak. Based on this review, they concluded that the use of PhibroBreak in the production of distillers byproducts is considered safe for use in this application. The use of PhibroBreak in the distillers oil production process may be properly categorized as Generally Recognized as Safe (GRAS). When PhibroBreak is used as instructed per label guidelines, the presence of PhibroBreak residues in distillers' byproducts (used as components of feed for food producing and companion animals) would not affect the status of those distillers' byproducts under the Federal Food, and Drug, and Cosmetic Act or the applicable animal feed regulations. The original PhibroBreak products from the P300 series from this determination may continue to be injected at levels up to 500 ppm into the thin stillage slipstream to the oil separation unit operation to remain compliant with this affirmation. The newer version of the product group, named P591, contains the same ingredients as the original products but in slightly different ratios in order to improve product economic performance and efficacy. The P591 product may be fed at rates up to 1,000 ppm into the thin stillage slipstream to the oil separation unit operation to remain compliant with the original affirmation.

If you have questions please contact your Phibro representative or you can reach me at 608-214-3660.

Sincerely,

Scott L. Gemmell
Vice President, The America's
Ethanol Performance Group
Phibro Animal Health Corporation
Mobile: 608-214-3660

Phibro Ethanol Performance Group (“Phibro”) currently markets its Phibrobreak™ product as a processing aid for the separation of corn oil from condensed solubles at ethanol production facilities. The product, when used within label guidelines, has been determined to be Generally Recognized as Safe (GRAS) in this application allowing the byproduct distillers streams produced from the process to be consumed as an animal feed.

It is Phibro’s intention to further expand the usage of this product in ethanol production in the same application but with the caveat that the oil produced in the process will be used for human consumption. As such the information contained within this document will evaluate the scientific reasons why Phibrobreak is acceptable for this application by reviewing the technical reason why the dominant component, the polymer, will not be expected to be present in the oil produced in any amount that would pose an unreasonable risk of a human health concern.

Background

Thin mid-stillage (syrup) in fuel ethanol plants is an oil-in-water emulsion which is more specifically known as a pickering emulsion. A pickering emulsion is an emulsion of two dissimilar phases stabilized by surface active agents as well as solids. In thin stillage (The heavy fraction from the evaporation bottoms after fermentation) the surface active agents consist of germ, gluten, proteins, and starchs; while the solids are mostly hull and fibers.

In an oil-in-water emulsion water (the large phase) is considered the continuous phase and the oil (the small phase) is considered the non-continuous phase. When these two phases are mixed in the presence of surface active agents (and solids) the non-continuous phase generates small droplets called micelles that are stabilized by the surface active agents.

Micelles are generated by surface active agents. Surface active agents typically are organic molecules that contain a hydrophilic (polar) head (or tail) and a hydrophobic (non-polar) tail that encapsulate the non-continuous phase (corn oil in this example). See Figure 1.

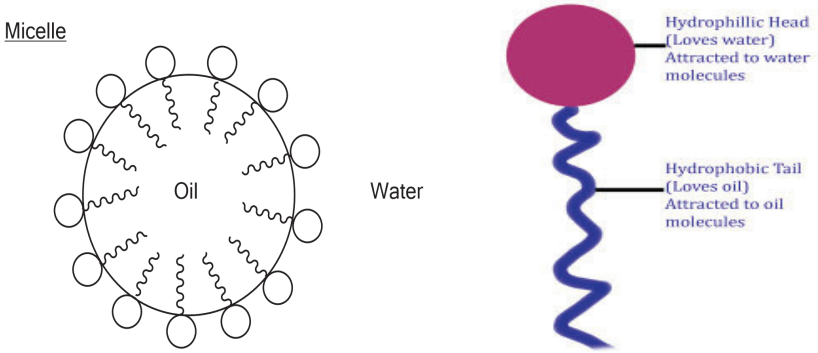

Figure 1
These micelles are encapsulated by a interfacial film of surface active agents (and solids) that result in very stable oil-in-water emulsions. The interfacial film is further stabilized by chemical forces between the oil phase, water phase and interfacial film, these include: attractive forces, repulsive forces, steric interaction and hydration forces. [2]

De-emulsification

There are several theories on de-emulisification. [1, 3, 4] De-emulsification occurs when the oil droplets bridge themselves, attach, and grow into larger droplets that eventually coagulate causing full coalescence of the oil phase and separation from the aqueous phase. For this to occur a force must breach the interfacial film disrupting the micelle’s structure and allowing the individual oil droplet to be released. When the individual droplets of oil come together through attractive forces they

coagulate. Once a number of the coagulants converge they coalesce and separate into oil and water phases.

Forces that can disrupt the micelle's interfacial film can include electrostatic forces (charge attraction / repulsion), surface tension reduction, and increases or decreases in temperature, among others.

Phibrobreak
Phibrobreak is made up of a surfactant, alumium sulfate, synthetic amorphous silica (SAS) and water. Each component contributes its own function to the de-emulsification of the thin stillage.

The surfactant has two functions. First to lower the surface tension of the thin stillage and help weaken the micelle. The surfactant also has a relatively low cloud point which enables it to cloud out at the thin stillage process temperature, effectively generating a very small size particulate with high surface area to mass.

The SAS also maintains two functions. The SAS is an insoluble particulate with very high surface area. The SAS, although somewhat polar is also somewhat hydrophobic and is a good nucleation agent.

The aluminum sulfate acts as a cationically charged species that is attracted to the anionically charged interfacial film (proteins, gluten, germ etc). This in conjunction with the lower surface tension weakens and breaks the interfacial film. Once the interfacial film is broken the clouded surfactant along with the SAS nucleates and begins to coagulate the interfacial film layers one after another releasing the corn oil. The lower surface tension also allows the oil droplets to more rapidly attach and eventually coalesce and separate from the aqueous phase.

Conclusion

The chemical nature of the components of Phibrobreak yield a response allowing for oil coalescence and simultaneous migration of the Phibrobreak components primarily into the rag layer between the separated oil and aqueous phases, which in turn ends up in the defatted mid-stillage. The defatted mid-stillage is further evaporated to increase solids. The evaporated stillage becomes what is referred to as “syrup” or “solubles”. The syrup is applied to the distillers grains during the drying process. It would be expected, based on the nature of the chemical components in Phibrobreak, that only a relatively small amount of residues would be possible in the separated oil phase and that the majority of the chemical components would end up in the various distillers grains products once the syrup is applied.

12-03-18

Christopher Murphy — Date

Director Research and Development Polymer Ventures, Inc

M.S. Polymer Science from Illinois Institute of Technology

20+ years of experience in water treatment and polymer formulation

References

1. E. Dickenson Interfacial interactions and the stability of oil-inwater emulsions, Pure & Appl. Chem. 64 (1992) 1721-1724
2. S.H. Shin, D.S. Kim Studies on the interfacial characterization of O/W emulsion for the optimization of its treatment, Environ. Sci. Technol. 35 (2001) 3040-3047
3. A.I. Zouboulis, A. Avranas Treatment of oil-in-water emulsions by coagulation and dissolved air flotation, Colloid Surf. A 172 (2000) 153-161
4. G. Rios, C. Pazos, J. Coca, Destabilization of cutting oil emulsions using inorganic salts as coagulants, Colloid Surf. A 138 (1998) 383-389

SAFETY DATA SHEET

PHIBROBREAK P391

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

GHS Product Information

Product Name: PHIBROBREAK P391
Business Unit PhibroEPG
Other means of identification: Not available

Safety data sheet number: 4021-210 -US-E

Recommended use of the chemical and restrictions on use

Recommended use: No information available.

Uses advised against: No information available

Details of the supplier of the safety data sheet

Supplier:
Phibro EPG
Glenpointe Centre East, 3rd FL
300 Frank W. Burr Blvd., Ste 21
Teaneck, NJ 07666-6712
Tel: (201) 329-7300
Toll free: (888) 475-7355
Fax: (201) 329-7070
Toll Free: 888-475-7355

SDS Contact (email of responsible person): phibroehs@pahc.com

24 Hour Emergency Phone Number: Chemtrec 1-800-424-9300 (CCN17224)

International: +1 703-527-3887

2. HAZARDS IDENTIFICATION

Classification

OSHA Regulatory Status
This chemical is not considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Not a dangerous substance or mixture according to the Globally Harmonized System (GHS)

Label elements

Emergency Overview

The product contains no substances which at their given concentration, are considered to be hazardous to health

Appearance liquid cloudy **Physical state** liquid **Odor** Slight

Hazards not otherwise classified (HNOC)

Other Information

3. COMPOSITION/INFORMATION ON INGREDIENTS

Pure substance/mixture Mixture

*The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST AID MEASURES

First aid measures

Eye contact: Rinse thoroughly with plenty of water for at least 15 minutes, lifting lower and upper eyelids. Consult a physician.

Inhalation: Remove to fresh air.

Skin Contact: Wash skin with soap and water.

Ingestion: Consult a physician if necessary.

Most important symptoms and effects, both acute and delayed

Symptoms: No information available.

Indication of any immediate medical attention and special treatment needed

Note to physicians: Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Extinguishing media

Suitable extinguishing media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media: Caution: Use of water spray when fighting fire may be inefficient.

Specific hazards arising from the chemical: No information available.

Explosion data

Sensitivity to Mechanical Impact: None.

Sensitivity to Static Discharge: None.

Protective equipment and precautions for firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal precautions: Ensure adequate ventilation, especially in confined areas.

For emergency responders: Use personal protection recommended in Section 8. Use personal protective equipment as required.

Environmental precautions: See Section 12 for additional ecological information.

Methods and material for containment and cleaning up

Methods for containment: Prevent further leakage or spillage if safe to do so.

Methods for cleaning up: Use personal protective equipment as required. Dam up. Cover liquid spill with sand, earth or other non-combustible absorbent material. Take up mechanically, placing in appropriate containers for disposal. Clean contaminated surface thoroughly.

Personal precautions, protective equipment and emergency procedures

Personal precautions: Ensure adequate ventilation, especially in confined areas.

For emergency responders: Use personal protection recommended in Section 8. Use personal protective equipment as required.

Environmental precautions: See Section 12 for additional ecological information.

Methods and material for containment and cleaning up

Methods for containment: Prevent further leakage or spillage if safe to do so.

Methods for cleaning up: Use personal protective equipment as required. Dam up. Cover liquid spill with sand, earth or other non-combustible absorbent material. Take up mechanically, placing in appropriate containers for disposal. Clean contaminated surface thoroughly.

7. HANDLING AND STORAGE

Precautions for safe handling

Advice on safe handling: Handle in accordance with good industrial hygiene and safety practice.

Conditions for safe storage, including any incompatibilities

Storage Conditions: Keep containers tightly closed in a dry, cool and well-ventilated place.

Incompatible materials: None known based on information supplied.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines .
NIOSH IDLH Immediately Dangerous to Life or Health

Other Information: Vacated limits revoked by the Court of Appeals decision in AFL-CIO v. OSHA, 965 F.2d 962 (11th Cir., 1992).

Appropriate engineering controls

Engineering Controls: Showers
Eyewash stations
Ventilation systems.

Individual protection measures, such as personal protective equipment

General Hygiene Considerations: Handle in accordance with good industrial hygiene and safety practice.

Eye/face protection: No special technical protective measures are necessary.

Skin and body protection: No special technical protective measures are necessary.

Respiratory protection: If exposure limits are exceeded or irritation is experienced, NIOSH/MSHA approved respiratory protection should be worn. Positive-pressure supplied air respirators may be required for high airborne contaminant concentrations. Respiratory protection must be provided in accordance with current local regulations.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical state	liquid		
Appearance	liquid, cloudy	**Odor**	Slight
Color	No information available	**Odor threshold**	No information available

Property	**Values**	**Remarks • Method**
pH	4-8	
Melting Point / Freezing Point	No information available	
Boiling point / boiling range	No information available	
Flash point	> 201 °F	
Evaporation rate	No information available	
Flammability (solid, gas)	No information available	
Flammability Limit in Air		
Upper flammability limit:	No information available	
Lower flammability limit:	No information available	
Vapor pressure	No information available	
Vapor density	No information available	
Specific Gravity	No information available	
Water solubility	dispersible	
Solubility in other solvents	No information available	
Partition coefficient	No information available	
Autoignition temperature	No information available	
Decomposition temperature	No information available	
Kinematic viscosity	No information available	
Dynamic viscosity	No information available	
Explosive properties	No information available	
Oxidizing properties	No information available	

Other Information

Softening point	No information available
Molecular weight	No information available
VOC Content (%)	No information available
Density	No information available
Bulk density	No information available
Percent Volatile	No information available

10. STABILITY AND REACTIVITY

Reactivity
No data available

Chemical stability
Stable under recommended storage conditions.

Possibility of Hazardous Reactions
None under normal processing.

Conditions to avoid
Extremes of temperature and direct sunlight.

Incompatible materials
None known based on information supplied.

Hazardous Decomposition Products
None known based on information supplied.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Product Information: No data available

Inhalation: No data available.

Eye contact: No data available.

Skin Contact: No data available.

Ingestion: No data available.

Information on toxicological effects

Symptoms: No information available.

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Sensitization: No information available.
Germ cell mutagenicity: No information available.
Carcinogenicity: The table below indicates whether each agency has listed any ingredient as a carcinogen.

IARC (International Agency for Research on Cancer)
Not classifiable as a human carcinogen

Reproductive toxicity: No information available.
STOT - single exposure: No information available.
STOT - repeated exposure: No information available.
Target Organ Effects: Respiratory system, Skin.
Aspiration hazard: No information available.

Numerical measures of toxicity - Product Information

The following values are calculated based on chapter 3.1 of the GHS document .
ATEmix (oral) 3285 5998

12. ECOLOGICAL INFORMATION

Ecotoxicity

Harmful to aquatic life with long lasting effects

94.4% of the mixture consists of components(s) of unknown hazards to the aquatic environment

Persistence and degradability
No information available.

Bioaccumulation
No information available.

Mobility
No information available.

Other adverse effects: No information available

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes: Refer to all federal, state and local regulations prior to disposal of container and unused contents by reuse, recycle or disposal. Disposal should be in accordance with applicable regional, national and local laws and regulations. Avoid runoff to waterways and sewers. Recover or recycle if possible. Send to a licensed recycler, reclaimer or incinerator.

Disposal methods: Do not reuse container.

14. TRANSPORT INFORMATION

Note: Store in a closed container. Keep container upright.

DOT Not regulated

IATA Not regulated

IMDG Not regulated

15. REGULATORY INFORMATION

International Inventories

TSCA:	Complies
DSL/NDSL:	Complies
EINECS/ELINCS:	Not Determined
ENCS:	Not Determined
IECSC:	Complies
KECL:	Complies
PICCS:	Complies
AICS:	Complies

Legend:
TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances
PICCS - Philippines Inventory of Chemicals and Chemical Substances
AICS - Australian Inventory of Chemical Substances

US Federal Regulations

SARA 313
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312 Hazard Categories

Acute health hazard	No
Chronic Health Hazard	No
Fire hazard	No
Sudden release of pressure hazard	No
Reactive Hazard	No

CWA (Clean Water Act)
This product contains the following substances which are regulated pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

CERCLA
This material, as supplied, contains one or more substances regulated as a hazardous substance under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302)

FIFRA

Not applicable

US State Regulations

California Proposition 65
This product does not contain any Proposition 65 chemicals

U.S. State Right-to-Know Regulations

No information available

Canada

No information available

16. OTHER INFORMATION

NFPA	**Health hazards** 1	**Flammability** 1	**Instability** 0	**Physical & Chemical Properties** 0
HMIS	**Health hazards** 1	**Flammability** 1	**Physical hazards** 0	**Personal protection** D

Document Review
Revision Number: 1

Revision Note: No information available

Key or legend to abbreviations and acronyms used in the safety data sheet:
Bioconcentration factor (BCF)
International Air Transport Association (IATA)
Globally Harmonized System (GHS)
International Maritime Dangerous Goods (IMDG)

Disclaimer

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End of Safety Data Sheet

SAFETY DATA SHEET

Phibro AC

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

GHS Product Information

Product Name: Phibro AC
Business Unit PhibroEPG
Other means of identification: Not available

Safety data sheet number: 4012-210 -US-E

Recommended use of the chemical and restrictions on use

Recommended use: No information available.

Uses advised against: No information available

Details of the supplier of the safety data sheet

Supplier:
Phibro EPG
Glenpointe Centre East, 3rd FL
300 Frank W. Burr Blvd., Ste 21
Teaneck, NJ 07666-6712
Tel: (201) 329-7300
Toll free: (888) 475-7355
Fax: (201) 329-7070
Toll Free: 888-475-7355

SDS Contact (email of responsible person): phibroehs@pahc.com

24 Hour Emergency Phone Number: Chemtrec 1-800-424-9300 (CCN17224)

International: International Number: +1 703-527-3887

2. HAZARDS IDENTIFICATION

Classification

OSHA Regulatory Status
This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Skin corrosion/irritation	Category 1 Sub-category A
Serious eye damage/eye irritation	Category 1

Label elements

Emergency Overview

Danger

Hazard statements
Causes severe skin burns and eye damage

Appearance liquid **Physical state** liquid **Odor** No information available

Precautionary Statements - Prevention
Do not breathe dust/fume/gas/mist/vapors/spray
Wash face, hands and any exposed skin thoroughly after handling
Wear protective gloves/protective clothing/eye protection/face protection

Precautionary Statements - Response
Immediately call a POISON CENTER or doctor/physician
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
Immediately call a POISON CENTER or doctor/physician
IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower
Wash contaminated clothing before reuse
IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
Immediately call a POISON CENTER or doctor/physician
IF SWALLOWED: Rinse mouth. DO NOT induce vomiting

Precautionary Statements - Storage
Store locked up

Precautionary Statements - Disposal
Dispose of contents/ container to an approved landfill

Hazards not otherwise classified (HNOC)

Other Information

3. COMPOSITION/INFORMATION ON INGREDIENTS

Pure substance/mixture Mixture

Chemical Name	CAS No	Weight-%	Trade Secret
Nitric Acid	7697-37-2	10 - 30	*
Trade Secret	Proprietary	1 - 5	*

*The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST AID MEASURES

First aid measures

General advice: Immediate medical attention is required.

Eye contact: Immediate medical attention is required. Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Keep eye wide open while rinsing. Do not rub affected area.

Inhalation: Remove to fresh air. Call a physician or poison control center immediately. If not breathing, give artificial respiration. If breathing is difficult, give oxygen.

Skin Contact: Immediate medical attention is required. Wash off immediately with soap and plenty of water while removing all contaminated clothes and shoes.

Ingestion: Immediate medical attention is required. Do NOT induce vomiting. Drink plenty of water. Never give anything by mouth to an unconscious person. Remove from exposure, lie down. Clean mouth with water and drink afterwards plenty of water. Call a physician or poison control center immediately.

Self-protection of the first aider: Use personal protective equipment as required. Avoid contact with skin, eyes or clothing.

Most important symptoms and effects, both acute and delayed

Symptoms: No information available.

Indication of any immediate medical attention and special treatment needed

Note to physicians: Product is a corrosive material. Use of gastric lavage or emesis is contraindicated. Possible perforation of stomach or esophagus should be investigated. Do not give chemical antidotes. Asphyxia from glottal edema may occur. Marked decrease in blood pressure may occur with moist rales, frothy sputum, and high pulse pressure. Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Extinguishing media

Suitable extinguishing media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media: Caution: Use of water spray when fighting fire may be inefficient.

Specific hazards arising from the chemical: The product causes burns of eyes, skin and mucous membranes. Thermal decomposition can lead to release of irritating and toxic gases and vapors. In the event of fire and/or explosion do not breathe fumes.

Explosion data

Sensitivity to Mechanical Impact: None.

Sensitivity to Static Discharge: None.

Protective equipment and precautions for firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal precautions: Evacuate personnel to safe areas. Use personal protective equipment as required. Avoid contact with skin, eyes or clothing. Keep people away from and upwind of spill/leak.

For emergency responders: Use personal protection recommended in Section 8. Use personal protective equipment as required.

Environmental Precautions: Do not allow into any sewer, on the ground or into any body of water. Should not be released into the environment. Prevent further leakage or spillage if safe to do so. Prevent product from entering drains. See Section 12 for additional ecological information.

Methods and material for containment and cleaning up

Methods for containment: Prevent further leakage or spillage if safe to do so.

Methods for cleaning up: Dike far ahead of liquid spill for later disposal. Soak up with inert absorbent material. Take up mechanically, placing in appropriate containers for disposal. Clean contaminated surface thoroughly. Prevent product from entering drains. Dam up. After cleaning, flush away traces with water.

Personal precautions, protective equipment and emergency procedures

Personal precautions: Evacuate personnel to safe areas. Use personal protective equipment as required. Avoid contact with skin, eyes or clothing. Keep people away from and upwind of spill/leak.

For emergency responders: Use personal protection recommended in Section 8. Use personal protective equipment as required.

Environmental Precautions: Do not allow into any sewer, on the ground or into any body of water. Should not be released into the environment. Prevent further leakage or spillage if safe to do so. Prevent product from entering drains. See Section 12 for additional ecological information.

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7. HANDLING AND STORAGE

Precautions for safe handling

Advice on safe handling: Use personal protective equipment as required. Avoid contact with skin, eyes or clothing. Ensure adequate ventilation, especially in confined areas. In case of insufficient ventilation, wear suitable respiratory equipment. Use only with adequate ventilation and in closed systems.

Conditions for safe storage, including any incompatibilities

Storage Conditions: Keep out of the reach of children. Keep container tightly closed in a dry and well-ventilated place. Keep containers tightly closed in a dry, cool and well-ventilated place. Keep in properly labeled containers.

Incompatible materials: Incompatible with strong acids and bases. Incompatible with oxidizing agents.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines .

Chemical Name	CAS No	ACGIH TLV	OSHA PEL	NIOSH IDLH
Nitric Acid	7697-37-2	STEL: 4 ppm TWA: 2 ppm	TWA: 2 ppm TWA: 5 mg/m^3 (vacated) TWA: 2 ppm (vacated) TWA: 5 mg/m^3 (vacated) STEL: 4 ppm (vacated) STEL: 10 mg/m^3	IDLH: 25 ppm TWA: 2 ppm TWA: 5 mg/m^3 STEL: 4 ppm STEL: 10 mg/m^3

NIOSH IDLH Immediately Dangerous to Life or Health

Other Information: Vacated limits revoked by the Court of Appeals decision in AFL-CIO v. OSHA, 965 F.2d 962 (11th Cir., 1992).

Appropriate engineering controls

Engineering Controls: Showers
Eyewash stations
Ventilation systems.

Individual protection measures, such as personal protective equipment

General Hygiene Considerations: When using do not eat, drink or smoke. Wash contaminated clothing before reuse. Keep away from food, drink and animal feeding stuffs. Contaminated work clothing should not be allowed out of the workplace. Regular cleaning of equipment, work area and clothing is recommended. Avoid contact with skin, eyes or clothing. Take off all contaminated clothing and wash it before reuse. Wear suitable gloves and eye/face protection.

Eye/face protection: Tight sealing safety goggles. Face protection shield.

Skin and body protection: No special technical protective measures are necessary.

Respiratory protection: If exposure limits are exceeded or irritation is experienced, NIOSH/MSHA approved respiratory protection should be worn. Positive-pressure supplied air respirators may be required for high airborne contaminant concentrations. Respiratory protection must be provided in accordance with current local regulations.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical state	liquid		
Appearance	liquid	**Odor**	No information available
Color	No information available	**Odor threshold**	No information available

Property	**Values**	**Remarks • Method**
pH	0-3	
Melting Point / Freezing Point	No information available	
Boiling point / boiling range	No information available	
Flash point	No information available	
Evaporation rate	No information available	
Flammability (solid, gas)	No information available	
Flammability Limit in Air		
Upper flammability limit:	No information available	
Lower flammability limit:	No information available	
Vapor pressure	No information available	
Vapor density	No information available	
Specific Gravity	~1.10 g/cc	
Water solubility	No information available	
Solubility in other solvents	No information available	
Partition coefficient	No information available	
Autoignition temperature	No information available	
Decomposition temperature	No information available	
Kinematic viscosity	No information available	
Dynamic viscosity	No information available	
Explosive properties	No information available	
Oxidizing properties	No information available	

Other Information

Softening point	No information available
Molecular weight	No information available

VOC Content (%)	No information available
Density	No information available
Bulk density	No information available
Percent Volatile	No information available

10. STABILITY AND REACTIVITY

Reactivity
No data available

Chemical stability
Stable under recommended storage conditions.

Possibility of Hazardous Reactions
None under normal processing.

Conditions to avoid
Exposure to air or moisture over prolonged periods.

Incompatible materials
Incompatible with strong acids and bases. Incompatible with oxidizing agents.

Hazardous Decomposition Products
Thermal decomposition can lead to release of irritating and toxic gases and vapors.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Product Information: No data available

Inhalation: No data available.

Eye contact: No data available.

Skin Contact: No data available.

Ingestion: No data available.

Chemical Name	CAS No	Oral LD50	Dermal LD50	Inhalation LC50
Nitric Acid	7697-37-2	-	-	= 67 ppm (Rat) 4 h = 130 mg/m³ (Rat) 4 h
Trade Secret		1976 mg/kg	-	-

Information on toxicological effects

Symptoms: No information available.

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Sensitization:	No information available.
Germ cell mutagenicity:	No information available.
Carcinogenicity:	The table below indicates whether each agency has listed any ingredient as a carcinogen.
Reproductive toxicity:	No information available.
STOT - single exposure:	No information available.
STOT - repeated exposure:	No information available.
Chronic toxicity:	Avoid repeated exposure. Possible risk of irreversible effects.
Target Organ Effects:	Eyes, Respiratory system, Skin, Teeth.
Aspiration hazard:	No information available.

Numerical measures of toxicity - Product Information

The following values are calculated based on chapter 3.1 of the GHS document .

ATEmix (oral) 4167 mg/kg 4167

12. ECOLOGICAL INFORMATION

Ecotoxicity

Harmful to aquatic life with long lasting effects

0% of the mixture consists of components(s) of unknown hazards to the aquatic environment

Chemical Name	CAS No	Algae/aquatic plants	Fish	Crustacea
Nitric Acid	7697-37-2	-	72: 96 h Gambusia affinis mg/L LC50	-

Persistence and degradability
No information available.

Bioaccumulation
No information available.

Mobility
No information available.

Chemical Name	Partition coefficient
Nitric Acid	-2.3

Other adverse effects: No information available

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes: This material, as supplied, is a hazardous waste according to federal regulations (40 CFR 261).

Disposal methods: Do not reuse container.

14. TRANSPORT INFORMATION

Note: Store in a closed container. Keep container upright.

DOT

UN/ID no UN3264
Proper shipping name Corrosive liquid, acidic, inorganic, n.o.s. (Nitric Acid)
Hazard Class 8
Packing Group II
Special Provisions B2, IB2, T11, TP2, TP27
Description UN3264, Corrosive liquid, acidic, inorganic, n.o.s. (Nitric Acid), 8, II
Emergency Response Guide Number 154

IATA

UN/ID no UN3264
Proper shipping name Corrosive liquid, acidic, inorganic, n.o.s. (Nitric Acid)
Hazard Class 8
Packing Group II
ERG Code 8L
Special Provisions A3, A803

Description UN3264, Corrosive liquid, acidic, inorganic, n.o.s. (Nitric Acid), 8, II

IMDG

UN/ID no	UN3264
Proper shipping name	Corrosive liquid, acidic, inorganic, n.o.s. (Nitric Acid)
Hazard Class	8
Packing Group	II
EmS-No	F-A, S-B
Special Provisions	274
Description	UN3264, Corrosive liquid, acidic, inorganic, n.o.s. (Nitric Acid), 8, II

15. REGULATORY INFORMATION

International Inventories

TSCA:	Complies
DSL/NDSL:	Complies
EINECS/ELINCS:	Not Determined
ENCS:	Not Determined
IECSC:	Complies
KECL:	Complies
PICCS:	Complies
AICS:	Not Determined

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances
PICCS - Philippines Inventory of Chemicals and Chemical Substances
AICS - Australian Inventory of Chemical Substances

US Federal Regulations

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product contains a chemical or chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

Chemical Name	CAS No	SARA 313 - Threshold Values %
Nitric Acid	7697-37-2	1.0

SARA 311/312 Hazard Categories

Acute health hazard	Yes
Chronic Health Hazard	Yes
Fire hazard	No
Sudden release of pressure hazard	No
Reactive Hazard	No

CWA (Clean Water Act)

This product contains the following substances which are regulated pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

Chemical Name	CAS No	CWA - Reportable Quantities	CWA - Toxic Pollutants	CWA - Priority Pollutants	CWA - Hazardous Substances
Nitric Acid	7697-37-2	1000 lb	-	-	X

CERCLA

This material, as supplied, contains one or more substances regulated as a hazardous substance under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302)

Chemical Name	CAS No	Hazardous Substances RQs	CERCLA/SARA RQ	Reportable Quantity (RQ)
Nitric Acid	7697-37-2	1000 lb	1000 lb	RQ 1000 lb final RQ RQ 454 kg final RQ

FIFRA

Not applicable

US State Regulations

California Proposition 65
This product does not contain any Proposition 65 chemicals

U.S. State Right-to-Know Regulations

No information available

Chemical Name	CAS No	New Jersey	Massachusetts	Pennsylvania
Nitric Acid	7697-37-2	X	X	X

Canada

No information available

16. OTHER INFORMATION

NFPA	**Health hazards** 3	**Flammability** 0	**Instability** 0	**Physical & Chemical Properties** 0
HMIS	**Health hazards** *3	**Flammability** 0	**Physical hazards** 0	**Personal protection** H

Document Review
Revision Number: 8

Revision Note: No information available

Key or legend to abbreviations and acronyms used in the safety data sheet:

Bioconcentration factor (BCF)
International Air Transport Association (IATA)
Globally Harmonized System (GHS)
International Maritime Dangerous Goods (IMDG)

Disclaimer

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End of Safety Data Sheet