

Dispersants and Seafood Safety

Assessment of the potential impact of COREXIT® oil dispersants on seafood safety

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The April 20, 2010 explosion and subsequent sinking of the Deepwater Horizon oil production platform (DWH) resulted in the largest oil spill in U.S. history. On April 29th, a Spill of National Significance was declared as roughly 53 thousand barrels of oil per day flowed into the Gulf of Mexico (GOM). The U.S. Coast Guard estimated 4.9 million barrels of crude oil escaped before the damaged DWH wellhead was sealed on July 15, 2010 (National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling 2010). Oil spill clean-up methods included skimming operations, burning of surface oil, siphoning oil into tankers directly from the wellhead, and the application of chemical dispersants. The first 3 methods mentioned above physically removed spilled oil from GOM waters. The last method, chemical dispersion, distributed insoluble fractions of the oil into the water-column. This was done for 3 reasons: 1) to reduce the exposure of response personnel at-sea to volatile organic compounds emanating from the surface slick; 2) to prevent concentrated surface oil from reaching, and damaging, fragile coastal wetlands, beaches and shoreline ecosystems; and 3) to accelerate the break-down of spilled oil by natural microorganisms in the environment. During oil spill response, the Regional Contingency Plan (RCP) applicable to the GOM (EPA Regions 4 and 6 within the National Response Framework) pre-authorized the use of Nalco Co. (Naperville, IL) oil dispersants Corexit® 9527 and Corexit® 9500 among other pre-approved product formulations. From April 22 to July 19, 2010, an estimated 1.1 million gallons of Corexit® dispersant were applied over approximately 300 square miles of oiled surface waters in the GOM and 771,000 gallons were injected directly into the oil free-flowing from the wellhead 5,100 feet beneath the surface (National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling 2010). Corexit® 9527 comprised approximately 215,000 gallons (~11%) of the total dispersant volume applied to the surface oil slick and was discontinued on May 22. The unprecedented volume of chemical dispersants used to combat the DWH oil spill elicited public concerns for the health of responders, coastal communities, marine life, and the safety of seafood from impacted areas of the GOM. This document will address the latter of these concerns.

As part of the federal response to the DWH oil spill, the FDA and NOAA assessed Corexit® dispersant ingredients for toxicity and potential to bioconcentrate in seafood species. With the exception of one proprietary component, the chemical compositions of Corexit® 9527 and Corexit® 9500 were identified in material safety data submitted to EPA

as required by subpart J of the National Contingency Plan (NCP), Sec. 300.915 for RCP pre-authorization (EPA 2010a; 40 CFR 300.915). As it became apparent that large volumes of dispersants were being used to combat the subsurface and surface oil spill, EPA requested and received from the manufacturer disclosure of the proprietary component (i.e. dioctyl sodium sulfosuccinate, DOSS). Corexit® constituents are listed in Table 1 and described below.

Table 1. From <http://www.epa.gov/bpspill/dispersants-qanda.html#list>

CASRN	Name	Corexit® 9527	Corexit® 9500
111-76-2	2-Butoxyethanol (ethylene glycol mono-n-butyl ether)	X	n/a
57-55-6	Propylene glycol	X	X
29911-28-2	Dipropylene glycol monobutyl ether	X	X
577-11-7	Dioctyl sodium sulfosuccinate	X	X
64742-47-8	Petroleum distillates, hydrotreated light fraction	n/a	X
1338-43-8	Sorbitan, mono-(9Z)-9-octadecenoate	X	X
9005-65-6	Polyoxy-1,2-ethanediyl derivatives of sorbitan, mono-(9Z)-9-octadecenoate	X	X
9005-70-3	Polyoxy-1,2-ethanediyl derivatives of sorbitan, tri-(9Z)-9-octadecenoate	X	X

The solvent 2-butoxyethanol (CASRN 111-76-2) is a high production glycol ether and constituent of Corexit® 9527. It has other common uses as a solvent and degreaser in industrial, residential, and personal care products including protective surface coatings (spray lacquers and paints), agricultural chemicals, household cleaners, and liquid soaps and cosmetics at concentrations of up to 10%. This compound is approved by FDA as an indirect and direct food additive for use as an antimicrobial agent, defoamer, stabilizer and component of adhesives (21 CFR 175.105(FAP 1B0233); 178.1010(FAP 4A1375); 176.210(FAP 3B0899); 177.1650; 173.315(FAP 5A3079). FDA approval means that the compound is safe for its approved intended uses and the human exposures associated with those uses. 2-butoxyethanol has been well studied. Information is available on metabolism, mechanism of toxicity, pharmacokinetics and impact of exposure on human health. Primary effects are on the hematologic system with secondary renal effects. Acute oral LD₅₀ values in a variety of rodent animal models range from 200 to 12,750 mg/kg bw. The Agency for Toxic Substances and Disease Registry (ATSDR, 1998) derived minimal risk levels (MRL¹) of 0.4 mg/kg bw d⁻¹ for human acute-duration (14 d) and 0.07 mg/kg bw d⁻¹ for human intermediate-duration (15-364 d) oral exposures. Acute oral exposures of humans to large amounts of 2-butoxyethanol have been shown to cause coma and respiratory depression in addition to hematotoxic effects, although this route of exposure is the least likely for the general population. From quantitative structure-activity relationships, the bioconcentration

¹ An MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure. MRLs are derived when reliable and sufficient data exist to identify target organs(s) of effect or the most sensitive health effects(s) for a specific duration within a given route of exposure. MRLs are based on noncancer health effects only and do not reflect a consideration of carcinogenic effects. MRLs can be derived for acute, intermediate, and chronic duration exposures for inhalation and oral routes.

factor (BCF) for 2-butoxyethanol has been predicted to be 3, and experimentally estimated in fathead minnows (*Pimephales promelas*) to be 2 (ASTER 1995). The physical-chemical characteristics of 2-butoxyethanol include vapor pressure of 0.88 mm Hg at 25°C (ATSDR 1998), Henry's law constant estimates ranging from 2.08×10^{-8} to 3.61×10^{-6} atm·m³/mol at 25°C (HSDB 1995, ASTER 1995), and log octanol-water partition coefficient (log K_{ow}) of 0.83 suggesting a low probability of lipid uptake or bioconcentration in fish (ATSDR, 1998). The half-life of 2-butoxyethanol in surface waters is estimated to be in the range of 7-28 days, and the chemical is reported to be readily biodegraded in aerobic soil and aquatic environments (Howard et al., 1991, HSDB 2010).

Propylene glycol (CASRN 57-55-6) and dipropylene glycol monobutyl ether (CASRN 29911-28-2) are constituents of both Corexit® 9527 and 9500. Dipropylene glycol monobutyl ether is used as a solvent for industrial and residential cleaners/degreasers, paints and plasticizers. Propylene glycol is used in commercial formulations of foods, drugs, cosmetics, and personal care products (e.g. toothpaste, shampoo, mouthwash). Propylene glycol is approved by FDA as a Generally Recognized As Safe (GRAS) ingredient, direct food additive, and indirect food additive for many uses, including as an anticaking agent, antimicrobial agent, antioxidant, color or color adjunct, defoamer, dough strengthener, emulsifier, flavoring agent, formulation aid, humectant, processing aid, solvent, diluent or vehicle stabilizer, thickener or gelling agent, surfactant, and texturizer (21 CFR 175.105(FAP 1B0233, FAP 2B0650); 178.3300; 175.300; 175.320; 177.2420; 177.1680(FAP 5B1808); 184.1666). Propylene glycol ethers as a class are rapidly absorbed and exhibit low acute toxicity by oral exposure and **propylene glycol is infrequently associated with adverse effects**. Acute oral LD₅₀ values in a variety of rodent animal models range from 3,000 to 5,000 mg/kg bw for dipropylene glycol monobutyl ether and from 18,000 to 46,000 mg/kg bw for propylene glycol (OECD 2003, HSDB 2010). Some acute oral data exist for humans, but the information is limited and includes systemic and neurological effects at high levels of exposure. No MRL for oral exposure to propylene glycol in humans has been derived because data are insufficient (ATSDR, 1997). The FAO/WHO Joint Expert Committee on Food Additives (JECFA) determined 25 mg/kg bw d⁻¹ as the acceptable daily intake (ADI) for propylene glycol (FAO/WHO, 1997). Predicted BCFs for dipropylene glycol monobutyl ether and propylene glycol are <10 indicating a low potential for bioconcentration in aquatic food chains (OECD 2003, HSDB 2010). Physical-chemical characteristics include vapor pressures below 1 mm Hg, Henry's law constants ranging from $1.2 - 1.7 \times 10^{-8}$ atm m³/mol at 25°C, and log K_{ow} from -0.92 to 1.52 suggesting low probability of uptake in lipids or bioconcentration in fish. Propylene glycol and glycol ethers would be expected to be of low to moderate volatility from water and readily biodegradable in aquatic and terrestrial environments with half-lives of 7-28 days (Howard et al., 1991; ATSDR 1997; Staples and Davis 2002; OECD 2003; HSDB 2010).

Petroleum distillates, hydrotreated light fraction (CASRN 64742-47-8) are paraffinic dearomatized, and volatile solvents derived from crude petroleum, and constituents of Corexit® 9500. Production quality of light petroleum distillates is highly variable and common uses include as a solvent for paints, varnishes, polishes, and lubricants, and general purpose cleaners and degreasers. Hydrotreated light petroleum distillates Norpar 13 (food grade aliphatic n-alkanes ranging from nonane to hexadecane: CASRN 94094-93-

6) were reportedly substituted for 2-butoxyethanol in the formulation of Corexit 9500 (NRC 2005); however, CASRN do not align with that reported by EPA (Table 1). FDA has approved similar food grade odorless light petroleum hydrocarbons as indirect and direct food additives (21 CFR 172.884; 175.105; 176.200; 176.210; 178.3650). C₈ – C₂₀ range aliphatic hydrocarbons comprising petroleum distillates, hydrotreated light fraction exhibit low acute oral toxicity. Acute oral LD₅₀ values in rodent animal models are greater than 5,000 mg/kg (HSDB 2010). Subchronic toxicity studies suggest the aliphatic hydrocarbon fluids to be relatively non-toxic (EPA 2006). Predicted BCFs range from 60 to 80 and physical-chemical characteristics include vapor pressures below 2.0 mm Hg; Henry's law constant ranging from 0.2 – 3.4 atm-cu m³/mol, and log K_{ow} from 2.2 to 5.4. Some of the longer chain compounds in the mixture may have a high potential for concentration in aquatic organisms provided they are not volatilized or metabolized. Petroleum distillates are volatile from water and readily biodegradable in days to weeks (EPA 2006, HSDB 2010).

Diocetyl sodium sulfosuccinate (DOSS; CASRN 577-11-7) is an anionic surfactant (butanedioic acid, 2-sulfo-1,4-bis(2-ethylhexyl) ester, sodium salt) listed as a proprietary organic sulfonic acid salt constituent of both Corexit® 9527 and 9500 formulations. Other common uses include wetting and flavoring agent in food, industrial, and cosmetic applications, and a medicinal stool softener in over-the-counter use. FDA has approved this compound as a GRAS ingredient, and as indirect and direct food additives under prescribed conditions of use (21 CFR 73.1; 131.130; 133.124; 133.133; 133.134; 133.162; 133.178; 133.179; 163.117; 168.115; 172.520; 172.808; 172.810; 175.105). DOSS was determined to be essentially non-toxic by oral administration to rodent animal models with acute toxicity ranging from 2.6 to 5.7 g/kg bw. Diarrhea and signs of intestinal irritation were noted. Three-generation reproduction studies in rodent models did not reveal adverse effects; however, parental and weanling weight loss was noted at dose levels above 5 g/kg bw (FAO/WHO 1991a). JECFA determined 0.1 mg/kg bw d⁻¹ as the ADI for diocetyl sodium sulfosuccinate (FAO/WHO 1995). Predicted and experimentally derived BCFs are <10, indicating a low potential for bioconcentration and bioaccumulation (Goodrich et al., 1991). Physicochemical characteristics include vapor pressure of 2.17 x 10⁻¹¹ mm Hg, Henry's law constant 5 x 10⁻¹² atm m³/mol, and log K_{ow} 6.1. DOSS is essentially nonvolatile from water and several studies have reported >90% biodegradation in 3-12 days at freshwater concentrations of 3.3-12.9 ppm (HSDB 2010).

The nonionic surfactant Span 80 (CASRN 1338-43-8) is a trade name for sorbitan, mono-(9Z)-9-octadecenoate. The nonionic surfactant Tween 80 (CASRN 9005-65-6) is a trade name for a mixture of isomers and congeners of polyoxy-1,2-ethanediyl derivatives of sorbitan, mono-(9Z)-9-octadecenoate. The nonionic surfactant Tween 85 (CASRN 9005-70-3) is a trade name for a mixture of isomers and congeners of polyoxy-1,2-ethanediyl derivatives of sorbitan, tri-(9Z)-9-octadecenoate. Numerous chemical synonyms and trade names exist for these materials. Other common uses for Span and Tween products include as wetting agents, solubilizing agents, or emulsifying agents in cosmetic and personal care products. Span 80 and Tween formulations are widely used in food products, cosmetic and personal care products, oral pharmaceuticals, and parenteral products. They include GRAS direct and indirect food additives commonly known as polysorbates (21 CFR 73.1;

107.105; 172.515; 172.623; 172.836; 172.838; 172.840; 172.842; 173.310; 173.340; 175.105; 178.340). The National Toxicology Program reviewed Tween 80 (CASRN 9005-65-6) for developmental toxicity in rats and estimated a maternal LOAEL of 500 mg/kg-day based upon an increase in maternal liver weight at this dose. No definitive adverse effects on prenatal development were noted and the developmental NOAEL was projected to be greater than 5,000 mg/kg/day (NTP 1992). JECFA determined 25 mg/kg bw d⁻¹ as the ADI for Tween 80 and Span 80 (FAO/WHO, 1973). Predicted BCF/BAF for sorbitan oleates have been estimated from 36 to >300 suggesting potential for bioaccumulation. Physical-chemical characteristics of the sorbitan oleates include vapor pressures less than 1×10^{-10} mm Hg at 25°C; Henry's law constants $<1 \times 10^{-10}$; and Log K_{ow} from <1 to 6 (KOWWIN v1.54; v1.67; HENRYWIN v3.20; Rorije et al., 1997; EPA 2010c). Sorbitan oleates would not be expected to volatilize from water and are readily biodegradable (HSDB 2010).

The aquatic toxicity of dispersant formulations has been examined and debated over many years. Following extensive reviews in 1989 and 2005, and suggested standardization of testing methods, dispersants in use today are generally reported to be less toxic than formulations prior to 1970 (e.g. NRC 1989, 2005, Fingas 2008). Corexit® dispersants in particular have been well studied with most reports indicating lower aquatic toxicity in direct comparisons with water soluble, water accommodated and chemically dispersed oil fractions (e.g., George-Ares and Clark, 2000; Liu et al., 2006; Judson et al., 2010; Hemmer et al., 2011). Other studies have addressed dispersant influence on the bioavailability and uptake of aromatic and aliphatic constituents of oil by various aquatic species (e.g. Milinkovitch et al., 2011; Jung et al. 2009; Mielbrecht et al., 2005; Fuller et al., 2004; Ramachandran et al., 2004; Cohen et al. 2001; Gagnon et al. 2000; Singer et al., 1998). However, the potential for dispersant constituents themselves to accumulate in aquatic species has received less attention. Several studies investigating uptake and disposition of principal dispersant constituents, ionic and nonionic surfactants, in aquatic species suggest rapid uptake, metabolic conjugation, concentration in liver and bile with transient enterohepatic circulation, and rapid elimination (Alvarez-Munoz et al., 2010; Tolls et al., 2000; Tolls & Sijm 1999; Goodrich et al., 1991; Granmo & Kollberg 1976; Calamari & Marchetti 1973). Distribution of surfactants into muscle tissues was reported to be low order and low BCF values for edible tissues. In one of few studies to assess the uptake and disposition of Corexit® constituent dioctyl sodium sulfosuccinate in aquatic species, Goodrich et al. (1991) noted rapid uptake and concentration in viscera and bile of rainbow trout, at significantly higher levels than uptake in either blood and carcass. BCFs were not determined for viscera or bile due to the lack of steady state conditions. BCFs of 3.47 and 3.78 were derived for blood and carcass compartments, respectively, indicating little bioconcentration in edible tissues.

The initial federal chemical safety assessment of Corexit® dispersants in the context of seafood safety included structure-activity modeling to estimate BCFs for Corexit® constituents. Consistent with existing information, predictive BCFs for Corexit® constituents, other than the nonionic surfactants and light petroleum distillates, fell below 10, suggesting low potentials for bioconcentration and accumulation in edible tissues of aquatic species. The BCFs for light petroleum distillate mixtures ranged from 60 to 80.

Nonionic surfactant BCFs have been experimentally determined in fathead minnow with an average value of 39.6 and maximum value of 387, suggesting moderate potential for bioconcentration. However, high elimination rate constants indicated that these compounds are rapidly biotransformed *in vivo* and are thus unlikely to accumulate in fish (Tolls et al., 2000). Dispersant concentrations in DWH surface applications at sea were estimated by the manufacturer to be approximately 30 µg/L in the area of the oil slick to a depth of 10 meters (Nalco, 2010). Previous research (Georges-Ares & Clark, 2000; NRC 1989) indicates that dispersant would be expected to be rapidly diluted and biodegraded in the ocean environment to levels below detection. Analyses for Corexit® constituents in surface water and sediment samples from the GOM after dispersant applications had ceased did not detect dispersant chemicals above limits of detection (EPA 2010b). However, deep subsurface sampling and analyses detected trace levels (12 ppb) of DOSS entrained in a hydrocarbon plume at 1000-1200 m water depth, suggesting slow to negligible degradation at depth (Kujawinski et al., 2011).

In the development of a method for surveillance of dispersant residues in GOM seafood species, the FDA and NOAA performed controlled exposures of Corexit® 9500 to live Eastern oyster (*Crassostrea virginica*), blue crab (*Callinectes sapidus*), and red snapper (*Lutjanus campechanus*) to generate incurred residues (Benner et al., 2010). DOSS was selected as the indicator compound for potential Corexit® contamination in seafood due to its inclusion in both Corexit® formulations, extremely low volatility, and potential to persist in the environment. The laboratory exposure studies were designed to generate incurred residues in seafood species to support method development and validation under a compressed time schedule, and therefore procedural design was not intended to be sufficient for rigorous pharmacokinetic assessment and environmental relevance. Nevertheless, it was possible to incorporate a limited sampling of uptake and depuration time points in the species exposed.

Performance testing of a rapid extraction procedure and liquid chromatography tandem mass spectrometry (LC-MS/MS) method for DOSS showed an average recovery of 92% and relative standard deviation of 11%. The method limits of detection (LOD) for DOSS in seafood species ranged from 0.003 µg/g (FDA Forensic Chemistry Center) to 0.015 µg/g (NOAA Northwest Fisheries Science Center) and limits of quantitation (LOQ) from 0.010 µg/g to 0.045 µg/g (Flurer et al., 2011). Mean DOSS concentrations in laboratory exposed and depurated oysters exposed to 100 mg/L Corexit® 9500 were 18 and 12 µg/g after 24 and 48 h of exposure, respectively. Levels of DOSS declined by >99%, to 0.023 µg/g within 72 h of depuration in clean water. In crabs exposed to Corexit® 9500 (100 mg/L) for 24 h, mean DOSS level in muscle was 0.9 µg/g, with levels declining to 0.023 µg/g (>97%) within 72 h of depuration in clean water. After 24 h of exposure, mean DOSS concentration in crab hepatopancreas was 11 µg/g, more than 10-fold higher than corresponding muscle tissue. Levels increased initially during the first 24 h of depuration, possibly as a result of the re-distribution of residues within the body during elimination. Levels subsequently declined >95% to 2.4 µg/g after 72 h of depuration. DOSS concentrations in muscle tissues of red snapper exposed to 100 mg/L Corexit® 9500 for 24 h were near or below the LOQ at all sampling times (Benner et al., 2010).

In retrospective analyses of 393 GOM fisheries re-opening samples collected from June 2010 through March 2011, DOSS was not detected in 116 of 119 samples collected from State waters. Three samples from State waters showed DOSS levels ranging from 0.011 to 0.013 $\mu\text{g/g}$ (FDA 2010a). Of 274 samples analyzed from Federal waters, 12 finfish samples contained DOSS ranging from 0.037 to 0.41 $\mu\text{g/g}$. Overall, DOSS was detected at or above the LOQ in less than 3.6% (14/393) of the re-opening samples tested and all were below safety thresholds determined for DOSS in finfish (100 $\mu\text{g/g}$), shrimp and crabs (500 $\mu\text{g/g}$), and oysters (500 $\mu\text{g/g}$). Safety thresholds were derived by combining the 2005-2006 National Health and Nutrition Examination Survey (NHANES) 90th percentile finfish, shrimp or crab meal size adjusted by the 90th percentile consumption frequency with the acceptable daily intake for DOSS developed by the World Health Organization, Food and Agriculture Organization, Joint Expert Committee for Food Additives (FAO/WHO 1991a, 1995, FDA 2010b).

Conclusions:

In considering the potential for chemical dispersants to compromise the safety of GOM seafood, initial questions concerned the potential toxicity of dispersant constituents, their concentrations, fate and persistence in the environment, their potential for bioconcentration in seafood species, and their disposition and persistence in seafood species. With the exception of dipropylene glycol monobutyl ether, the constituents of Corexit® dispersants are recognized direct or indirect food additives under prescribed conditions of use. Corexit® dispersants used to treat the DWH oil spill were rapidly and extensively diluted in GOM waters, and environmental concentrations, estimated and measured, were commensurately low when detected. The physical-chemical characteristics and scientific literature indicate that dispersant constituents are susceptible to chemical and biological degradation, and that the potential for bioconcentration and persistence in the edible tissues of seafood species is low. The modeling, experimental, and field assessments performed during the response to the DWH oil spill, as well as the knowledge base accessed through scientific literature, indicated that Corexit® dispersants did not pose a threat to the safety of GOM seafood during or after their use. However, oil spills in different parts of the world differ in the nature and extent of public and environmental health hazards entailed, and consequently response strategies are rarely the same. There are numerous dispersant formulations available to responders, and in development for mitigation of oil spills under varying conditions. Future responders would benefit from a systematic assessment of all dispersant constituents, and their fate in aquatic species. A review of the existing knowledge base for dispersant constituents that are listed on the NCP product schedule should be performed to determine chemical makeup, environmental fate, kinetics, BCF/BAF, and potential human toxicity through direct or indirect exposure in order to identify constituents of potential public health concern. Some level of standardization of experimental designs informed by the needs of risk analysis, and testing methods for toxicologically valid markers of dispersant contamination in aquatic species would benefit risk managers and responders in the event of future oil spills.

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