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Toxicology Directorate

Toxicology Assessment for Safer Alternatives for Readiness (SAFR) Program Work Unit ALR 18-01: Green Improved Process: DBX-1 Lab-RAM March 2018—July 2020

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14. ABSTRACT
This report is a Toxicology Assessment for the components of an improved method of loading percussion primers for small arms. The automated filling process eliminates the hazard to ammunition plant workers who have been hand filling caps for decades. The filling suspension is DBX-1 in isopropyl alcohol. The human and environmental hazard from the process is assessed to be low.

15. SUBJECT TERMS
DBX-1, isopropanol, percussion primers, small arms

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1 SUMMARY

1.1 Overview

Research, development, testing, training, and use of substances potentially less hazardous to human health and the environment is vital to the readiness of the U.S. Army. Safeguarding the health of Soldiers, civilians, and the environment requires an assessment of alternatives before they are fielded. Continuous assessments begun early in the Research, Development, Testing and Evaluation (RDT&E) process can save significant time and effort during RDT&E, as well as over the life cycle of the items developed. Residues of pyrotechnics, propellants, explosives and incendiaries that were part of mission-essential activities have been found in soil, air, surface and groundwater samples. Remediation of the contaminated areas has cost the Department of Defense (DOD) millions of dollars and can interfere with training activities.

1.2 Purpose

Primer caps are necessary to initiate the combustion process for all types of munitions. These caps are filled with an impact-sensitive formulation that typically contains both lead azide and/or lead styphnate. These caps are very small, typically just 2-3 millimeters (mm) in diameter and are loaded by hand in a process that has not changed significantly in decades. Workers involved in this process are potentially exposed to quantities of lead-containing materials that could have adverse health effects, as well as hazardous solvent vapors. In addition, the hand application process is outmoded and inefficient. Additionally, Soldiers are increasingly exposed to higher concentrations of lead vapors from use of lead-based primers, some at levels that have been shown to adversely affect health. The Army is in the process of eliminating the lead-based primers with lead-free alternatives, and this is the ideal opportunity to update the filling process. The purpose of this project is to develop an automated means of filling these primer caps with a DBX-1 formulation that would reduce human exposure and be a more efficient way of producing these items.

1.3 Conclusions

Overall, this formulation is assessed to be of low to moderate toxicity, and suggests lower toxicity than the lead compounds that are being replaced. Given current data and testing already underway, little if any additional testing is considered necessary at this time.

Occupational health risks appear to be low overall, but the formulation suggests environmental releases may constitute an ecotoxicity hazard, and should therefore not be released into the environment. Ecotoxicity evaluations should be considered if there is the prospect of significant environmental release.

DBX-1 in aqueous solutions limits the applicability for most *in vitro* and aquatic toxicity testing.

2 REFERENCES

See Appendix A for list of references.

3 AUTHORITY

Funding for this work was provided under Military Interdepartmental Purchase Request No. 10453954 dated March 2014. This Toxicology Assessment addresses, in part, the environment, safety and occupational health (ESOH) requirements outlined in Army Regulation (AR) 200-1, Environmental Protection and Enhancement, 2007; AR 40-5, Army Public Health Program, 2020; and AR 70-1, Army Acquisition Policy, 2018; Department of Defense Instruction (DODI) 4715-series and Army Environmental Requirement and Technology Assessment (AERTA) requirement PP-3-02-07, *Compliant Munitions Lifecycle for Warfighter Readiness* (AERTA 2018). The Sponsor is the Army Safer Alternatives for Readiness (SAFR) Program. The Principle Investigator is Ms. Neha Mehta of the Combat Capabilities Development Command-Armaments Center (CCDC-AM), Picatinny Arsenal, NJ.

4 BACKGROUND

Current regulations require assessment of human health and environmental effects arising from exposure to substances in soil, surface water, and groundwater. Applied after an item has been fielded, these assessments can reveal the existence of adverse environmental and human health effects that must be addressed, often at substantial cost. It is more efficient to begin the assessment of exposure, effects, and environmental transport of military-related compounds/ substances early in the RDT&E process in order to avoid unnecessary costs, conserve physical resources, and sustain the health of our forces and others potentially exposed.

In an effort to support this preventive approach, the U.S. Army Public Health Center (APHC) has been tasked with creating a phased process to identify ESOH effects impacting readiness, training, and development costs. This report represents the status of information available for this work unit as of the date of publication.

5 STATEMENT OF THE PROBLEM

Methods used for filling primer caps used in military munitions have not changed since World War II, and involve workers squeegeeing the primer paste over a tray containing empty primer cups. This method is labor-intensive, wasteful of primer chemical formulations and potentially

puts workers involved in filling the caps at risk from solvent vapors, lead-based materials and the explosive nature of the chemical formulations. The objective of this project is to develop an

automated process for loading newly-developed lead-free primer formulations, eliminating the problems associated with the current method.

6 METHODS

To determine the human health and environmental impact of compounds employed in these formulations, it is necessary to correctly identify each compound and to determine its physical, chemical, and toxicological properties. The primary means of identification employed for each compound in this program is its Chemical Abstracts Service Registry Number (CAS RN) (Table-1). While all compounds do not necessarily have a single CAS RN, the CAS RN is an unambiguous way of accessing information for chemical substances. The CAS RN is readily used as a keyword for searching online databases and is often cross-referenced with both systematic and trivial (i.e., “common” or non-systematic) names for chemical substances. In some cases, synonyms and trade names are also used to identify structures.

Table 1. Formulation Components

Section	Chemical Substance	CAS RN
7.3	DBX-1	957133-97-0
7.4	Isopropyl alcohol	67-63-0

The physicochemical properties necessary to assess environmental fate and transport include:

- Molecular weight (MW in grams (g) per mol; g/mol)
- Boiling point (bp) in degrees Celsius (^{O}C)
- Octanol-water partition coefficient (log K_{OW})
- Organic carbon partition coefficient (log K_{OC})
- Water solubility (milligrams (mg) or milliliters (mL) per liter (L) e.g., mg/L or mL/L)
- Henry’s Law constant (K_H)
- Vapor pressure (vp) in millimeters (mm) of mercury (Hg) – mmHg

Basic physical and chemical properties are usually determined by consulting tertiary sources when such information is available.

Toxicological information needed to estimate potential human health risks includes reported toxicity effects of oral, inhalation, dermal, and ocular exposures; potential for developmental or reproductive toxicity, neurotoxicity, genotoxicity and carcinogenicity; and modes and mechanisms of toxicity. Values reported herein include lethal dose 50% (LD_{50}; reported in milligrams (mg) per kilogram (kg) i.e., mg/kg), no observed adverse effect level (or concentration) (NOAEL/C), lowest observed adverse effect level (or concentration) (LOAEL/C) reported in mg/kg or mg/liter (mg/L), 50% effect concentration (EC_{50}), lethal concentration 50%

(LC_{50}) typically reported as mass (g or mg) per cubic meter (m^3) or mg/L, clinical chemistry values may be reported in deciliters (dL) and some water quality values may be reported in micrograms/liter (µ/L) or parts per million (ppm). Toxicological information is derived directly from primary sources whenever possible. Sources used in this search included publications from peer-reviewed journals, official government publications and websites, and tertiary reference sources such as *The Merck Index*. Commercial suppliers may provide results of in-house research that do not appear in the open literature.

In the absence of published information, *in silico* quantitative structure-activity relationship (QSAR) models, such as TOPKAT (Toxicity Prediction Komputer Assisted Technology; BIOVIA 2015), EPI Suites (Estimation Program Interface) 2012, and ECOSAR (Ecological Structure Activity Relationships Predictive Model, Versions 1.11 and 2.0) 2018 may be used (if applicable to the type of molecule under consideration) to predict toxicity endpoints, physical properties, and ecotoxicity endpoints, respectively.

Persistence, bioaccumulation, human health toxicity, and ecotoxicity were assigned to general categories of risk (i.e., low, moderate, or high) using criteria modified from Howe et al. (2006). Table B-1 describes the criteria used in the categorization, though the relative proportions of each substance were also factored into the final assessment. In addition, classification in the Globally Harmonized System (GHS) is also included for many of these compounds in Appendix B (OSHA 2012).

7 RESULTS

7.1 Physicochemical Properties

Selected physicochemical properties that are relevant for evaluating toxicity and environmental fate are summarized in Appendix C- Table C-1. Physical properties include melting/boiling points and molecular weight; solvation properties include phase partitioning and solubility. The primary sources for these properties include PubChem®, Safety Data Sheets (SDS) (when available) and EPI Suites (when experimentally measured data are not available).

7.2 Compound Summaries

Summaries of mammalian toxicity data are collected in Appendix C- Table C-2. Assessments of human health and environmental toxicity for each of the formula components are presented in Appendix C- Tables C-3 and C-4, respectively. Each characterization is generally based on the criteria set forth in Table B-1. Where applicable, the GHS categories may be included (see Appendix B for details). The final risk characterization also incorporates assessment of the uncertainty associated with available data, the amount of each compound present in the formulation, and the nature of potential exposure associated with use of the end-item.

7.3 Copper(I) 5-nitrotetrazole [DBX-1]

7.3.1 General Information

DBX-1 is under evaluation as a replacement for lead azide in primary detonators. As shown in Figure 1, DBX-1 is a complex of two nitrotetrazole molecules and Cu(I). However, a review of available information indicates there are several different molecular representations in the energetics literature for the DBX-1 compound—from monomers to substituted tetramers. These different isomers and concatamers may have unique properties. Investigating all the molecular permutations of DBX-1-based structures is beyond the scope of this toxicity assessment. No toxicological information was found in the literature search. This substance profile addresses only the organic anion component of DBX-1 (i.e., 5-nitrotetrazole (5-NT); QSAR predictions were conducted using the 5-NT SMILES); the copper (I) cation is not expected to be the limiting factor for toxicity for this compound.

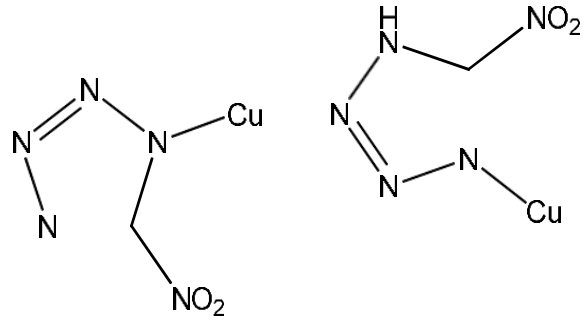

Figure 1. DBX-1 Structure as Determined by Single Crystal X-ray Crystallography (Sabatini and Oyler 2016)

7.3.2 Toxicology Data

7.3.2.1 Oral

No experimental data were found. TOPKAT modeling predicts an oral lethal dose of 50% (LD_{50}) of 421 mg/kg with low confidence. The chronic LOAEL is predicted to be 90 mg/kg-day at low confidence. These values classify DBX-1 as moderately toxic under the APHC system, and Category (Cat.) 4 for acute oral toxicity in the GHS.

In vitro testing of 5-NT using the Neutral Red Uptake test predicts an oral toxicity of 2372 mg/kg, indicating low toxicity and GHS Cat. 5 (USAPHC 2013).

7.3.2.2 Inhalation

No experimental data were found. TOPKAT modeling predicts an inhalation LC_{50} of 0.636 g/m^3-hour at low confidence. This correlates to moderate toxicity in the APHC system, and GHS Cat. 3.

7.3.2.3 Dermal

No experimental data were found. TOPKAT modeling predicts DBX-1 is a mild skin irritant (GHS

Cat. 3) with low confidence and a strong sensitizer with high confidence.

7.3.2.4 Ocular

No experimental data were found. TOPKAT modeling predicts DBX-1 is a moderate ocular irritant (GHS Cat. 2B) with high confidence.

7.3.2.5 Development and Reproduction

No experimental data were found. TOPKAT modeling predicts DBX-1 will not be a developmental or reproductive toxicant at high confidence.

7.3.2.6 Genotoxicity

No experimental data were found. TOPKAT modeling predicts DBX-1 and 5-NT will be mutagenic in the Ames assay at high confidence.

7.3.2.7 Carcinogenicity

No experimental data were found. TOPKAT modeling predicts DBX-1 is not a carcinogen; however, modeling predicts 5-NT is carcinogenic. These data present an equivocal assessment for carcinogenicity.

7.3.2.8 Neurotoxicity

No data for DBX-1 or 5-NT were found.

7.3.2.9 Mechanism/Mode of Action

No data for DBX-1 or 5-NT were found.

7.3.3 Ecological Data

7.3.3.1 Fate and Transport

With an estimated water solubility of 6.7×10^4 mg/L, 5-NT is highly soluble, and with a log K_{OC} estimated at 0.244, mobility in ground water is expected to be high. DBX-1 has been observed experimentally to dissolve only slowly in water (USAPHC 2014), likely resulting in restricted mobility if released to soil. TOPKAT modeling predicts a vapor pressure of 8.41×10^{-4} mmHg, indicating DBX-1 would be relatively volatile in air and exist as a vapor. This has not been experimentally observed, probably due to the de-facto higher molar mass from the formation of dimers and higher order crystals. The DBX-1 log K_{OW} is -0.76 and log bioconcentration factor (BCF) is 0.50, indicating low to no bioaccumulation potential.

7.3.3.2 Ecotoxicity

No experimental data were found. TOPKAT predicts an LC_{50} in *Daphnia* of 9.67 mg/L and LC_{50} in fathead minnow of 26.7 mg/L, both with very low confidence.
The U.S. Environmental Protection Agencies (EPA) ECOSAR program models DBX-1 as a neutral organic with a 96-hour LC_{50} in green algae are 1.61×10^4 mg/L, a 48-hour LC_{50} for *Daphnia* of 9.1×10^4 mg/L, and a 96-hour LC_{50} in fish of 2.27×10^5 mg/L, which is expected to exceed the solubility of the compound. These values suggest DBX-1 is not toxic toward aquatic species.

7.3.3.3 Degradation and Treatment

DBX-1 dissolves only slowly in water. When solubilized with a co-solvent such as dimethyl sulfoxide (DMSO) and then transferred to water, degradation occurs rapidly producing a flocculent precipitate (USAPHC 2014).

DBX-1 is predicted by EPI Suite modeling to be poorly removed by wastewater treatment processes, however its relative insolubility in water will likely make it easily removed via precipitation.

7.4 Isopropyl Alcohol [IPA]

7.4.1 General Information

IPA is a volatile, colorless liquid with a sharp odor characteristic of rubbing alcohol. Vapors are heavier than air and mildly irritating to the eyes, nose, and throat. IPA is used in making cosmetics, skin and hair preparations, pharmaceuticals, perfumes, lacquer formulations, dye solutions, antifreezes, soaps and window cleaners. It is sold commercially as a 70% solution in water (PubChem 2018). Synonyms include propan-2-ol (IUPAC name), 2-propanol, isopropyl alcohol, rubbing alcohol, and isopropanol (density = 1 ppm) = 2.46 mg/m^3)).

7.4.2 Toxicology Data

IPA and ethyl alcohol have been used as low-level disinfectants in healthcare settings for many years. Recent studies have found that ethyl alcohol inhibits protein synthesis in *E. coli* by direct effects on ribonucleic acid nucleic (RNA) polymerase and that 60-70% solutions have *in vitro* efficiency against murine noroviruses, Ebola viruses, and several corona viruses; IPA may function in a similar way (Boyce 2018).

7.4.2.1 Oral

According to clinical experience, IPA is more toxic than ethyl alcohol but less toxic than methanol. Its acute potency as a central nervous system (CNS) depressant is about twice that of ethanol. A single lethal dose for humans is about 250 mL, although as little as 100 mL can be fatal (PubChem 2018).

The oral LD_{50} in rats is reported to be between 4710 and 5840 mg/kg. The oral LD_{50} in mice is

reported to be 3600-4475 mg/kg; in rabbits it is 6410-7990 mg/kg, and in dogs 4797-4830 mg/kg (PubChem 2018).

7.4.2.2 Inhalation

Vapors of IPA are mildly irritating to the nose and throat. The lowest published toxic concentrations in humans are 35 ppm for 4 hours, 150 ppm for 2 hours, and 3000 ppm for 6 minutes (PubChem 2018).
The inhalation LC_{50} in the rat is reported to be 53 mg/L for a 2-hour exposure, 72.6 mg/L for a 4-hour exposure, and 51.04 mg/L for an 8-hour exposure (PubChem 2018).

The lowest published LC_{50} values in mice are 53,000 mg/m^3 and 12,800 ppm for a 3-hour exposure. The comparable numbers in rats are 72,600 mg/m^3 and 16,000 ppm for an 8-hour exposure (PubChem 2018).

Biological effects of a single exposure to moderate or high concentrations of 2-propanol were investigated in Sprague-Dawley rats (Laham 1980). Acute toxicity (LC_{50}, 8-hour exposure) was reported as 19,000 ppm (17,380-20,760 ppm) for females and 22,500 ppm (19,200-26,400 ppm) for males. Determination of blood levels of 2-propanol and its metabolite acetone was carried out during and after a single 4-hour exposure (concentration range: 500 to 8000 ppm). The amount of acetone and IPA was directly related to the various concentrations of alcohol inhaled. Increase of exposure time to 8 hours considerably increased the amount of blood acetone which could be observed even 20 hours after exposure. Histopathological examination of rats exposed to high levels of IPA shows typical lesions of chemical pneumonitis and pulmonary edema accompanied by foamy vacuolization of liver cells and severe focal cytoplasmic degradation (Laham et al. 1980).

Ohashi et al. (1988) evaluated the recovery of the nasal mucosa of the guinea pig after exposure to a concentration of 400 ppm IPA. At this dose level, the test animals recovered from tissue degeneration in about 2 weeks. However, at a higher dose (5500 ppm) the recovery period exceeded 2 weeks, suggesting workers exposed to higher concentrations will need longer recovery periods.

7.4.2.3 Dermal

The rabbit dermal LD_{50} is reported to be 12,800-12,870 mg/kg (PubChem 2018). Skin absorption is a significant factor in IPA toxicity. Twelve rabbits (body weights = 2-2.6 kg) were divided into 4 groups of 3 each. Groups 1 and 2 were given isopropyl alcohol, 2 and 4 mL/kg respectively, by gavage. Groups 3 and 4 were placed in an inhalation chamber with group 3 having a towel soaked with isopropyl alcohol applied to the chest. Group 4 had a similar towel placed on the chest but with a plastic layer to preclude skin contact. Average blood levels of isopropanol/acetone were then measured over 4 hours. Oral absorption produced the highest levels of isopropyl alcohol and acetone, followed by inhalation and dermal. Inhalation alone was of little significance. Acetone levels continued to rise even as isopropyl levels fell following oral exposure. With the inhalation plus skin absorption group, both isopropyl and acetone levels continued to rise throughout the 4-hour time period (Martinez et al. 1986).

Long-term exposure to IPA de-fats the skin, which may cause dryness and cracking (PubChem 2018).

7.4.2.4 Ocular

Vapors of IPA are mildly irritating to the eyes while liquid IPA is listed as causing serious eye irritation (GHS H319; PubChem 2018).

7.4.2.5 Development and Reproduction

In a rat developmental study, female Sprague-Dawley rats were dosed by oral gavage with either 0, 400, 800, or 1200 mg/kg IPA during gestation days 6 to 15 (Tyl 1994). One rat died in the 800 mg/kg-day group and two rats died in the 1200 mg/kg-day dose group. In the high dose animals, reduced maternal gestation weight gain (days 0 through 20) was associated with significantly reduced gravid uterine weight. Although gestational parameters were equivalent across the dose groups, reduced fetal weights were observed in the 800 and 1200 mg/kg-day dose groups. No adverse maternal or developmental effects were noted at 400 mg/kg (= rat NOAEL). No teratogenic effects were noted at any dose tested (Tyl 1994).

A developmental toxicity study was conducted in rabbits and reported with the rat study (Tyl 1994). Groups of 15 pregnant New Zealand white rabbits were orally dosed daily with IPA at 0, 120, 240, or 480 mg/kg-day. Four does in the 480 mg/kg-day died. No differences between the treatment groups were noted for gestational or teratogenic endpoints; maternal toxicity was significant in the highest dose. The rabbit NOAEL for maternal toxicity was 240 mg/kg-day and 480 mg/kg-day for developmental toxicity.

7.4.2.6 Genotoxicity

IPA tested negative in the Ames mutagenicity test, sister chromatid exchange (SCE) test, micronuclei in mice, and for aneuploidy in *Neurospora crassa* (PubChem 2018).

7.4.2.7 Carcinogenicity

The carcinogenicity of IPA has been evaluated in animal models for inhalation, dermal and oral exposures (IARC 1977). No increases in tumor incidence or cancers were observed in animals exposed to IPA. In humans, IPA occupational exposures were associated with increased nasal and laryngeal cancers; however, due to concurrent chemical exposures the increases cannot be definitively to IPA.

7.4.2.8 Neurotoxicity

Isopropanol is a CNS depressant and intoxication causes dizziness, headache, coma and death (when sufficient quantities are ingested- IPA is approximately twice as toxic as ethanol) (NRC 1984). The NOAEL in a rat inhalation neurotoxicity assay is 10000 ppm, 1200 mg/kg-day (rat, oral) and 700 mg/kg-day (rat, oral, developmental neurotoxicity) (EPA 2021).

7.4.2.9 Mechanism/Mode of Action

IPA is oxidized by liver alcohol dehydrogenase to acetone (PubChem 2018). Acetone is excreted slowly via the kidney and lung. Acetone may be further oxidized to acetate, formate and CO_2. The TOXCAST summary data for isopropanol shows it is positive in 37 of 235 assays; however, none of the EC_{50}s are below the cytotoxicity cutoff limit of 21.4µM (micromolar)-indicating toxicity is associated with general cell and membrane disruption rather than a specific molecular pathway (EPA 2021).

7.4.3 Ecological Data

7.4.3.1 Fate and Transport

If released to soil, IPA is expected to have a high mobility in groundwater and pose a hazard to surface and drinking water based upon miscibility with water and a low log K_{OC} value. Volatilization from water or wet or dry surfaces is expected to be a significant fate process. IPA will exist in the atmosphere exclusively as a vapor. An estimated bioconcentration factor of 3 suggests the potential for bioaccumulation is low (PubChem 2018).

7.4.3.2 Ecotoxicity

The effects of 2-propanol on the rate of seed germination were investigated on several occasions. Total inhibition of the germination of barley grains were reached after incubation for 4 days at 18°C on filter papers, absorbing a solution containing 39,420 mg/L of 2-propanol in water. The germination of white amaranth (*Amaranthus albus*) seeds were not affected after 5 hours of incubation at 25°C on filter papers moistened with a solution containing 36,050 mg/L. The EC_{50} for inhibition of germination in lettuce (*Lactuca sativa*) seeds after incubation for 3 days at 30°C on agar containing IPA was calculated as >36,000 mg/L (IPCS 1990).

The LC_{50} for the protozoa *Spirostomum ambiguum* was determined to be 6970 mg/L for a 24-hour exposure and 7150 mg/L for a 48-hour exposure. The LC_{50} for a 24-hour exposure of *Daphnia magna* was determined to be 10,000 mg/L. The LC_{50} for fathead minnows (*Pimephales promelas*) for a period of 48-, 72-, or 96-hours was 11,130 mg/L. Other fish species tested had comparable LC_{50} values (PubChem 2018). IPA is essentially non-toxic to aquatic species.

7.4.3.3 Degradation and Treatment

Biodegradation is expected to be an important fate process based upon the results of microbial screening tests. Vapor phase IPA will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with a half-life of about 3.2 days (PubChem 2018).

8 DISCUSSION

8.1 Compound Summaries

8.1.1 DBX-1

No experimental toxicological information is available for DBX-1. Where applicable, data for the related 5-NT were evaluated. QSAR modeling predicts that DBX-1 will be moderately toxic by the oral route of exposure. Dermal and ocular hazards are also predicted to be moderate based upon skin sensitization and ocular irritation predictions. Modeling predicts DBX-1 will be mutagenic in the Ames assay, but this should be experimentally confirmed.

Ecotoxicity is low across prospective receptors, and transport in the environment will be limited by solubility. Degradation of DBX-1 is likely to occur upon solubilization, and release of copper ions may pose a hazard to algal species with subsequent impact on higher trophic levels. However, this is not expected to be a serious issue unless large quantities of DBX-1 are released to the environment.

8.1.2 Isopropyl Alcohol

IPA has low toxicity by all routes of exposure. It is a mild ocular irritant, and defatting of the skin with subsequent penetration may occur upon prolonged exposure. IPA is neither genotoxic or carcinogenic.

Ecotoxicity is also low, and persistence in the environment will be limited by biological degradation and atmospheric hydrolysis.

8.2 Regulations and Standards

8.2.1 DBX-1

DBX-1 is a primary explosive and is subject to transportation restrictions. While mutagenicity appears to be the primary concern, and because DBX-1 is a high-nitrogen organometallic compound that is poorly handled by contemporary QSAR models, it is recommended that *in vitro* testing be performed on DBX-1 for acute toxicity (Neutral Red Uptake assay) and aquatic toxicity (luminescent bacteria test) as a preliminary to *in vivo* testing.

8.2.2 Isopropyl alcohol

The NIOSH-REL (National Institute Occupational Safety and Health - Recommended Exposure Limit) for IPA is a time-weighted 400 ppm (980 mg/m^3) with a 15-minute Short-Term Exposure Limit (STEL) of 500 ppm (1225 mg/m^3). The OSHA-PEL (Occupational Safety and Health Administration - Permissible Exposure Limit) is also a time-weighted average 400 ppm (NIOSH 2018).

The state of Connecticut has established a drinking water guideline of 2300 µg/L (PubChem 2018).

8.3 Formulation Summary

Overall, this formulation is assessed to be of low to moderate toxicity, and available data

suggest it is less toxic and persistent than the lead compounds that are being replaced. The toxicity of isopropanol is generally well-understood, but there are toxicity data gaps for DBX-1. The toxicity of DBX-1 related compounds 5-aminotetrazole and 5-NT are low to moderate. DBX-1 is predicted to be a mutagen but not a carcinogen. DBX-1 is predicted to have low bioavailability, which supports the finding of a low hazard from exposure. No additional toxicity testing is recommended for parent compounds or combustion products at this time.

Occupational health risks appear to be low overall, but the formulation may present an ecotoxicity hazard; therefore environmental releases could represent a concern. Ecotoxicity evaluations should be considered if there is the prospect of significant environmental release.

9 RECOMMENDATIONS

In vitro toxicity testing is recommended for DBX-1, if feasible. The low solubility of DBX-1 limits the potential testable concentration range for it; however, conducting solubility limit and stability tests would provide useful data for estimating the environmental hazard of DBX-1. Based on measured stability, especially in aquatic systems, ecotoxicity testing should also be considered.

10 POINT OF CONTACT

The point of contact for this report is Dr. William Eck, telephone 410-436-3980, DSN: 584-3980; email: usarmy.apg.medcom-phc.mbx.tox-info@mail.mil.

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APPENDIX A

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APPENDIX B

ENVIRONMENTAL SAFETY AND OCCUPATIONAL HEALTH SEVERITY CATEGORIZATION

B.1 APHC CATEGORIZATION CRITERIA

Table B-1. Categorization Criteria used in the Development of Environmental Safety and Occupational Health Severity[a]

	Low	Moderate	High	Unknown
PERSISTENCE	Readily biodegrades (<28 days)	Degradation ½ life: water <40 days, soil <120 days	Degradation ½ life: water >40 days soil > 120 days	Data are unavailable, insufficient, or unreliable.
TRANSPORT	Water sol. < 10 mg/L log K_{OC} > 2.0	Water sol. 10–1000 mg/L log K_{OC} 2.0–1.0	Water sol. > 1000 mg/L log K_{OC} <1.0	
BIOACCUMULATION	log K_{OW} <3.0	log K_{OW} 3.0–4.5	log K_{OW} >4.5	
TOXICITY	No evidence of carcinogenicity/ Mutagenicity (IARC group 3 & 4); Subchronic LOAEL > 200 mg/kg-d	Mixed evidence for carcinogenicity/mutagenicity (IARC group 2B) Subchronic LOAEL 5–200 mg/kg-d	Positive corroborative evidence for carcinogenicity (IARC group 1 & 2A)/ mutagenicity; LOAEL < 5 mg/kg-d	
ECOTOXICITY	Acute LC_{50}/LD_{50} >1 mg/L or 1,500 mg/kg; Subchronic EC_{50} >100 µg/L or LOAEL >100 mg/kg-d	Acute LC_{50}/LD_{50} 1-0.1 mg/L or 1,500–150 mg/kg; Subchronic EC_{50} 100-10 µg/L or LOAEL – 10–100 mg/kg-d	Acute LC_{50}/LD_{50}<100 µg/L or <150 mg/kg; Subchronic LOAEL <10 mg/kg-d	

Legend:
mg/L = milligrams per liter
K_{OC} = soil organic carbon-water partitioning coefficient
K_{OW} = octanol-water partition coefficient
IARC = International Agency for Research on Cancer
mg/kg-d = milligrams per kilogram per day
LOAEL = lowest-observed adverse effect level
LC_{50} = median lethal concentration; concentration expected to result in 50% mortality to a population of test animals
LD_{50} = median lethal dose; dose resulting in 50% mortality
EC_{50} = half maximal effective concentration
µg/L = micrograms per liter
Note:
[a]Modified from Howe, et al. (Howe 2006)

B.2 GLOBALLY HARMONIZED SYSTEM

GHS is the acronym for the Globally Harmonized System of Classification and Labeling of Chemicals. The GHS attempts to establish international consensus for defining health, physical, and environmental hazards of chemicals; creating a classification process for comparison with defined hazard criteria; and communicating hazard information and protective measures on labels and Safety Data Sheets (SDS, formerly known as Material Safety Data Sheets). The GHS attempts to reduce differences among levels of protection for workers established by the different countries and reduce regulatory burden and barriers to commerce while establishing consistent standards for classification. The GHS is the result of an international mandate adopted in the 1992 United Conference on Environment and Development, often called the "Earth Summit." The harmonization and classification of chemicals was one of six program areas endorsed by the United Nations General Assembly to strengthen international efforts in the environmentally sound management of chemicals.

While there are several aspects of the GHS, the one most important area for our purposes is classification of chemicals into various hazard categories based upon their effects and the route of exposure. Tabular extracts of the criteria for acute toxicity (both oral and inhalation), dermal, and ocular effects are included below. More information can be found in the original source (OSHA 2012).

Table B-2. GHS Acute Toxicity

	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg)	≤5	>5 ≤50	>50 ≤300	>300 ≤2000	Criteria: -Anticipated LD_{50} between 2000 and 5000 mg/kg -Indication of significant effects in humans. -Any mortality in Category 4 -Significant clinical signs in Category 4 -Indications from other studies. *If assignment to a more hazardous class is not warranted.
Dermal (mg/kg)	≤50	>50 ≤200	>200 ≤1000	>1000 ≤2000	
Gases (ppm)	≤100	>100 ≤500	>500 ≤2500	>2500 ≤5000	
Vapors (mg/L)	≤0.5	>0.5 ≤2.0	>2.0 ≤10	>10 ≤20	
Dusts & Mists (mg/L or g/m^3)	≤0.05	>0.05 ≤0.5	>0.5 ≤1.0	>1.0 ≤5	

Legend:
mg/kg = milligrams per kilograms
ppm = parts per million
mg/L = milligrams per liter
LD_{50} = dose resulting in 50% mortality

Table B-3. GHS Skin Corrosion/Irritation

Category 1A	Category 1B	Category 1C	Category 2	Category 3	Not Categorized
Corrosion < 3 minutes Observation < 1 hour	**Corrosion** < 1 hour Observation < 14 days	**Corrosion** < 4 hours Observation < 14 days	**Irritation** Reversible adverse effects in dermal tissue Draize score: ≥ 2.3, <4.0, or persistent inflammation	**Mild Irritation** Reversible adverse effects in dermal tissue Draize score: ≥ 1.5, <2.3	Corrosion and irritation not observed
Destruction of dermal tissue; visible necrosis in at least one animal.					

Table B-4. GHS Eye Effects

Category 1	Category 2A	Category 2B	Not categorized
Irreversible damage 21 days after exposure	**Irritant** Reversible in 21 days	**Mild irritant** Reversible in 7 days	**Non-irritating**

Table B-5. GHS Acute and Chronic Aquatic Toxicity

Acute Aquatic Toxicity				
Category I	**Category II**	**Category III**		**Not Categorized**
Acute toxicity ≤ 1.00 mg/L	Acute toxicity > 1.00 but ≤10.0 mg/L	Acute toxicity > 10.0 but < 100 mg/L		Acute toxicity > 100 mg/L
Chronic Aquatic Toxicity when biodegradation ½ life is > 7 days				
Category I	**Category II**	**Category III**	**Category IV**	**Not Categorized**
Acute Cat I and log K_{ow} ≥ 4, unless BCF < 500; Or chronic toxicity ≤ 0.01 mg/L	Acute Cat II and log K_{ow} ≥ 4, unless BCF < 500; Or chronic toxicity 0.01-0.1 mg/L .	Acute Cat III and log K_{ow} ≥ 4, unless BCF < 500; Or chronic toxicity 0.1-1.0 mg/L	Acute toxicity > 100.0 mg/L, biodegradation ½ life >7 days, and log K_{ow} ≥ 4, unless BCF < 500; Or chronic toxicity > 1.0 mg/L	Acute toxicity >100 mg/L, Log K_{ow} < 4, BCF< 500 and chronic toxicity > 1.0 mg/L

Legend:
mg/L = milligrams per liter
BCF = Bioconcentration factor

APPENDIX C

DATA TABLES

Table C-1. Physicochemical Properties

Compound	Molar Mass (g/mol)	Melting Point (ºC)	Boiling Point (ºC)	Aqueous solubility (mg/L) @ 25ºC	log K_{OW}	log K_{OC}	Henry's Law Constant (atm-m^3/mol) @ 25ºC	Vapor Pressure mmHg @ 25°C
DBX-1	178.59[a]	99.4[b]	284.4[b]	6.7E+04[b,c]	-1.76[b]	0.244[b]	2.41E-09[b]	8.41E-04[b]
IPA	60.09[c]	-89.5[c]	82.3[c]	Miscible[c]	0.05[c]	1.5[c]	8.10E-06[c]	45.4[c]

Legend:
g/mol = grams per mole
mg/L = milligrams per liter
atm-m^3/mol = air to mol per cubic meter

Notes:
[a] = Calculated from molecular formula and standard atomic weights
[b] = Values determined for the neutral base form of 5-nitrotetrazole
[c] = PubChem 2018

Table C-2. Toxicity Data

Compound	Acute Oral LD_{50} (mg/kg)	Chronic Oral LOAEL (mg/kg- d)	Inhalation LC_{50} (g/m^3-h)	Dermal	Ocular	Genotoxicity	Carcinogenicity
DBX-1	937[a]	132.5[a]	5.5[a]	Probable moderate sensitizer[a]	Possible moderate irritant[a]	Positive[a]	Indeterminate[a]
IPA	4710-5840[b]	ND	5.3[b]	LD_{50} = 12.8 g/kg	GHS Cat 2	Negative[b]	Negative[b]

Legend:
mg/kg = milligrams per kilograms
mg/kg-d = milligrams per kilograms per day
g/m^3-h = grams per cubic meter per hour
ND = No data
Notes:
[a] TOPKAT model estimate
[b] PubChem 2018

Table C-3. Toxicity Assessment

Compound	Oral	Inhalation	Dermal	Ocular	Carcinogenicity	Comments
DBX-1	Cat 4	Cat 3	Irritation Cat 3 Strong Sensitizer	Cat 2B	Unk	
IPA	Cat 5	Cat 5	Low	Cat 2A	Low	Commonly used industrial and consumer product. Dizziness and narcosis with high exposure levels.

Table C-4. Ecotoxicity Assessment

Compound	Aquatic	Terrestrial Invertebrates	Terrestrial Plants	Mammals	Birds	Comments
DBX-1	Low	Low	Unknown	Moderate	Unknown	Insolubility may contribute to low toxicity.
IPA	Low	Low	Low	Low	Unknown	High levels have narcotic effects.