U.S. Army Public Health Center

Technical Guide No. 389

Guide to Performing a Developmental Environment, Safety, and Occupational Health Evaluation (DESHE)

Approved for public release; distribution unlimited.

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APHC

Disclaimer:

This Guide to Performing a Developmental Environment, Safety, and Occupational Health Evaluation (DESHE) is intended to provide the user (e.g. researcher, acquisition Program Manager) with guidance for collecting environment, safety, and occupational health data for materials considered for use in Department of Defense technologies in development. It does not establish performance standards for implementation of the DESHE. Subsequent policy or instruction may provide direction.

A DESHE is a hazard assessment rather than a risk assessment tool. The data collected from this process are intended to be incorporated into existing risk and impact models to provide a more complete understanding of the hazards and enable earlier assessment of data needs. The DESHE does not include specific collection of exposure data as this guide is intended to provide hazard information where specific exposure data are often lacking. Exposure potential should be considered as part of the material evaluation process as users approach acquisition requirements pre-Milestone B and beyond.

Preface

Department of Defense and U.S. Army policies require acquisition program managers (PMs) to identify, document, and manage environment, safety, and occupational health (ESOH) risks throughout the acquisition lifecycle. However, the regulations fail to provide guidance as to what data are needed or at which evaluation points the data should be presented. As a result, PMs are likely to encounter downstream schedule delays and unexpected expenses due to a lack of hazard data early in the development process. The Developmental Environment, Safety, and Occupational Health Evaluation (DESHE) is a framework to guide PMs in obtaining the most appropriate ESOH data at the most appropriate time in the development process. The goal of the DESHE framework is to enable PMs to meet regulatory requirements, include ESOH risk profiling with regards to lead candidate down selection, and inform early risk mitigation considerations. Implementation of the DESHE framework early in the process will streamline the development process, allowing more accurate assessments of environmental and human health hazards, manufacturing costs, schedule, program sustainment, and maintaining military readiness.

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Guide to Performing a Developmental Environment, Safety, and Occupational Health Evaluation (DESHE)

SECTION 1: BACKGROUND

Department of Defense (DOD) and U.S. Army policies require acquisition program managers (PMs) to identify, document, and manage environment, safety, and occupational health (ESOH) risk throughout the acquisition lifecycle. However, the ESOH hazard data that PMs need is not often available at the appropriate acquisition milestones because there is no requirement to develop and collect such data during Research, Development, Test and Evaluation (RDT&E). This approach has failed to provide program managers (PMs) with timely information they need to fulfill these requirements and accurately understand the potential hazards. Furthermore, PMs need to understand ESOH data requirements for manufacture and use and to accurately assess lifecycle costs. Examples include information needed to assess permits for wastewater discharge (e.g., aquatic toxicity data), rodent toxicity bioassays that could be used to develop a safe level of exposure to workers or Soldiers, and analytical chemistry methods needed to assess proper industrial hygiene protocols. As a result, Army RDT&E programs have been either transitioning materials with limited or no ESOH performance data into acquisition programs without sound knowledge of risks to workers, Soldiers, the surrounding community, the environment, or have found the requirements for ESOH data late in the acquisition process, resulting in unanticipated costs and scheduling delays for implementation. Multiple legacy examples exist of fielding having taken place prior to a complete understanding of the associated manufacturing and use hazards, leading to cessation of training activities, injured personnel, environmental contamination, and costly remediation.

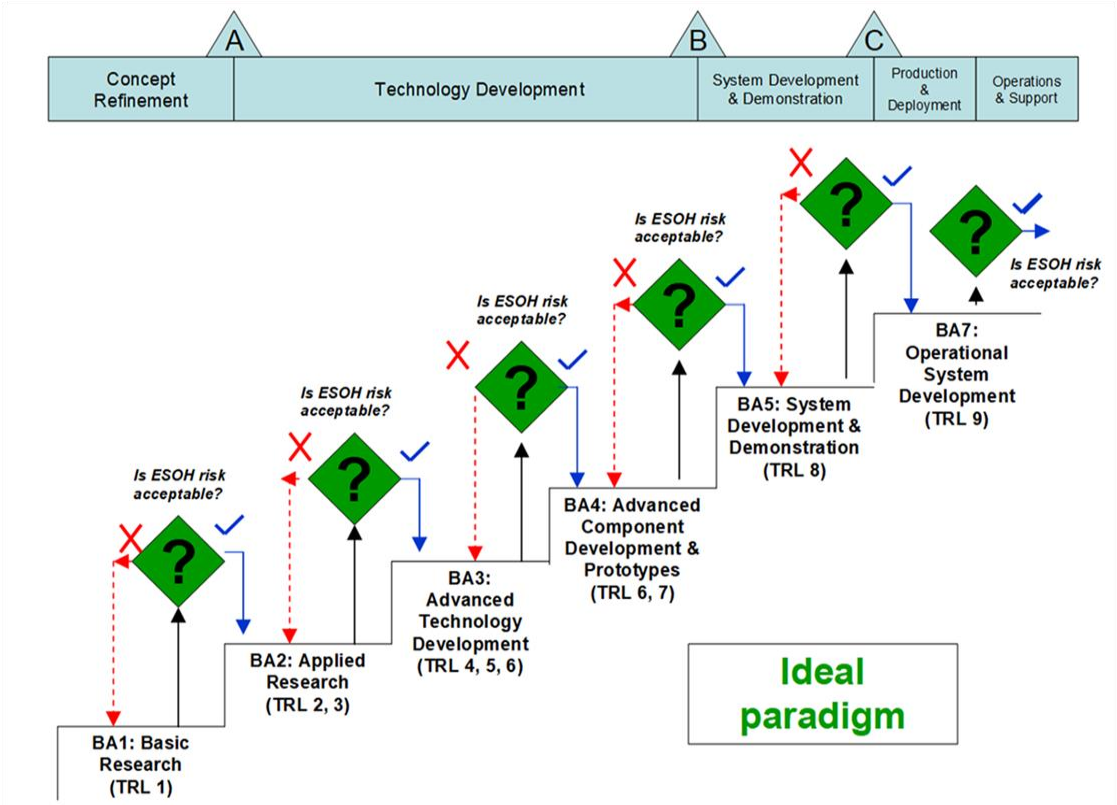
Regulatory agencies are taking action towards requiring specific toxicity data. In 2006, the European Union (EU) enacted a sweeping regulation known as Registration, Evaluation, Authorization and Restriction of Chemicals (REACH). REACH requires manufacturers and importers responsible for assessing and managing the risks posed by their materials to provide appropriate ESOH information to their users. REACH requires a defined, minimum ESOH data set for all materials. Similarly in 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act was signed into law in the U.S., thus amending the Toxic Substances Control Act (TSCA) of 1976. The reformed TSCA law sets a mandatory requirement for the U.S. Environmental Protection Agency (EPA) to evaluate existing materials and implements a new risk-based safety standard for materials entering into commerce. This law does not establish a defined, minimum ESOH data set for materials, but it does provide the EPA the authority to force industry to provide specific toxicity data from manufacturers. Appendix A provides a list of the references applicable to this guide.

Lack of specific hazard data can have serious, costly impacts to manufacturing, use, and sustainability.

In response to this changing regulatory landscape, the U.S. Army Public Health Center (APHC), Combat Capabilities Development Command, and Army Environmental Command collaborated to create the Developmental Environment, Safety, and Occupational Health Evaluation (DESHE) framework guidance to provide the Army research and acquisition community with a logical, step-wise approach to gathering ESOH data throughout RDT&E for materials in the acquisition pipeline.

What is a DESHE?

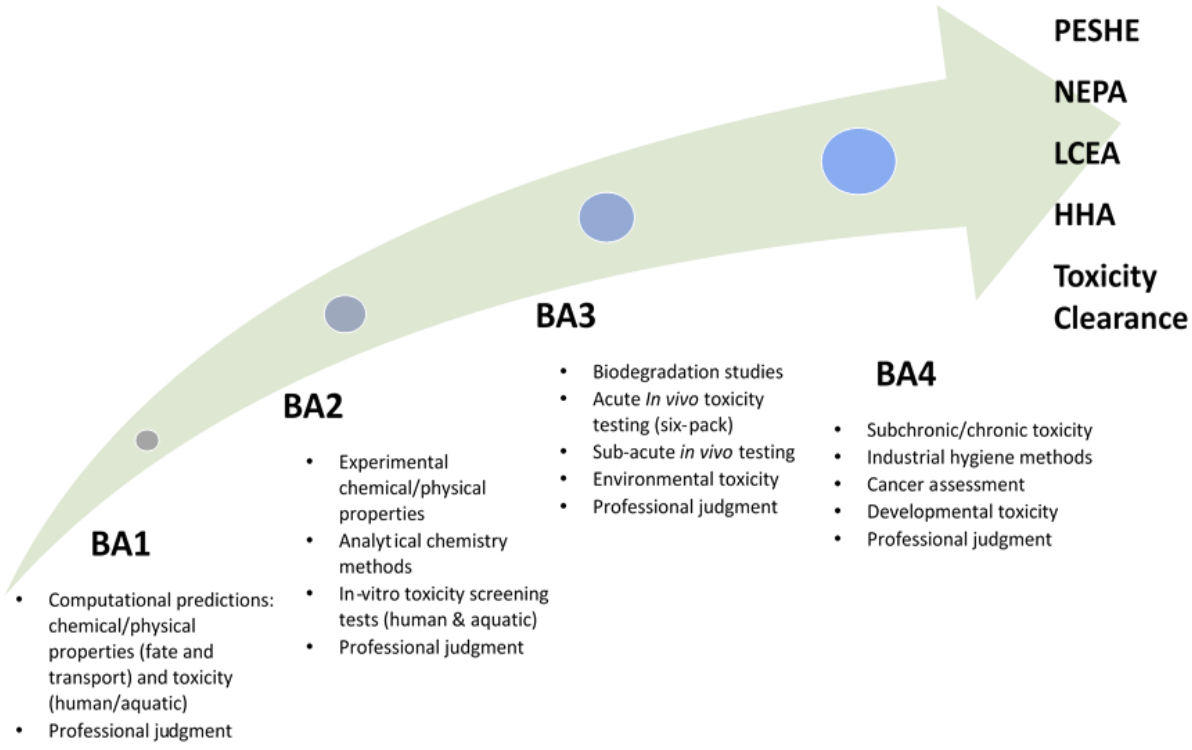
The DESHE is a framework to guide the collection and interpretation of ESOH data at the most appropriate time in the development process. The DESHE guidance provides specific criteria representing a minimum ESOH data set (e.g., toxicity, chemical fate, environmental transport) that can be used to directly populate a Toxicity Assessment (TA) (i.e., an ESOH profile or hazard assessment) for the material under development. The TA synthesizes the data set, puts the information into context, explains potential ESOH hazards, and provides recommendations to the PM that enable accurate risk-based decisions and a streamlined transition from RDT&E to an acquisition program (Figure 1).



Legend:
BA= Budget Activity TRL = Technology Readiness Level

Figure 1. Conceptual Process for Assessing ESOH Hazard Data at each Stage of Material Development

The DESHE is an iterative, phased (i.e., tiered) approach to gathering and developing ESOH data for materials under development based on the level of investment associated with the TRL of the material. The level of effort in gathering ESOH data is proportionate to the technology maturity level of the material. The ESOH data recommended for collection in the early stages of development are relatively quick and inexpensive to gather, yet are uncertain. As the material progresses to higher maturity levels, the ESOH data progress to more robust, accurate, and specific information to supplement previously obtained data (Figure 2). This phased, iterative approach retains material options and begins the process for gathering information during the RDT&E levels, allowing for an informed selection of alternatives that enables and increases the probability for savings in lifecycle costs. The DESHE ensures flexible decision-making and, ideally, will preserve innovation in material solutions. Appendix B provides a detailed list of the minimum suggested ESOH data requirements by Budget Activity (BA) level.



Legend:
BA = Budget Activity
HHA = Health Hazard Assessment
LCEA = Lifecycle Environmental Assessment
NEPA = National Environmental Policy Act
PESHE = Programmatic ESHE

Figure 2. Conceptual Representation of Suggested ESOH Data suggested Collection Associated with Budget Activity Level

The DESHE is not intended to provide the complete ESOH data set needed to transition a fully characterized material to the field; rather, it provides information to the developer regarding potential ESOH issues that should be addressed. Additional data may need to be collected to satisfy regulatory requirements and to ensure an acceptable risk level to the user. Examples include industrial hygiene methods for evaluations, development of additional data needed to determine a safe level of exposure for Soldiers and workers, and data needed to determine environmental criteria (e.g., lifetime drinking water health advisories). Additional data may be needed based on proposed uses, output from conceptual models, or site-specific concerns. Other examples include specific organism toxicity testing required by regional regulators in locations where the system will be manufactured (e.g., to obtain a wastewater discharge permit), or specific concerns identified through previous operation of similar systems. This DESHE guide also includes a recommended list of additional data that may need to be collected by the acquisition community after the DESHE (see Appendix C). These examples are provided for planning purposes.

The DESHE does not supersede or replace other acquisition ESOH requirements. Instead, data collected through the DESHE process enable the collection of vital ESOH technical information to produce the TA, which interprets this technical information and serves as a technical foundation to other ESOH requirements, such as the PESHE, Toxicity Clearance (TC), and HHA. This information also informs the implementation of NEPA statutory requirements (e.g., the LCEA) and the development of industrial hygiene (IH) programs.

Why is the DESHE needed?

Implementation of the DESHE for phased data collection will allow the development of risk mitigation strategies in parallel with material implementation. A consistent process will reduce uncertainty, prioritize human health and the environment, potentially reduce costs, encourage innovation, and streamline implementation of new and novel materials.

The intent of collecting the DESHE-guided minimum ESOH data set is to ultimately provide accurate technical information for ESOH requirements. Collecting toxicity data through this process will instill awareness of data needs before technology progression or budget limitations prohibit adequate material characterization prior to integration of the material into a specific materiel solution. This process also allows for informed assessment and prioritization of alternatives should there be options in material development.

Army Regulations (ARs) 70–1, 40–5, 200–1, and Military Standard (MIL-STD) 200–1 require that ESOH risks be assessed for new systems through the PESHE, HHA, TC, LCEA, and NEPA documentation. AR 40–5 also includes a provision for the development of a TA to assist in interpreting the data and to inform subject matter expert (SME) recommendations. However, there is no guidance available as to the specific data or information needed to perform these assessments or how to collect that information. Therefore, researchers and acquisition programs have collected ESOH data *ad hoc*. The consequences of an *ad hoc* approach are variable data and limited data sets providing disparate information that fails to address specific ESOH requirements (e.g., IH methods and determination of safe levels of exposures for workers). Additionally, data tend to be collected post-RDT&E, following determination of

materiel solutions and the realization that data were either required by regulators, required to facilitate warfighter or worker protection, or required by regulators (e.g., wastewater discharge permits; see Appendix D). Taken together, the range of data quality and utility hampers consistency in decision-making and material selection. This outcome causes confusion about which data points are needed, and when, and limits the potential for early awareness of critical data gaps. Such an awareness is necessary to address specific ESOH questions that may magnify over the course of a program's lifecycle.

Historically, the burden of collecting ESOH data has fallen to the acquisition community. These data are often collected retrospectively after environmental regulators, IH practitioners, or installation personnel have requested or required it for clean-up purposes. This reactionary approach is costly, both in time and resources, makes budgeting difficult, and burdens individual end users with unknown ESOH risk. Such risk leads to increased personal protective equipment (PPE) requirements and management of worker behaviors versus more effective preventative controls (NIOSH 2015).

The DESHE assists ESOH professionals, fellow researchers, laboratory managers, PMs, and other acquisition personnel to anticipate the ESOH risks throughout the acquisition lifecycle. The DESHE will enable PMs to meet regulatory requirements and include ESOH risk profiling throughout the process with regard to decisions concerning alternatives or risk mitigation strategies, for example. Implementation of the DESHE framework early in the process improves combat readiness and streamlines acquisition processes through more accurate assessment of manufacturing costs, schedules, Soldier health, and sustainment.

The DESHE framework is not intended to be prescriptive or simply another "box to check" within an RDT&E or acquisition program. It is meant to be an active and flexible process that encourages ESOH SME engagement through the development process. This guidance has been developed based on recommendations from the Army acquisition, environmental, and public health communities. Ultimately, the ESOH data collected through the DESHE process should be used to make more informed, risk-based decisions.

How are ESOH data used?

Guided by the DESHE, the ESOH data build the underlying knowledge base for material hazard characterization while revealing potential data gaps to be resolved as that material progresses through the Army acquisition pathway. These data also proactively fulfill acquisition requirements established by the DOD/Army, and *a priori* satisfies regulatory requirements set by the EPA, the Occupational Safety and Health Administration (OSHA), and other agencies to develop safe handling procedures and clean-up levels for installation managers. While domestic regulations do not require specific ESOH data points, many of the recommended data points have been used in regulatory risk assessments or to establish exposure/clean-up limits. In the absence of specific data, users and regulators must develop actionable values (e.g., occupational exposure levels (OELs), clean-up limits, etc.) using uncertainty factors, which can reduce acceptable levels by orders of magnitude, or by comparing to an analog material, which introduces additional uncertainty. Both of these approaches are more likely to produce overly restrictive and potentially inaccurate values.

When followed, the DESHE provides data that assist in hazard assessment and inform decision-makers about the potential ESOH impacts of new technologies (i.e., coupled with ESOH impact models and used to perform risk assessments per MIL-STD-882, TAs, Toxicity Clearances (TCs), and HHAs). The data are evaluated in a comparative approach (e.g., evaluating the inhalation toxicity of combustion products from a fielded explosive formulation to a new one) and are compared with other important hazard criteria such as bioaccumulation, environmental persistence, and fate and transport. TAs provide those data within a hazard context and provide recommendations.

Following are examples of how ESOH data may be used across a variety of areas to satisfy regulatory requirements. These examples demonstrate the flexibility needed in tiered testing to meet individual program needs, dependent on proposed uses and output from other models, while considering site-specific requirements and concerns.

Department of Defense/Army Acquisition Documentation

The DOD and Army regulations below require that ESOH risks are considered, documented, and mitigated throughout the acquisition lifecycle. However, they do not require collection of specific data points and must rely on “sufficient” data that have been collected by RDT&E or acquisition programs. Hazard assessments are performed according to MIL-STD-882.

- *DoD Directive 5000.01* identifies the PM as the single point of accountability for meeting program objectives for total lifecycle systems management and requires the PM to consider and prevent ESOH related risks.

- *DoD Instruction 5000.02* requires the PM to integrate ESOH risk management into the overall systems engineering process, eliminate ESOH risks where possible, manage hazards that cannot be eliminated, and document associated risks. PMs document ESOH planning in the PESHE and compliance schedule required by the NEPA and Executive Order 12114. DoD 5000.02 requires that the PM prepare and maintain a PESHE to document data generated by ESOH analyses conducted in support of program execution. This documentation includes identification of ESOH risks and their status; identification of hazardous materials, wastes, and pollutants associated with the system and its support; and plans for safe disposal and/or minimizing releases/use.

- *AR 70–1* requires the PM to assess and accept ESOH risks (identified in the PESHE) by Milestone B. PMs plan and execute the requirements for HHAs and TCs per AR 40–5 and AR 40–10.

- *AR 40–5* requires the Army to ensure all new equipment and materials acquired by the Army are subjected to an HHA and that all new chemicals and materials added to the Army Supply System undergo a TA during RDT&E and a TC for acquisition.

- *AR 40–10* requires the completion of an HHA. In support of the Army acquisition process, the HHA utilizes a composite risk assessment approach to identify health

hazards, demonstrate compliance, and assess the level of risk associated with each hazard. Health hazards will be considered in the PESHE. PMs will ensure that HHA recommendations are integrated in the risk management process. PMs will include HHA data requirements and issues in test plans to ensure sufficient health hazard data are collected to support the completion of HHAs.

- *AR 200–2, Environmental Analysis of Army Actions*, implements the NEPA by requiring environmental analysis of Army actions affecting human health and the environment (32 Code of Federal Regulation (CFR) 651).

- The U.S. Army Public Health Center (APHC) executes a *toxicology assessment program* to document and interpret available fate, transport, and toxicology data for materials. This is a voluntary program instituted by APHC to support the TC process. Data are collected as per American Society for Testing and Materials (ASTM) E2552-16, *Standard Guide for Assessing the Environmental and Human Health Impacts of New Compounds for Military Use.* The TC does not require the collection of specific ESOH data; however, a TC can be denied due to incomplete information. Neither TAs nor TCs require funding support; however, studies that are needed to develop data are externally funded and can be conducted at the APHC Toxicology Directorate (TOX).

Commerce Regulations

- *Domestic:* The EPA regulates materials that enter into commerce through the TSCA New Chemicals Review Program. The 2016 Lautenberg amendment to the TSCA requires that the EPA make an affirmative safety finding prior to the materials entering into commerce. This is required for new materials and for new uses of existing materials. Although the law does not establish a minimum ESOH data set, the EPA can request additional ESOH data from manufacturers through Consent Orders after an initial review of available data. Materials with limited data can be restricted or delayed from use while the manufacturer collects more data, or the risks posed by their use can be evaluated using computational models or comparisons to other similar materials.

- *International:* The European Union (EU) REACH regulation set a tiered minimum ESOH data set based on production volumes for all materials that enter into commerce. This data set is outlined in Annexes VIII, IX, and X for substances manufactured or imported in quantities of 10, 100, and 1,000 metric tons or more, respectively. This data set includes chemical/physical properties, human health information, and ecotoxicity data consistent with the DESHE; additional data points are required for larger quantities. All materials must be registered with the European Chemicals Agency with a complete ESOH data set. Although not directly applicable to the U.S. Army, REACH could impact operations at Army installations outside of the U.S. or could become an issue in Foreign Military Sales.

Occupational Health and Safety

IH programs provide guidance for PPE, engineering controls, and safe exposure levels for all materials in the workplace. IH programs rely on multiple toxicological and chemical/physical data points that are evaluated against potential exposures collected through sampling programs to correct, reduce, or eliminate workplace hazards. These data points can be used to establish non-regulatory OELs (e.g., American Industrial Hygiene Association Workplace Environmental Exposure Levels) used as a benchmark for safe handling of materials prior to a regulatory limit. Typically, regulatory workplace limits lag behind development of new materials, but ESOH data can be used to establish OSHA Permissible Exposure Limits, National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limits, or American Conference of Governmental Industrial Hygienists (ACGIH®) Threshold Limit Values.

Clean-up Programs

If materials are released to the environment, the DOD/Army may need to establish range and installation clean-up programs in compliance with Resource Conservation and Recovery Act (RCRA) requirements. Facilities that produce, handle, test, or store these materials could be at risk for violation of RCRA Land Disposal Regulations (LDR) per 40 CFR 268. Violation of LDR can result in significant fees, clean-up requirements, operational shut downs, and negative public relations.

ESOH data points, specifically ecotoxicity and fate/transport data, can be used to establish industrial soil, residential soil, and water quality guidelines, which establish installation clean-up levels, or to complete a Superfund Ecological Risk Assessment under Section 104 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Clean-up levels or compliance actions can also be driven by a variety of species-specific regulations, including the Migratory Bird Treaty Act (1918), the Bald and Golden Eagle Protection Act (1940), and the Endangered Species Act of 1973 (ESA). ESOH data are needed for compliance with these regulations. As an example, the current U.S. Fish & Wildlife Service List of Threatened and Endangered Species includes plants and terrestrial invertebrates that have at least one lifecycle stage in soil. Ecotoxicity data using surrogate species can be used to develop Incidental Take Statements to comply with the ESA.

Wastewater Treatment and Release

The Clean Water Act requires a permit for discharge of a material into a body of water through the National Pollutant Discharge Elimination System (under 33 U.S. Code 1251 et seq § 402). To issue such permits for materials that will be produced by the Army or used in production processes at Army industrial base installations, regulators need ecotoxicity data with a focus on aquatic toxicity in multiple species, as well as treatability data. However, there is no fixed set of data points required to satisfy the permitting process, so it is handled on a case-by-case basis. Each state can request data for region-specific species as it sees fit.

Other Documentation

Guidance for selecting alternative chemicals has been provided by the National Academy of Sciences (NRC 2014) and recommendations by others (Jacobs et al. 2016). The guidance in this TG provides for data collection that is consistent with those recommendations.

Additional details on which data are needed for regulatory decision-making are provided in Appendix D.

SECTION 2: COMPLETING THE DESHE

The DESHE uses a tiered approach to gather ESOH data based on the RDT&E BA level or the TRL of the project. Data collected at previous levels are intended to be built upon in subsequent BA and TR levels.

The final scope of the DESHE for each individual material depends on user interpretation, professional judgment, and recommendations from the ESOH/public health community based on exposure risk, proposed uses, and preliminary data findings. It is recommended that the user consult with the public health/toxicology SMEs and support staff to identify and prioritize data points for the DESHE, as well as to analyze and evaluate the data.

The DESHE follows three steps: 1) Gather existing ESOH data for the material used in technology under development (e.g., literature review), 2) Develop new ESOH performance data parameters to fill any gaps in the minimum ESOH data set, and 3) Document and interpret these findings. These steps are repeated as the RDT&E project advances to higher BAs or TRLs.

Step 1: Problem Formulation/Gather Existing ESOH Data

Problem Formulation:

- Define how the compound/material may be used.
- Identify probable exposure routes or pathways for individuals.
- Trace potential release points from synthesis to disposal.

Problem formulation is critical in defining downstream ESOH performance data requirements. Effective problem formulation guides the prioritization and directs the collection of ESOH performance data.

APHC Toxicology SMEs can provide support in developing an effective problem formulation and conceptual exposure pathway models.

Gather Existing ESOH Data:

ESOH data for existing materials proposed for new uses may be available from reliable material sources (e.g., the National Institutes of Health, ACGIH, NIOSH, ECHA, etc.). Appendix B provides specific guidance, data points, and test standards. Apply extreme caution when using SDS information, as SDSs have no quality requirement, and their content may be erroneous.

Methods described in Appendix B are not meant to be either all-inclusive or required in total; rather, they serve as a set of study methods that can provide answers to hazard issues. It is recommended that users consult their problem formulation plan when deciding what methods are appropriate for each chemical or system. Specific methods will depend on use, quantity, and likely exposure pathway. Subject matter experts may be able to offer alternative solutions (e.g., use of read across techniques) that may address these data gaps without need to perform specific studies.

Few ESOH data may be available for novel materials under development. In such cases, predictions/modelled data are recommended (e.g., *in silico* Quantitative Structural Activity Relationships (QSAR), qualitative read-across methods). Figure 3 provides an example of a modeled approach.

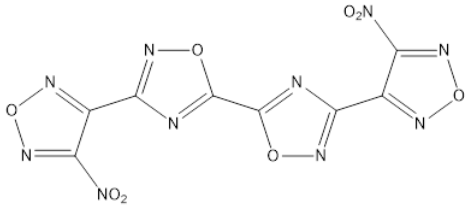


Figure 3. Example: Abbreviated Profile of a Developmental Energetic using QSAR

- Rat LD_{50}: 3100 mg/kg (moderate oral toxicity)
- Chronic LOAEL: 29.0 mg/kg (moderate chronic oral toxicity)
- Inhalation LC_{50}: 70.8 µg/m^3 (high inhalation toxicity)
- Skin irritant: Predicted to not be an irritant
- Skin sensitizer: Mild sensitizer
- Ocular irritant: Mild irritant
- Developmental toxicity: Unlikely
- Mutagenicity: Predicted to be Positive (experimental, without metabolic activation)
- Solubility: 139.6 mg/L (moderately soluble)

- Mobility: Moderate
- Aquatic toxicity: Low
- Persistence: High

The DESHE does not prescribe the collection of all necessary data points for materials. Rather, the DESHE should be used to guide the collection of a minimally required data set necessary to inform the next tier of testing commensurate with technology maturity. Next-tier testing requirements can be determined based on previously collected data, professional judgement, program and user needs, and other site-specific information.

Step 2: Develop New ESOH Data

A suggested minimum required data points with standard test methods and cost/time estimates (where available) are provided for each BA/TRL in Appendix B. APHC TOX can support data collection needs, if needed.

Typically, only chemicals that can be inhaled, ingested, or absorbed through the skin need to be evaluated. These include combustion products, starting materials, maintenance, and products of environmental breakdown.

ESOH performance data will be collected using approved and validated methodologies (e.g., ASTM standards, Organization for Economic Co-operation and Development (OECD) guidelines, EPA methodologies) at an experienced laboratory, using Good Laboratory Practices, where applicable.

Three types of data are recommended:

1. Chemical/Physical Properties – include descriptions of the chemical such as molecular mass, boiling point, melting point, and solubility. Physical properties also include vapor pressure, Henry's Law constant, partitioning characteristics, and other properties that are used to predict bioaccumulation, absorption if ingested, probability to be inhaled, probability to be absorbed through the skin, and transport in the environment (e.g., water solubility, fat solubility (log K_{OW}), affinity to organic carbon, etc.). Long-term fate in the environment (e.g., persistence, hydrolysis, etc.) and treatability/degradation for wastewater treatment can also be inferred. Chemical/physical characterization data are partitioned into compartment-specific parameters. The data for these criteria include physical constants and data that are determined based on specific conditions in water and soil/sediment compartments. The data for water and soil/sediment compartments can vary based on environmental conditions. Many of these criteria also require analytical methods for detection in various matrixes (e.g., air, water, soil).

2. Human Health Data Points – include *in silico* (modelled), *in vitro,* and mammalian toxicity data that can be extrapolated to estimate the toxic end points in humans. The DESHE includes acute and repeated dose *in vivo* toxicity studies. Additional sub-chronic and chronic toxicity testing is recommended post-DESHE (see Appendix C). These data are

primarily used in determining safe levels of exposure for warfighters, workers, and the environment (e.g., remediation concentrations, water reuse, etc.).

3. Ecotoxicity Data Points – are used to estimate the toxicity of a material to terrestrial and aquatic species, using representative species. These methods include commonly used species for acute and chronic testing (aquatic and terrestrial invertebrates). Additional species may be required by regulators to develop a species sensitivity distribution (SSD). These data are used for environmental permitting and clean-up requirements.

The DESHE does not provide an exposure assessment. Additional models and data are used to define use-specific exposure pathways and criteria. All data collected in the DESHE can be incorporated into any impact or risk assessment model that evaluates exposure and hazard to determine overall risk.

Data Development Guidance Based on BA/TRL Maturity (Figure 2):

- BA1/TRL 1–2: Basic RDT&E. Because products in the early research stage generally maintain significant uncertainly in future application and transition, collection of experimental data is not recommended until further developed. However, it is appropriate to begin *in silico* modeling of ESOH data at this stage.

- BA2/TRL 3–4: Applied Research. At this stage of development, the DESHE recommends small scale testing. At this TRL, the focus is on establishing basic properties that can be used to predict fate and transport in the environment (chemical/physical properties), *in vitro* screening for mutagenicity, dermal sensitization and irritation, and acute toxicity (human health), and potential environmental effects using laboratory species (surrogates for ecotoxicity). These data will provide an initial understanding of the relative toxicity of the material, how it may transport in the environment, its potential for no-human impact, and its potential for bioaccumulation and persistence.

  Because mixtures, formulations, or alloys can vary (e.g., during research, during manufacturing, by abiotic processes if released to the environment), all ESOH data of the constituent materials are considered. Potential exposure routes and applications may not be well-defined at this stage and are only considered qualitatively within the DESHE. Combined mixture effects may occur, and toxicity studies may be warranted at further stages (e.g., smokes and obscurants).

- BA3/TRL 5: Advanced Technology Development. At this TRL, the researcher will be able to identify potential applications for the material. These can be used to inform specific data collection requirements based on potential environmental and occupational exposures.

  The goal of DESHE data collection during this phase is to be able to develop a preliminary understanding of the material's fate and persistence in the environment (e.g., photolysis potential, microbial breakdown, hydrolysis, leachability, Henry's Law, etc.),

acute exposure issues for workers (e.g., personal protective equipment (PPE) needed) and acute effects in aquatic and terrestrial environments.

Researchers will gather experimental chemical/physical characterization data for material persistence in the environment and potential pathways to degradation. These data may include *in vitro* measurements for specific toxicity to expected target organs, bioaccumulation, and possibly metabolism as implications for anticipated human exposure.

Collection of experimental data for human health effects is focused on toxicity testing for acute exposures, including ingestion or inhalation (based on the potential exposure risks), dermal exposure, and ocular exposure. The minimal necessary data for human health can be collected though the cumulative outcomes of the assays included in a test panel known as the “Six-Pack”: Ames assay (genotoxicity screen), acute oral/inhalation, ocular irritation, dermal irritation, dermal toxicity, and dermal sensitization. These data are essential for mitigating risks of material handling in a production environment.

“Six Pack”
Ames assay (genotoxicity screen)
Acute oral/inhalation
Eye irritation
Dermal irritation
Dermal sensitization
Dermal toxicity

- BA4/TRL 6-7: Advanced Component Development and Prototypes. During this stage, the material will be produced and tested in larger quantities, often scaling up for improved synthesis/production processes, increasing human exposure risks. As such, data are collected to support eventual development of exposure levels that could be used in an occupational setting to protect workers as well as researchers. Industrial hygienists use these values, referred to as occupational exposure levels (OELs), to protect workers. At a minimum, a 90-day subchronic toxicity test in rodents is needed to develop an OEL or similar toxicity-based benchmark.

  Chemical/physical data requirements during this phase may include bioaccumulation/biodegradation and wastewater treatability; analytical detection methods for discerning the material-/chemical-of-interest from the background environmental matrices; or biological tissue anticipated from intended use and release conditions.

Human health data are focused on repeated-dose mammalian toxicity (sub-acute, sub-chronic) data that will be used to down-select specific target organ testing that may need to be performed post-RDT&E for the protection of human health.
Ecotoxicity data focus on chronic aquatic and terrestrial species toxicity, including longer-term chronic/reproduction or growth data for multiple species from relevant ecological groups (both aquatic and terrestrial exposure media) that may be used to develop a Species Sensitivity Distribution (SSD) for each material.

At each stage, information should be presented, evaluated, interpreted, and weighed relative to other evidence in a TA where sound recommendations are made (see AR 40–5), providing the researcher with an analysis of potential system Soldier, occupational, and environmental impacts, including an assessment of exposure routes. These exposure pathways, along with the results from previous toxicity studies, are used to select additional toxicity testing that may be needed. Additional recommended data points are provided in Appendix C.

Step 3: Document ESOH Data

Development of a TA at the conclusion of each maturity level step is recommended to place existing and newly collected ESOH data into proper context, thus allowing for accurate interpretation and sound judgment. Phased collection and contextual interpretation of ESOH performance data should be used in conjunction with other performance criteria to inform decisions and down-select possible alternatives at each TRL. Conclusions and recommendations are made during each phase as new data are collected and evaluated, allowing continuity and alignment within the context established in previous steps. Appendix D provides examples of regulatory drivers for specific ESOH data, and Appendix E provides an example TA format for interpreting and presenting ESOH data in context. Appendix F provides additional methods for generating data that may be needed based on system-specific needs and concerns.

It is recommended that data collected for materials be published on the Defense Technical Information Center website and shared with the U.S. Army Combat Capabilities Development, Safer Alternatives for Readiness (SAFR) office. For use in future risk assessment and program requirements (such as a PESHE), the DESHE should be transitioned to the customer (funding proponent), RDT&E program, and potential end user within acquisition of the technology.

Requests for TAs, SME support, or toxicity data collection can be made to APHC TOX by email: usarmy.apg.medcom-aphc.mbx.tox-info@mail.mil or phone: 410-436-3980.

Other Considerations:

Collection of the data prescribed by this guide will assist in the development of other criteria to necessary for production, training, maintenance, and other activities to protect Soldiers, workers, civilians, and the environment. Examples include the use of personal protective equipment (PPE), industrial hygiene methods, and occupational exposure levels. Other

examples include the development of risk-based remediation values and other criteria to assist decision makers when there are environmental releases.

The science of toxicology is increasing and new alternative methods are constantly being developed. Users are recommended to employ only those methods that have been adequately verified, validated, and recommended by national and international regulatory authorities to ensure the accuracy and applicability of those data collected by new and evolving methodologies.

Appendix A. References

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Appendix B. Recommended Minimum ESOH Performance Data by Budget Activity Level

Data	Standard Test Methods	Cost ($K)	Time (days)
BA2			
Chemical/Physical Characterization			
Material purity	Thermogravimetric analysis, Differential Scanning Calorimetry, Fourier Transform Infrared/Raman spectroscopy, Nuclear Magnetic Resonance, Gas Chromatography Mass Spectrometry	$25K	Varies (approximately 30 d)
pH or pKa	OECD 122, OECD 112		
Vapor pressure	ASTM E1194-07 (withdrawn 2013); OECD 104; ARL-TR-6887, *New Micro-Method for Prediction of Vapor Pressure of Energetic Materials*, July 2014		
Water solubility	ASTM E1148-02 (withdrawn 2013, no replacement); OECD 105		
Hydrolysis*	ASTM E895, OECD 111, the EPA 712-C-08-012		
Octanol water partition coefficient (K_{ow})	ASTM E1147 (withdrawn 2013), OECD 123, OPPTS 830.77550		
Affinity to organic carbon (K_{oc}) (calculated)*	OECD 121; Estimate Koc using Mackay function (Koc = 0.41- Kow)		
Henry's Law constant (calculated)*	Calculated (H = (Vp * MW)/S, where Vp = vapor pressure (atm) at 25C, MW = molecular weight (g/mol), S = solubility in water (mg/L)		
Dissolution rate*	ASTM E1624-94 (2008; withdrawn 2013). See ERDC's method for munition dissolution, *Dissolution Kinetics of IMX 101 and IMX-104,* ERDC TR OP-F-15-1.		

*Needed only if expected to be released to the environment.

Human Health			
Endocrine disruption - *in vitro* estrogen and steroidogenesis	OECD 455-457 (estrogen); 458 (androgens), 456 (thyroid); see Day et al. 2018.	$10K	60
Mutagenicity, *in vitro*			
Bacterial reverse mutation (*Salmonella typhimurium)*	OECD 471	$6K	35
Cytotoxicity, *in vitro*			
Mammalian cell viability assay *(*e.g., Mammalian Cell Line - Neutral Red Uptake); phototoxicity	OECD 432	$6K	25
Skin sensitization (*in vitro*)	OECD 442C/442E	$10K	60
Eye irritation/corrosion screen	OECD 496	1K	20
Ecotoxicity			
Acute toxicity, bioluminescent bacteria (*Aliivibrio fischeri*), *in vitro*	ASTM STP766, *in vitro* assay	$7K	20
Aquatic bioconcentration factor	*Estimated from experimentally measured K_{OW} (if organic)	NA	1-7
BA3			
Chemical/Physical Characterization			
Hydrolysis (rate)*	ASTM 895, OECD 111, EPA 712-C-08-012	$10K	60 for all four
Photolysis (rate)*	ASTM E896, OECD 316, EPA 712-C-08-013	$10K	
Persistence*	OECD 301, 310, 302C, ASTM E1279, OPPTS 835.3180	$10K	
Koc (Kd)*	ASTM E1195-01 (Withdrawn 2013, No Replacement), OECD 106 (recommended), OECD 121	$10K	
Human Health (specific exposure tests determined by professional judgment)			
Acute oral toxicity	ASTM E1163, OECD 401, OECD 420, OECD 423, OECD 425, EPA 712-C-02-189, EPA 712-C-02-190	$13K	74

Acute inhalation toxicity	OECD 403, OECD 436, EPA 712-C-98-193	$15K	90
Acute dermal toxicity	OECD 402, EPA 712-C-98-192	$9K	30
Skin irritation/corrosion	OECD 439, OECD 404, EPA 712-C-98-196	$7K	30
Skin sensitization (3-pack *in vitro*)	OECD 442	$16K	50
Additional *in vitro* genotoxicity tests (if reverse mutation results are positive):			
Genotoxicity, Chinese Hamster Ovary Test, *in vitro*	ASTM E1262, OECD 473	$21K	65
Genotoxicity, Mouse Lymphoma Assay, *in vitro*	ASTM E1280, OECD 490	$21K	56
Ecotoxicity*			
Aquatic toxicity - *in vivo*			
Acute aquatic organism toxicity*	ASTM E729, ASTM E1192, EPA-821-R-02-012	$25K	60
Chronic aquatic organism toxicity*	EPA-821-R-02-013	$20	60
Aquatic plant (algae) toxicity*	OECD 201	$8	60
BA4			
Chemical/Physical Characterization			
Biodegradation (rate)*	ASTM E1279	$15	30
Leaching study*	OPPTS 835.1240	NA	
Treatability (select the test most relevant to manufacturing conditions and facility capabilities)			
Aerobic sewage treatment*	OECD 303, ASTM E1625	$15	30
Biodegradation in activated sludge*	OECD 311, ASTM E2170	$17	30
Biodegradation in wastewater*	OECD 314	$10	30
Human Health (specific exposure tests determined by professional judgment)			

28-day repeated dose, oral	OECD 407, EPA 712-C-00-366	$94K	125
28- or 14-day repeated dose, inhalation	OECD 412	$180K	120
Additional genotoxicity tests (if *in vitro* genotoxicity results are positive):			
Genotoxicity, *in vivo* (mouse micronucleus)	OECD 474	$17K	65
Genotoxicity, Hepatic COMET Assay, *in vivo*	OECD 489	$15K	65
Ecotoxicity*			
Bioconcentration and bioaccumulation*	ASTM E1676, OECD 317	varies	
Aquatic toxicity (chronic/sub-lethal) *in vivo* (three species)*			
Water flea (*Ceriodaphnia dubia*) (7 day)*	EPA-1002.2; ASTM E1295; ISO 20665	50K (all three)	30
Fathead Minnow *(Pimephales promelas)* (7 day)*	OECD 229		
Green algae *(Pseudokirchneriella subcapitata or Raphidocelis subcapitata)**	OECD 201		
Freshwater Whole Effluent Aquatic Toxicity	EPA-821-R-02-013, EPA 821-B-00-004	$11-19	60
Terrestrial/soil invertebrate toxicity (chronic)		$80-130K	90
Earthworm reproduction *(Eisenia fetida/Eisenia andrei)* - 56 day*	ISO 11268-2; OECD 222	$70	90

Legend:
ASTM = American Society for Testing and Materials
EPA = U.S. Environmental Protection Agency
ERDC = Engineer Research Development Center
ISO = International Organization for Standardization
NA = Not Applicable
OECD = Organization for Economic Co-operation and Development
OPPTS = EPA Office of Prevention, Pesticides and Toxic Substances
*Needed only if expected to be released to the environment

Appendix C. Additional Data Points, Post-RDT&E

Data	Standard Test Methods	Cost ($K)	Time (days)
Human Health			
Mammalian Toxicity: Sub-chronic			
Subchronic (90-day) mammalian oral toxicity†	ASTM E1372, OECD 408 (see OECD 422)	$300K	180
Subchronic (90-day) mammalian inhalation toxicity†	OECD 413	$350	180
Subchronic (90-day) mammalian dermal toxicity	OECD 411	$300	180
Reproductive/Developmental Screen	OECD 421, OECD 422, EPA 712-C-00-367, EPA 712-C-00-368, EPA 712-C-98-208	$190K	220
One Generation Reproduction/Developmental	OECD 415	$330K	300
Mammalian Toxicity: Chronic			
Chronic oral toxicity – 1 Year	OECD 452	$705K	685
Chronic oral toxicity – 2 Year (cancer bioassay)	OECD 453	$3000K	1200
Developmental neurotoxicity, oral dose	OECD 426	$422	120
Advanced toxicokinetics	OECD 417	varies	30
Ecotoxicity*			
Avian Acute Oral Toxicity*	OECD 223	$25	60
Avian Subchronic oral*	60-d gavage (see: Johnson et al. 2005)	$170	90
Avian Reproduction Test (eight weeks)*	OECD 206	$160	160
Toxicity Benchmarks			
Occupational Exposure Levels (OELs), e.g., Threshold Limit Values (TLVs®), Workplace Environmental Exposure Levels (WEEL) ™).	ACGIH, AIHA/OARS	varies	365
Toxicity Reference Values (TRVs)*	CHPPM 2000	varies	
Tolerable Daily Intake (TDI)*		varies	
Lifetime Drinking Water Health Advisory*		varies	

Data	Standard Test Methods	Cost ($K)	Time (days)
Wastewater Treatability*			
Aerobic sewage treatment*	OECD 303	$12	30
Biodegradation in activated sludge*	OECD 311	$12	30
Biodegradation in wastewater*	OECD 314	$30	90
Whole effluent toxicity (WET) testing*	EPA 821-B-00-004; EPA-821-R-02-013	$11-19	60

Legend:
ACGIH = American Conference of Governmental Industrial Hygienists®
AIHA: = American Industrial Hygiene Association
ASTM = ASTM International (formerly American Society for Testing and Materials)
CHPPM = Center for Health Promotion and Preventive Medicine (now the U.S. Army Public Health Center)
EPA = U.S. Environmental Protection Agency
NA = Not Applicable
OECD = Organization for Economic Co-operation and Development
TERA = Toxicology Excellence for Risk Assessment
*Needed only if expected to be released to the environment
† Minimum data requirement for development of an occupational exposure level; oral or inhalation depends on predominant exposure pathway.

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Appendix D. Regulations and Other Drivers that use Data in the DESHE

	Acquisition Documents	Commerce	REACH Annex X	Occupational Safety	Range Clean-Up	Wastewater Discharge / Treatment
Material Purity						
pH	x	x		x	x	x
Vapor pressure	x	x	x	x	x	
Water solubility	x	x	x	x	x	x
Hydrolysis	x		x	x	x	x
K_{oc} (K_d)	x				x	
K_{ow}			x		x	
Henry's Law Constant	x	x		x	x	x
Dissolution Rate					x	
Hydrolysis	x		x		x	x
Photolysis	x				x	x
Persistence	x				x	x
Photolysis	x				x	x
Leaching Study					x	
Aerobic sewage treatment	x	x				x
Biodegradation in activated sludge	x	x	x			x
Biodegradation in wastewater	x	x				x
Mutagenicity (*in vitro*): Ames (*Salmonella typhimurium*)	x	x	x	x	x	
Cytotoxicity (*in vitro*): Mammalian cell viability assay	x	x	x	x	x	
Genotoxicity (*in vivo*): Mouse Micronucleus	x	x	x	x	x	
Genotoxicity (*in vitro*): Chinese Hamster Ovary (CHO) Test	x	x	x	x	x	
Genotoxicity (*in vitro*): Mouse Lymphoma Assay	x	x	x	x	x	

	Acquisition Documents	Commerce	REACH Annex X	Occupational Safety	Range Clean-Up	Wastewater Discharge / Treatment
Genotoxicity (*in vivo*): Hepatic COMET Assay	x	x	x	x	x	
Acute oral toxicity (*in vivo*)	x	x	x	x	x	
Acute inhalation toxicity (*in vivo*)	x	x	x	x		
Acute dermal toxicity (*in vivo*)	x	x	x	x		
Skin irritation/corrosion (*in vivo)*	x	x	x	x		
Eye irritation/corrosion (*in vivo*)	x	x	x	x		
Skin sensitization (3-pack) (*in vitro*)	x	x	x	x		
28-day Repeated dose oral (in vivo)	x	x	x	x	x	
28- or 14-day Repeated dose inhalation (*in vivo*)	x	x	x	x	x	
Biodegradation	x		x		x	x
Bioconcentration and bioaccumulation	x		x		x	x
Acute toxicity, bioluminescent bacteria (vibrio fisheri), in vitro	x	x			x	x
Aquatic toxicity (acute) - *in vivo*	x	x	x		x	x
Aquatic toxicity (chronic/sublethal)	x	x	x		x	x
Aquatic bioconcentration factor	x	x			x	x
Sediment Bioaccumulation by benthic invertebrates					x	

Appendix E. Example of Documenting DESHE Data: Toxicity Assessment Requirements

Summarizing environment, safety and occupational health (ESOH) data in a format that provides context and recommendations to the investigator and program manager is critical. The information below provides an example outline of a Toxicity Assessment (TA) report.

Summary:

The summary should be concise and should provide the following information:

- A brief overview of the Research, Development, Test, and Evaluation (RDT&E) project and purpose
- An overall review of the ESOH data collected and hazards identified relative to use (conclusions)
- Recommendations

Background (Project Overview):

This section provides an overview of the RDT&E project. The background also describes the purpose of the TA relative to the materials under development.

Statement of the Problem:

This section describes the purpose of the new technology in the context of lifecycle production and use and described relevant pathways for exposure and environmental release (i.e., problem formulation).

Methods:

Description of ESOH Data

Provide search strategies to acquire all pertinent information on chemical physical properties, toxicity, and toxicity guidelines, and present the criteria used to assess this information. Include only those chemicals that could conceivably be inhaled (including combustion products), ingested (possibly from environmental releases), or splashed in the eyes or on skin. Interpretation and categorization of these data should employ the use of the Globally Harmonized System (GHS).

Results: Substance Toxicity Profiles

Present the chemical physical properties, such as water solubility, fat solubility (log octanol/water partition coefficient), affinity to organic carbon (K_{oc}), vapor pressure, Henry's law coefficient, bioaccumulation factors, etc. Provide toxicity information relative to exposure route and length of exposure according to the GHS. Summarize this information in relative risk charts (Tables E-1 through E-3). Presenting various ESOH data simultaneously is often challenging. The ToxPi system is useful for displaying both toxicity hazards and important chemical property

information useful in predicting environmental transport and exposure in a relative manner (Figure E-1).

Table E-1. Global Harmonized Acute Toxicity Categories

Global Harmonized System; Acute toxicity categories					
	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg)	≤5	>5 ≤50	>50 ≤300	>300 ≤2000	Criteria: -Anticipated LD50 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	

Source: United Nations Economic Commission for Europe, 2011

Table E-2. Categorization Criteria used in the Development of Environmental Safety and Occupational Health Severity[1]

	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 Koc <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 (IARC group 3 & 4)/ mutagenicity; Subchronic LOAEL >200 mg/kg-d	Mixed evidence for Carcinogenicity (IARC group 2B)/ mutagenicity; 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 >1500 mg/kg; Subchronic EC_{50} >100 µg/L or LOAEL >100 mg/kg-d	Acute LC_{50}/LD_{50} 0.1-1 mg/L or 150-1500 mg/kg; Subchronic EC_{50} 10-100 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	

Note: [1]Adapted from Howe et al. 2007.

Table E-3. Example: Summary Toxicity Assessment Stoplight Chart*

Compound	Oral	Inhalation	Dermal	Ocular	Carcinogenicity	Aquatic	Invertebrates	Plants	Mammals	Birds	Comments
DBX-1	Mod	Low	Mod	Mod	Unk	Low	Low	Unk	Mod	Unk	Chemical instability limited experimental testing
TTZ	Mod	Mod	Mod	Mod	Unk	Low	Unk	Unk	Mod	Unk	
KNO_3	Low	Low	Low	Low	Low	Low	Low	Low	Low	Unk	Toxicity would be expected from the nitrate anion (expected low for all species).
B_4C	Low	Low	Low	Low	Low	Unk	Unk	Low	Unk	Unk	No experimental data available; Likely low, inert compound
Al	Low	Mod	Low	Low	Low	Low	Mod	Low	Low	Unk	Moderate toxicity toward shellfish
Selvol 523	Low	Low	Mod	Mod	Low	Low	Unk	Unk	Low	Unk	Concern due to sensitization

*Applying criteria from Table E-2.

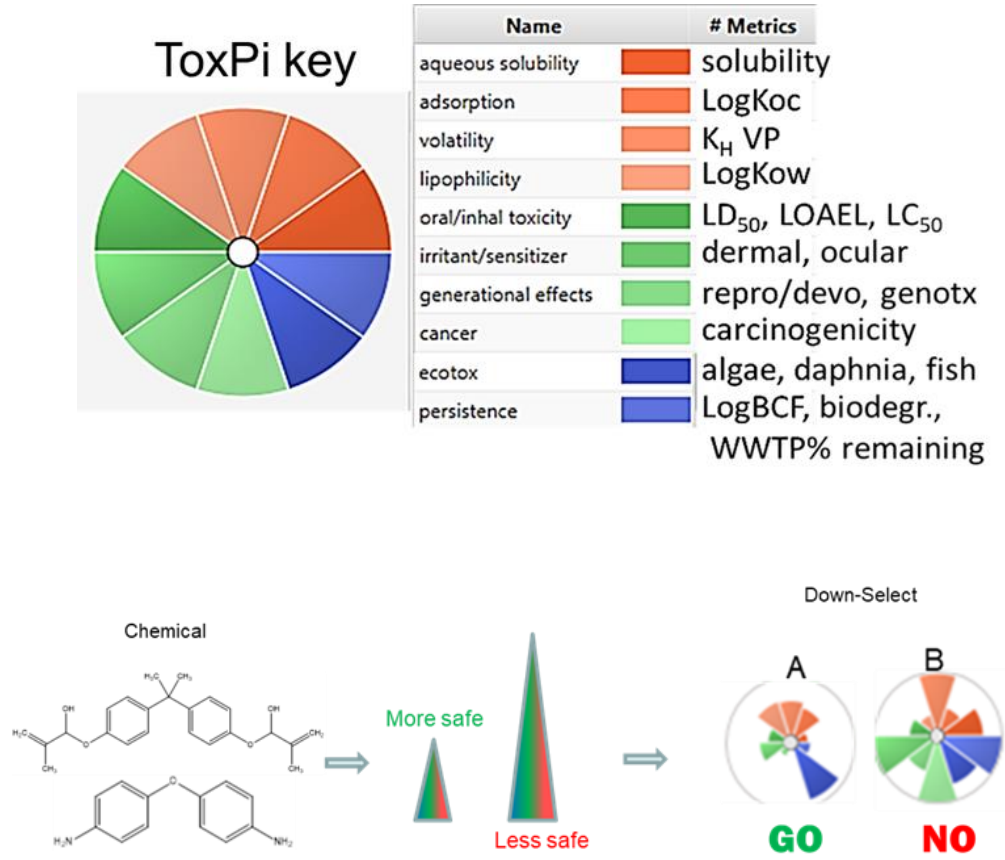

Figure E-1. ToxPi Example to Illustrate Relative Magnitude of Concern for Various Hazard Properties

Discussion:

Discuss the summaries of toxicity for each compound of interest; provide regulatory values and standards. Present the general conclusion, highlighting any pathways of concern.

Assumptions/Uncertainties:

Discuss information that was extrapolated, modeled, or estimated; and the relative uncertainty associated with any extrapolations or generalizations. Describe data gaps and potential impact of information either not provided or unavailable.

Recommendations:

Present general recommendations relative to exposure pathways and existing data, and discuss any further needs for information or data.

Points of Contact:

Contact information is provided in the DESHE to accommodate additional questions or information needs.

Appendix F. Additional Guidance

Additional environment, safety, and occupational health (ESOH) guidance documents are available to support the safe development of new materials. The following are provided as examples of methods sufficiently reviewed and verified for use.

- American Society for Testing and Materials (ASTM). 2016. ASTM E2552-16, *Standard Guide for Assessing the Environmental and Human Health Impacts of New Compounds.*
- The Technical Cooperative Program. 2014. Key Technical Area KTA 4-42, *Development of a Framework to Assess the Environmental Impacts of Green Munition Constituents and of New Energetic Formulations*.

Table F-1 provides a complete listing of applicable ASTM International, Organization for Economic Co-operation and Development (OECD), Environmental Protection Agency (EPA), International Organization for Standardization (ISO), and Department of Defense (DOD)-developed test methodologies.

Table F-1. Test Methods

ASTM International Standards	
D1252-06	Standard Test Methods for Chemical Oxygen Demand (Dichromate Oxygen Demand) of Water
E1023	Standard Guide for Assessing the Hazard of a Material to Aquatic Organisms and Their Uses
E1055-99R03	Standard Test Method for Evaluation of Eye Irritation in Albino Rabbits
E1103-96R04E01	Standard Test Method for Determining Subchronic Dermal Toxicity
E1147	Standard Test Method for Partition Coefficient (N-Octanol/Water) Estimation by Liquid Chromatography
E1148-02R08	Standard Test Method for Measurements of Aqueous Solubility
E1163	Standard Test Method for Estimating Acute Oral Toxicity in Rats
E1192-97R08	Standard Guide for Conducting Acute Toxicity Tests on Aqueous Ambient Samples and Effluents with Fishes, Macroinvertebrates, and Amphibians
E1194	Standard Test Method for Vapor Pressure
E1195	Standard Test Method for Determining a Sorption Constant (Koc) for an Organic Chemical in Soil and Sediments
E1197-87R04	Standard Guide for Conducting a Terrestrial Soil-Core Microcosm Test
E1241	Standard Guide for Conducting Early Life-Stage Toxicity Tests with Fishes
E1262 – 88 (2013)	Standard Guide for Performance of Chinese Hamster Ovary Cell/Hypoxanthine Guanine Phosphoribosyl Transferase Gene Mutation Assay
E1279	Standard Test Method for Biodegradation By a Shake-Flask Die-Away Method
E1280-97 (2008)	Standard Guide for Performing the Mouse Lymphoma Assay for Mammalian Cell Mutagenicity (Withdrawn 2015)
E1291-99R03	Standard Test Method for Conducting a Saturated Vapor Inhalation Study with Rats (Withdrawn 2009)
E1295	Standard Guide for Conducting Three-Brood, Renewal Toxicity Tests with *Ceriodaphnia dubia*
E1372	Standard Test Method for Conducting a 90-Day Oral Toxicity Study in Rats

E1373-01R05E01	Standard Test Method for Conducting a Subchronic Inhalation Toxicity Study in Rats (Withdrawn 2009)
E1415	Standard Guide for Conducting Static Toxicity Tests With *Lemna gibba* G3
E1525	Standard Guide for Designing Biological Tests with Sediments
E1624	Standard Guide for Chemical Fate in Site-Specific Sediment/Water Microcosms
E1625	Standard Test Method for Determining Biodegradability of Organic Chemicals in Semi-Continuous Activated Sludge (Withdrawn 2013)
E1676	Standard Guide for Conducting Laboratory Soil Toxicity or Bioaccumulation Tests
E1688	Standard Guide for Determination of Bioaccumulation of Sediment-Associated Contaminants by Benthic Invertebrates
E1689	Standard Guide for Developing Conceptual Site Models for Contaminated Sites
E1798 - 96	Standard Test Method for Assessing Treatability or Biodegradability, or Both, of Organic Chemicals in Porous Pots (Withdrawn 2013)
E1811	Standard Test Method for Oncogenicity Study in Rats and Mice (Withdrawn 2010, no replacement)
E1963-02	Standard Guide for Conducting Terrestrial Plant Toxicity Tests
E1963-09	Standard Guide for Conducting Terrestrial Plant Toxicity Tests
E2170	Standard Test Method for Determining Anaerobic Biodegradation Potential of Organic Chemicals Under Methanogenic Conditions
E729	Standard Guide for Conducting Acute Toxicity Tests on Test Materials with Fishes, Macroinvertebrates, and Amphibians
E895 – 89 (2008)	Standard Practice for Determination of Hydrolysis Rate Constants of Organic Chemicals in Aqueous Solutions
E896 – 92 (2005)e1	Standard Test Method for Conducting Aqueous Direct Photolysis Tests
G115-98	Standard Guide for Measuring and Reporting Friction Coefficients
OECD	
102	Melting Point/ Melting Range
103	Boiling Point
104	Vapor Pressure
105	Water Solubility
106	Adsorption - Desorption Using a Batch Equilibrium Method
109	Density of Liquids and Solids
111	Hydrolysis as a Function of pH
112	Dissociation Constants in Water
113	Screening Test for Thermal Stability and Stability in Air
114	Viscosity of Liquids
115	Surface Tension of Liquids
120	Solution/Extraction Behavior of Polymers in Water
121	Estimation of Adsorption Coefficient (Koc) on Soil and on Sewage Sludge Using High Performance Liquid Chromatography
122	Determination of pH, Acidity and Alkalinity

201	Freshwater Alga and Cyanobacteria, Growth Inhibition Test
202	Daphnia sp. Acute Immobilisation Test
203	Fish, Acute Toxicity Test
205	Avian Dietary Toxicity Test
206	Avian Reproduction Test
208	Terrestrial Plant Test: Seedling Emergence and Seedling Growth Test
209	Activated Sludge, Respiration Inhibition Test
210	Fish, Early-Life Stage Toxicity Test
211	Daphnia magna Reproduction Test
212	Fish, Short-term Toxicity Test on Embryo and Sac-Fry Stages
215	Fish, Juvenile Growth Test
220	Enchytraeid Reproduction Test
221	*Lemna sp*. Growth Inhibition Test
222	Earthworm Reproduction Test (*Eisenia fetida/Eisenia andrei*)
223	Avian Acute Oral Toxicity Test
227	Terrestrial Plant Test: Vegetative Vigour Test
229	Fish Short Term Reproduction Assay
230	21-day Fish Assay: A Short-Term Screening for Oestrogenic and Androgenic Activity, and Aromatase Inhibition
232	Collembolan Reproduction Test in Soil
234	Fish Sexual Development Test
236	Fish Embryo Acute Toxicity (FET) Test
301	Ready Biodegradability
302C	Inherent Biodegradability: Modified MITI Test (II)
303	Simulation Test - Aerobic Sewage Treatment
304A	Inherent Biodegradability in Soil
306	Biodegradability in Seawater
307	Aerobic and Anaerobic Transformation in Soil
308	Aerobic and Anaerobic Transformation in Aquatic Sediment Systems
310	Ready Biodegradability - CO2 in sealed vessels (Headspace Test)
311	Anaerobic Biodegradability of Organic Compounds in Digested Sludge: by Measurement of Gas Production
312	Leaching in Soil Columns
314	Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater
315	Bioaccumulation in Sediment-dwelling Benthic Oligochaetes
316	Photo-transformation of Chemicals in Water – Direct Photolysis
317	Bioaccumulation in Terrestrial Oligochaetes
401	Acute Oral Toxicity

402	Acute Dermal Toxicity
403	Acute Inhalation Toxicity
404	Acute Dermal Irritation/Corrosion
405	Acute Eye Irritation/Corrosion
406	Skin Sensitization
407	Repeated Dose 28-day Oral Toxicity Study in Rodents
411	Subchronic Dermal Toxicity: 90-day Study
412	Subacute Inhalation Toxicity: 28-day Study
415	One-Generation Reproduction Toxicity Study
416	Two-Generation Reproduction Toxicity
417	Toxicokinetics
418	Delayed Neurotoxicity of Organophosphorus Substances Following Acute Exposure
420	Acute Oral Toxicity - Fixed Dose
421	Reproduction/Developmental Toxicity Screening Test
422	Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test
423	Acute Oral Toxicity – Acute Toxic Class Method
425	Acute Oral Toxicity - Up and Down Procedure
426	Developmental Neurotoxicity Study
429	Skin Sensitization
436	Acute Inhalation Toxicity – Acute Toxic Class Method
439	*In Vitro* Skin Irritation: Reconstructed Human Epidermis Test Method
440	Uterotrophic Bioassay in Rodents
451	Carcinogenicity Studies
473	In vitro Mammalian Chromosome Aberration Test
474	Mammalian Erythrocyte Micronucleus Test
476	In vitro Mammalian Cell Gene Mutation Test
479	Genetic Toxicology: In vitro Sister Chromatid Exchange Assay in Mammalian Cells
482	Genetic Toxicology: DNA Damage and Repair, Unscheduled DNA Synthesis in Mammalian Cells in vitro
483	Mammalian Spermatogonial Chromosomal Aberration Test
486	Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells in vivo
489	In Vivo Mammalian Alkaline Comet Assay
490	In Vitro Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene

EPA Standards	
712-C-00-366	Repeated Dose 28-Day Oral Toxicity Study in Rodents
712-C-02-189	Acute Toxicity Testing - Background
712-C-02-190	Acute Oral Toxicity
712-C-03-197	Skin Sensitization
712-C-08-010	Leaching Studies
712-C-08-012	Hydrolysis
712-C-08-013	Photo-degradation in Water
712-C-96-038/ OPPTS 830.77550	Partition Coefficient (n-Octanol/Water), Shake Flask Method
712-C-98-192	Acute Dermal Toxicity
712-C-98-193	Acute Inhalation Toxicity
712-C-98-195	Acute Eye Irritation
712-C-98-196	Acute Dermal Irritation
821-R-02-012	Methods for Measuring the Acute Toxicity of Effluents and Receiving Waters to Freshwater and Marine Organisms
821-R-02-013	Short-term Methods for Estimating the Chronic Toxicity of Effluents and Receiving Waters to Freshwater Organisms
OPPTS 835.3180	Sediment/Water Microcosm Biodegradation Test
ISO Standards	
11268-1	Soil quality — Effects of pollutants on earthworms; Part 1: Determination of acute toxicity to *Eisenia fetida/Eisenia andrei*
16387	Soil quality — Effects of contaminants on Enchytraeidae (*Enchytraeus* sp.) -- Determination of effects on reproduction
20665	Water quality — Determination of chronic toxicity to *Ceriodaphnia dubia*
Additional Test Methods developed by the DOD	
Vapor Pressure	Army Research Laboratory (ARL) method: ARL-TR-6887, New Micro-Method for Prediction of Vapor Pressure of Energetic Materials, July 2014. Prepared by R.A. Pesce-Rodriguez and E. Klier. https://apps.dtic.mil/dtic/tr/fulltext/u2/a603833.pdf
Dissolution Rate	Engineer Research Development Center (ERDC) method for munition dissolution: ERDC/CRREL TR-14-23, Dissolution of NTO, DNAN, and Insensitive Munitions Formulations and Their Fates in Soils, September 2014. U.S. Army Corps of Engineers, ERDC Cold Regions Research and Engineering Laboratory (CCREL), Hanover, New Hampshire. https://apps.dtic.mil/dtic/tr/fulltext/u2/a609594.pdf

Glossary. Acronyms and Abbreviations

ACGIH
American Conference of Governmental Industrial Hygienists

APHC
U.S. Army Public Health Center

AR
Army Regulation

ASTM
American Society for Testing and Materials (ASTM International)

BA
Budget Activity

CFR
Code of Federal Regulations

DESHE
Developmental Environment, Safety, and Occupational Health Evaluation

DOD/DoD
Department of Defense

DoDD
Department of Defense Directive

DoDI
Department of Defense Instruction

EPA
U.S. Environmental Protection Agency

EPISuite
Estimation Programs Interface Suite

ESOH
Environment, safety, and occupational health

ETAP
Environmental Technology Acquisition Program

EU
European Union

HHA
Health Hazard Assessment

IH
Industrial Hygiene

LCEA
Lifecycle Environmental Assessment

LDR
Land Disposal Regulations

LOAEL
Lowest Observable Adverse Effect Level

NEPA
National Environmental Policy Act

NIOSH
National Institute for Occupational Safety and Health

NOAEL
No Observable Adverse Effect Level

OECD
Organization for Economic Co-operation and Development

OSHA
Occupational Safety and Health Administration

PESHE
Programmatic Environment, Safety, and Occupational Health Evaluation

PM
Program manager

PPE
Personal protective equipment

QSAR
Quantitative Structural Activity Relationships

RCRA
Resource Conservation and Recovery Act

RDT&E
Research, Development, Test, and Evaluation

REACH
Registration, Evaluation, Authorisation and Restriction of Chemicals

SDS
Safety Data Sheet

TRL
Technology Readiness Level

TSCA
Toxic Substances Control Act

U.S.C.
United States Code