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Standard Guide for Assessing the Environmental and Human Health Impacts of New Compounds for Military Use[1]

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INTRODUCTION

Sustaining training operations while maintaining force health is vital to national security. Research efforts are underway to identify new substances that have negligible environmental impacts and implement them in military weapon systems and applications. This guide is intended to provide a standardized method to evaluate the potential human health and environmental impacts of prospective candidate substances. This guide is intended for use by technical persons with a broad knowledge of risk assessment, fate and transport processes, and toxicology to provide recommendations to the research chemist or systems engineer regarding the environmental consequences of use.

1. Scope

1.1 This guide is intended to determine the relative environmental influence of new substances, consistent with the research and development (R&D) level of effort and is intended to be applied in a logical, tiered manner that parallels both the available funding and the stage of research, development, testing, and evaluation. Specifically, conservative assumptions, relationships, and models are recommended early in the research stage, and as the technology is matured, empirical data will be developed and used. Munition constituents are included and may include propellants, oxidizers, explosives, binders, stabilizers, metals, dyes, and other compounds used in the formulation to produce a desired effect. Munition systems range from projectiles, grenades, rockets/missiles, training simulators, to smokes and obscurants. Given the complexity of issues involved in the assessment of environmental fate and effects and the diversity of the systems used, this guide is broad in scope and not intended to address every factor that may be important in an environmental context. Rather, it is intended to reduce uncertainty at minimal cost by considering the most important factors related to human health and environmental impacts of energetic materials. This guide provides an outline for collecting data useful in a relative ranking procedure to provide the systems scientist with a sound basis for prospectively determining a selection of candidates based on environmental and human health criteria. The general principles in this guide are applicable to substances other than energetics if intended to be used in a similar manner with similar exposure profiles.

1.2 The scope of this guide includes:

1.2.1 Energetic and other new/novel materials and compositions in all stages of research, development, test and evaluation.

1.2.2 Environmental assessment, including:

1.2.2.1 Human and ecological effects of the unexploded energetics and compositions on the environment.

1.2.2.2 Environmental transport mechanisms of the unexploded energetics and composition.

1.2.2.3 Degradation and bioaccumulation properties.

1.2.3 Occupational health impacts from manufacture and use of the energetic substances and compositions to include load, assembly, and packing of the related munitions.

1.3 Given the wide array of applications, the methods in this guide are not prescriptive. They are intended to provide flexible, general methods that can be used to evaluate factors important in determining environmental consequences from use of new substances in weapon systems and platforms.

1.4 Factors that affect the health of humans as well as the environment are considered early in the development process. Since some of these data are valuable in determining health effects from generalized exposure, effects from occupational exposures are also included.

1.5 This guide does not address all processes and factors important to the fate, transport, and potential for effects in every system. It is intended to be balanced effort between scientific and practical means to evaluate the relative environmental effects of munition compounds resulting from intended

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use. It is the responsibility of the user to assess data quality as well as sufficiently characterize the scope and magnitude of uncertainty associated with any application of this standard.

1.6 Integration of disparate information and data streams developed from using the methods described in this guide is challenging and may not be straight-forward. Professional assistance from subject matter experts familiar with the fields of toxicology and risk assessment is advised.

1.7 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.8 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D5660 Test Method for Assessing the Microbial Detoxification of Chemically Contaminated Water and Soil Using a Toxicity Test with a Luminescent Marine Bacterium (Withdrawn 2014)[3]

E729 Guide for Conducting Acute Toxicity Tests on Test Materials with Fishes, Macroinvertebrates, and Amphibians

E857 Practice for Conducting Subacute Dietary Toxicity Tests with Avian Species

E943 Terminology Relating to Biological Effects and Environmental Fate

E1023 Guide for Assessing the Hazard of a Material to Aquatic Organisms and Their Uses

E1147 Test Method for Partition Coefficient (N-Octanol/Water) Estimation by Liquid Chromatography (Withdrawn 2013)[3]

E1148 Test Method for Measurements of Aqueous Solubility (Withdrawn 2013)[3]

E1163 Test Method for Estimating Acute Oral Toxicity in Rats

E1193 Guide for Conducting *Daphnia magna* Life-Cycle Toxicity Tests

E1194 Test Method for Vapor Pressure

E1195 Test Method for Determining a Sorption Constant (K_{oc}) for an Organic Chemical in Soil and Sediments (Withdrawn 2013)[3]

E1241 Guide for Conducting Early Life-Stage Toxicity Tests with Fishes

E1279 Test Method for Biodegradation By a Shake-Flask Die-Away Method (Withdrawn 2013)[3]

E1372 Test Method for Conducting a 90-Day Oral Toxicity Study in Rats (Withdrawn 2010)[3]

E1415 Guide for Conducting Static Toxicity Tests With *Lemna gibba* G3

E1525 Guide for Designing Biological Tests with Sediments

E1624 Guide for Chemical Fate in Site-Specific Sediment/Water Microcosms (Withdrawn 2013)[3]

E1676 Guide for Conducting Laboratory Soil Toxicity or Bioaccumulation Tests with the Lumbricid Earthworm *Eisenia Fetida* and the Enchytraeid Potworm *Enchytraeus albidus*

E1689 Guide for Developing Conceptual Site Models for Contaminated Sites

E1706 Test Method for Measuring the Toxicity of Sediment-Associated Contaminants with Freshwater Invertebrates

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *conception, n*—refers to part of the munition development process whereby molecules are designed through software and modeling efforts though not yet synthesized.

3.1.2 *demonstration, n*—refers to testing munition compounds in specific configurations that may use other substances to maintain performance specifications.

3.1.3 *engineering and manufacturing development, n*—involves the process of refining manufacturing techniques and adjusting formulations to meet production specifications.

3.1.4 *environmental, adj*—used to describe the aggregate of a receptor's surroundings that influence exposure, used in the holistic sense that may include human exposures in a variety of conditions.

3.1.5 *energetic materials, n*—chemical compounds or compositions that contain both fuel, binder, and potentially oxidizer and rapidly react to release energy and other products of combustion. Examples of energetic materials are substances used in high explosives, gun propellants, rocket & missile propellants, igniters, primers, initiators, and pyrotechnics (for example, illuminants, smoke, delay, decoy, flare and incendiary) and compositions. Energetic materials may be thermally, mechanically, and electrostatically initiated and do not require atmospheric oxygen to sustain the reaction.

3.1.6 *munition, n*—refers to weapon systems or parts of platforms that have a military application. Includes the use of energetic substances in addition to stabilizers, plasticizers, and other substances to the final combined formulation referred to as energetic material.

3.1.7 *production, n*—includes activities involved in the finalized manufacturing and use of the munition compound and accompanying system.

3.1.8 *synthesis, n*—process in which minute (gram) quantities of the energetic material are made, often using laboratory desktop equipment.

3.1.9 *testing and refinement, n*—includes preliminary small-scale tests to large-scale testing and range operations that require refined synthesis techniques within the research and

[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] The last approved version of this historical standard is referenced on www.astm.org.

development phase for new energetic compounds. Energetic materials may be combined with other ingredients at this stage to tailor specific performance properties.

4. Summary of Guide

4.1 In the evaluation of the probability of adverse environmental effects, measures of exposure are compared with measures of toxicity to evaluate relative risk. These methods and data requirements are balanced with the level of funding used in military system development. This guideline, therefore, provides a tiered approach to data development necessary for various levels of hazard assessment. Often it results in a relative ranking of properties, not a robust estimation of exposure. Initially, physical/chemical properties necessary for fate, transport, and exposure estimation may be derived and estimated from conceptual compounds developed from computer model simulations. Quantitative structural activity relationships (QSARs) and quantitative structural property relationships (QSPRs) may be useful in estimating toxicity and chemical properties important in estimating environmental fate and transport, respectively. Following successful synthesis of compounds, key properties may be experimentally determined (for example, water solubility, vapor pressure, sorption (K_{oc}), octanol/water partition coefficients (K_{ow}), boiling point, and molecular weight). These properties can be used in a relative manner or quantitatively to determine potential for transport and bioaccumulation. Given the expense involved, toxicity studies are tiered, where lower cost *in vitro* methods are used early in the process and more expensive *in vivo* methods are recommended later in the development process. Acute mammalian toxicity data may be generated, along with soil, water, and sediment toxicity to invertebrates (Tier I tests). Earthworm bioaccumulation tests may also be conducted, along with an evaluation of plant uptake models. At advanced stages, sublethal mammalian testing shall be conducted along with avian and other limited vertebrate toxicity tests (Tier II tests).

5. Significance and Use

5.1 The purpose of this guide is to provide a logical, tiered approach in the development of environmental health criteria coincident with level and effort in the research, development, testing, and evaluation of new materials for military use. Various levels of uncertainty are associated with data collected from previous stages. Following the recommendation in the guide should reduce the relative uncertainty of the data collected at each developmental stage. At each stage, a general weight of evidence qualifier shall accompany each exposure/effect relationship. They may be simple (for example, low, medium, or high confidence) or sophisticated using a numerical value for each predictor as a multiplier to ascertain relative confidence in each step of risk characterization. The specific method used will depend on the stage of development, quantity and availability of data, variation in the measurement, and general knowledge of the dataset. Since specific formulations, conditions, and use scenarios may not be known until the later stages, exposure estimates can be determined when practical (for example, Engineering and Manufacturing Development; see 6.6). Exposure data can then be used with other toxicological data collected from previous stages in a quantitative risk assessment to determine the relative degree of hazard.

5.2 Data developed from the use of this guide are designed to be consistent with criteria required in weapons and weapons system development (for example, programmatic environment, safety and occupational health evaluations, environmental assessments/environmental impact statements, toxicity clearances, and technical data sheets).

5.3 Information shall be evaluated in a flexible manner consistent with the needs of the authorizing program. This requires proper characterization of the current problem. For example, compounds may be ranked relative to the environmental criteria of the prospective alternatives, the replacement compound, and within bounds of absolute environmental values. A weight of evidence (evaluation of uncertainty and variability) must also be considered with each criterion at each stage to allow for a proper assessment of the potential for adverse environmental or occupational effects; see 6.8.

5.4 This standard approach requires environment, safety, and occupational health (ESOH) technical experts to determine the magnitude of the hazard and system engineers/researchers to evaluate the acceptability of the risk. Generally, the higher developmental stages require a higher managerial level of approval.

6. Procedure

6.1 *Problem Evaluation*—The first step requires an understanding of the current problem. Often, specific attributes of existing compounds drive the need for a replacement. For example, increased water solubility may indicate a propensity of the compound to contaminate groundwater. Environmental persistence and biomagnification may cause concerns regarding exposures to predatory animals and in human fish consumption. Increased vapor pressure may lead to significant inhalation exposures in confined spaces that would increase the probability of toxicity to workers or troops. A sound understanding of the factors principally attributed to the environmental problem is required to focus relative evaluation of these properties. A conceptualization of potential exposure pathways given specific chemical properties can be helpful in ascertaining likelihood for adverse effects. Guide E1689 can be helpful in that regard. Table 1 provides stages of technical development of munition compounds and corresponding suggested data requirements.

6.2 *Conception*—At this stage of energetic material development, molecular relationships and characteristics are examined to evaluate the properties of a new material. These include molecular and electronic structure, stability, thermal properties, performance and sensitivity requirements, and decomposition pathways. Since these substances are still conceptual, no empirical data exist.

6.2.1 The predicted molecular and electronic structural properties can be used in quantitative structure-activity relationship (QSAR) or other approaches to determine chemical/physical properties relating to toxicity, fate, and transport. These properties can be gleaned from computer-modeled estimations using quantitative structure-property relationship

TABLE 1 Life-Cycle Munition Development Stage Relative to the Collection of Data Important to the Evaluation of Environmental Criteria

Developmental Stage	Action	Data Requirement
Conception	Computer modeling (QSAR), computational chemistry	Chem/phys properties; toxicity estimates (mammalian and ecotoxicity)
Synthesis	Develop experimental chemical property data; conduct relative toxicity screen	Chem/phys properties (estimate fate, transport, bioaccumulation), *in vitro* mammalian toxicity screen, *in vitro* ecotoxicity screen (for example, luminescent bacteria)
Testing	Conduct Tier I mammalian toxicity testing	Acute/subacute rodent toxicity data; *in vitro* cancer screen
Demonstration	Conduct Tier II mammalian toxicity testing; Tier I Ecotox screening	Subchronic rodent toxicity data; aquatic/plant/earthworm assays
Engineering and manufacturing development	Cancer studies[A] ; Tier II Ecotox studies, evaluate plant uptake	Rodent cancer evaluation; avian, amphibian studies; plant uptake models
Production	Evaluate exposure and effects	No additional data required[B]
Storage and use	Evaluate exposure and effects	No additional data required
Demilitarization	Evaluate exposure and effects	No additional data required

[A] Only necessary if *in vitro* screens are predominantly positive and potential for exposure is relatively high.
[B] In certain cases, it may be necessary to verify predictions through environmental monitoring procedures.

(QSPR)-like or quantum mechanical models. The properties that are useful in estimating the extent of fate and transport include the following:

6.2.1.1 Molecular weight;
6.2.1.2 Water solubility;
6.2.1.3 Henry's law constant;
6.2.1.4 Vapor pressure;
(1) Liquid-phase vapor pressure;
(2) Solid-phase vapor pressure;
6.2.1.5 Affinity to organic carbon; sorption (log K_{oc});
6.2.1.6 Lipid solubility (octanol/water coefficient; log K_{ow});
6.2.1.7 Boiling point;
6.2.1.8 Melting point; and
6.2.1.9 Ionization potential.

6.2.2 When using existing materials, conduct a literature search to determine first if Chemical Abstract Service (CAS) registry numbers are available. A comprehensive database available from the National Institute of Health can be used to search for this information: (http://pubchem.ncbi.nlm.nih.gov). These CAS numbers may then be used to search for chemical/physical property values and toxicity information without significant risk of confusion regarding synonyms. In many cases PubChem offers links to additional sites, such as the archived Hazardous Substances Data Bank (HSDB) as well as European Chemical Agency sites

6.2.3 Models are available to predict environmental parameters that can be useful in predicting environmental fate and transport with an inherent degree of uncertainty. It is important that this uncertainty be captured using a qualitative or semi-quantitative approach (see 6.8). Examples of such models include those found in the EPA's Estimation Program Interface (EPI) suites.[4] EPI suites is available for download at https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-programinterface#download. EPI suites includes programs to estimate log Kow, Henry's Law constant, melting and boiling points, as well as several other parameters of environmental relevance.

6.2.4 Henry's law constant can also be calculated using the following equation:

$$H = \frac{Vp(MW)}{S} \quad (1)$$

where:

H = Henry's law constant (atm·m^3/mol),
Vp = vapor pressure (atm) at 25°C (298 K),
MW = molecular weight (g/mol), and
S = solubility in water (mg substance/L).

6.2.5 Octanol/water partition coefficients (log K_{ow}) can be predicted through the use of QSPR models. Models that predict sorption (affinity to organic carbon; log K_{oc}) are generally not required since log K_{oc} can be predicted from log K_{ow} values using the following equation:

$$K_{oc} = 10^{[0.0784+(0.7919+(\log K_{ow}))]} \quad (2)$$

where:

K_{oc} = soil organic carbon-water partition coefficient (mL water/g soil), and
K_{ow} = *n*-octanol/water partition coefficient (unitless).

6.2.6 QSAR approaches can also be used to estimate toxicological impact. Toxicity QSAR models can often predict many parameters before experimental toxicology testing but are dependent upon similar compounds that have toxicity data. These models produce estimates of toxicity (for example, rat subchronic benchmark dose response, low or no observed adverse effect levels (NOAELs)) are used to rank new energetic materials, not to evaluate them quantitatively. These methods provide a relatively fast, low-cost method for developing the minimum amount of environmental data necessary for an initial evaluation of environmental impacts. They can be used as a basis for go/no-go decisions regarding further development and can serve to focus further research. These rankings shall be based on measures of toxicity (for example, acute values such as LD50s, chronic/subchronic rat lowest observed adverse effect levels (LOAELs), benchmark dose response, etc.). QSARs may also be used in a qualitative sense to evaluate the need for focused developmental, reproductive (for example, endocrine-like functional groups) *in vivo* testing. Compounds with structure suggesting specific toxicity should be qualified for further testing at advanced stages in munition development (for example, engineering and manufacturing development).

[4] EPI Suite is a trademark of ImageWare Systems, Inc. 10883 Thornmint Road San Diego, CA 92127.

6.2.7 Following the problem evaluation procedure, pertinent properties are compared along with those of other candidate substances and, if applicable, with the currently used constituents marked for replacement. Estimates of the relative level of confidence (for example, high, medium, or low) shall also be assigned to each attribute. These qualifiers may be assigned a numerical weight and used in a semiquantitative approach. These substances are then ranked, evaluated based on absolute parameters, and/or assessed relative to the replacement substance configuration according to these criteria to provide the system investigator with a prioritized list from which to focus efforts or provide general recommendations regarding their use in an environmental or occupational context or both.

6.3 *Synthesis*—Following the conceptualization and successful assessment of a new material, it must be made. Once it is shown that small amounts of a new energetic material can be produced, small-scale screening tests shall be performed to establish performance characteristics. If the material can be synthesized at the gram level, risks from an environmental and occupational perspective can be more reliably determined through experimentally determining chemical properties in small-scale tests using actual material. If the candidate is suitable for further consideration, performance in gun or warhead configurations will be modeled to provide information on emissions. Amounts needed for each assay may need to be determined before initiation. These methods can be used to develop data that can increase confidence in risk (fate, transport, and toxicity) predictions. In addition, analytical chemistry methods are also needed at this stage.

6.3.1 Analytical chemistry and standard experimental methods can be used to develop the following data. The appropriate ASTM International standard is referenced where applicable.

6.3.1.1 *Water Solubility*—Test Method E1148.

6.3.1.2 *Vapor Pressure*—Test Method E1194.

6.3.1.3 *Log* K_{oc}—Test Method E1195.

6.3.1.4 *Log* K_{ow}—Test Method E1147.

6.3.1.5 *Boiling Point*—Organization for Economic Cooperation and Development (OECD) Test Guidelines 102 (**1**).[5]

6.3.1.6 *Relative Toxicity*—Use of *in vitro* techniques.

6.3.2 Increased water solubility suggests a propensity for increased bioavailability and transfer to groundwater. This parameter is also useful in predicting oral, inhalation, and dermal bioavailability and toxicity. This property, however, shall be compared with the affinity to organic carbon, since sorption assists in retarding migration to groundwater. As mentioned, log K_{oc} values may be derived from log K_{ow} values (**2**); however, experimentally derived data are recommended at this stage, if feasible.

6.3.3 Increased vapor pressure and a lower boiling point suggest a greater propensity for inhalation exposures and can be compared in a relative sense. Molecular weight is valuable in determining exposure within and between organ systems (**3, 4**).

6.3.4 Relative acute toxicity can be evaluated using low-cost and rapid in-vitro basal cytotoxicity assays (for example, Neutral Red Uptake (NRU) https://ntp.niehs.nih.gov/sites/default/files/iccvam/docs/protocols/ivcytonhk.pdf). Relative acute toxicity can be evaluated using relatively low-cost in-vitro cell culture techniques (for example, MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay, cell exclusion dyes, and propidium iodide (**5, 6**)). Specific assays that assess cellular function may be needed when toxicity for replacement compound is not mediated by changes in metabolism, necrosis or cell death. Screening-level ecotoxicological methods ((**7**), Test Method D5660) can be used to ascertain relative toxicity to the test organism and can be used for ranking purposes, though all have limitations (**7, 8**).

6.3.5 As before, these data are used to improve on the information and confidence estimates used in the previous evaluation. The relative weight of each ranking criterion depends upon the factors most important to the initial problem. Confidence estimates shall be used as ranking criteria in providing the hierarchical list of candidates.

6.4 *Testing*—This involves testing new materials in various systems and configurations to determine the best formulations to achieve specific performance characteristics. This often requires varying the proportions of various compounds to achieve performance goals. Other substances, such as binders or plasticizers, are used to meet specifications. This requires an understanding of the dynamics of these mixtures insofar as they affect transport and fate (for example, products of combustion) as well as attributes of any introduced compounds to the mixture. Since larger masses/volumes of compounds are needed at this stage, the probability for human exposure increases; therefore, it is important to have baseline human toxicity data (Tier I testing). At this stage, the following are important data to collect.

6.4.1 Sorption can be measured experimentally in various soil types using Test Method E1195. Modeled approaches using available software systems could be used to estimate biodegradation, persistence, bioaccumulation, and toxicity, respectively (**9**).

6.4.2 Animal data are now needed since potential for human exposure is likely and a higher degree of certainty is needed. Acute rodent studies shall be conducted before subacute (14-d) and subchronic (90-d) studies. Test Method E1163 describes the stagewise probit method to determine the median lethal dose and slope for 50 % of rats exposed to a single oral dose. Data from previous stages (for example, NRU test) can be used to refine and set parameters for the oral acute studies. Following the determination of the acute LD50, a 14-day range finding (subacute) study is required to refine sublethal levels of exposure useful for the 90-day subchronic tests (Test Method E1372); data from the latter are required to determine a chronic benchmark (for example, acceptable daily dose). Study conduct and hence data quality is important. It is therefore recommended that mammalian toxicity studies are conducted consistent with good laboratory practices (GLPs). Extent of sublethal mammalian toxicity (benchmark dose points of departure) shall be identified. If the compound has properties consistent with exposures via inhalation routes, then the inhalation counterpart to these tests shall be conducted. The

[5] The boldface numbers in parentheses refer to a list of references at the end of this standard.