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# Standard Guide for Assessing the Health Hazard of Pesticides to Applicators and Others with Potential Exposure[1]

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## 1. Scope

1.1 This guide covers a stepwise process for using information concerning biological, chemical, physical, and toxicological properties of a pesticide or other chemical(s), or of a formulation to identify adverse effects that may occur to pesticide applicators or others with potential exposure.

1.2 The health hazard assessment process is complex and requires decisions at a number of points; thus, the validity of the assessment depends on the soundness of those decisions, as well as the soundness of the information used. All decisions should be based on carefully documented analyses so that an appropriate assessment can be completed, at the least cost, which is consistent with scientific validity.

1.3 This guide assumes that the reader is knowledgeable in animal toxicology and related pertinent areas, and relies heavily on the judgment of the evaluator, particularly in the area of chronic hazards.

1.4 *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 and health practices and determine the applicability of regulatory limitations prior to use.*

## 2. Referenced Documents

2.1 *ASTM Standards:*

E 609 Definition of Terms Relating to Pesticides[2]

E 943 Terminology Relating to Biological Effects and Environmental Fate[2]

2.2 *OSHA Standard:*

29 CFR 1910.1200 Hazard Communication Standard[3]

## 3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *health hazard assessment*—the identification and evaluation of the adverse effects likely to result from specified release(s) of a material. The estimate is only semi-quantitative.

3.1.2 *hazard identification*—the process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect and whether the adverse health effect is likely to occur in humans.

3.1.3 *human exposure concentration* (HEC)—the concentration in the human environment based on application rate or distribution, persistence in the environment, the chemical form of the material, and location of the pesticide or formulation in the air, on surfaces, in vegetation, or in soil.

3.1.4 *maximum safe concentration for humans* (MSCH)—a prediction of the highest concentration of a material that would have no unacceptable adverse effect on humans based on toxicity testing in animals, clinical studies, and field experience.

## 4. Summary of Guide

4.1 This guide describes a stepwise process for assessing the risk of a pesticide, chemical, or formulation to applicators and other individuals susceptible to exposure of pesticides by considering the relationship between the material's measured or estimated human exposure concentration(s) and the adverse effects likely to result. Unavailable necessary information concerning human exposure concentrations and adverse effects is obtained through a stepwise program that starts with inexpensive information and progresses to expensive information if necessary. At the end of each iteration, the estimated or measured human exposure concentration(s) is compared with information on possible adverse effects to determine the adequacy of the available data for assessing the health hazard. If it is not possible to conclude that the health hazard is either minimal or potentially excessive, the available data are judged inadequate to characterize the health hazard. If desired, appropriate additional information is identified and obtained, so that the health hazard can be reassessed. The process is repeated until the health hazard is characterized adequately.

## 5. Significance and Use

5.1 Concern over the toxic effects observed in tests on animals has demonstrated the need to assess hazards of many new, and some presently used, materials. The process described herein will help producers, regulatory agencies, and others to compare alternative materials efficiently and adequately, completely assess a final candidate material, or reassess the health hazard of a material already in use. The process is not intended for pesticide registration; this guide provides techniques for health hazard assessment.

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[1] This guide is under the jurisdiction of ASTM Committee E-35 on Pesticides and is the direct responsibility of Subcommittee E35.26 on Safety to Man.

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[2] *Annual Book of ASTM Standards*, Vol 11.05.

[3] Available from Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.

5.2 Sequential assessment and feedback allow appropriate judgments concerning the efficient use of resources, thereby minimizing unnecessary testing and focusing effort on the information most pertinent to each material. For different materials and situations, hazard assessment will appropriately be based on substantially different amounts and kinds of biological, chemical, physical, and toxicological data.

5.3 Assessment of the health hazard of a material should never be considered complete for all time. Reassessment should be considered if new uses are discovered, the nature of the exposure changes, or new information on biological, chemical, physical, or toxicological properties becomes available.

5.4 Periodic review will help ensure that new information receives prompt and appropriate attention.

5.5 If a pesticide is transformed substantially into another chemical entity in the environment, the hazard of the transformed material(s) may need to be assessed.

## 6. Phase I—Use of Low-Cost Information

6.1 *Collection of Available Data*—The initial step in assessment of the hazard of a material is to assemble all of the available pertinent information concerning the following:

6.1.1 Recommended use, frequency of application, amounts of release, types of application, expected dispersion, and potential for accidental release.

6.1.2 Composition, structure, and chemical reactions of the test material, with emphasis on those chemical properties likely to affect the testing procedures, HECs, and biological effects.[4, 5, 6] Complete chemical characterization of the test material is important, but it is often difficult to obtain. Many industrial chemicals contain a mixture of isomers, homologs, or polymer chains of various lengths, as well as impurities or by-products. The manufacturer(s) of the chemical(s) of interest should supply this information.

6.1.3 Physical properties, with particular emphasis on volatility, evaporation rate, surface tension, dispersibility, sorption, and solubility.

6.1.4 Toxicity of the pesticide or similar materials to mammals and target organisms. If toxicity data on the material(s) of interest or similar materials are not available in the literature (see Appendix X1), some acute and subchronic testing of the test material is necessary. Sources for definitions and some test methods of acute animal toxicity are cited in Appendix X2. In some cases, it is highly desirable to compare the toxicity of the technical grade material with that of the purified active ingredient. Use of reagent-grade materials can simplify the development of structure-activity correlations, which may then allow estimates of the toxicity of more complex mixtures.

6.1.5 Efficacy data, particularly the nature of the target organism(s) and biological effects on this organism(s), may provide some information on the toxicity of the material.

6.1.6 Material Safety Data Sheet (MSDS). Obtain or prepare a MSDS (such as OSHA Form 174) for each material or formulation under evaluation; this information should comply with OSHA Standard 29 CFR 1910.1200. A revised MSDS should be prepared when a change in the composition of the material/product occurs which changes any of the information on the MSDS, or when the investigator becomes aware of any significant information regarding the health hazards of a chemical or ways in which to protect against the health hazards.

6.2 *Initial Estimates of Human Exposure Concentrations (HEC)*—Based on the available information on recommended usage, chemical and physical properties, and analogy with other pesticides for which data are available, an initial estimate should be made of the concentrations likely to be found on various surfaces and in the air. Information on persons who will be exposed (age and weight), the duration and frequency of exposures, and the potential for drift during application, and possible misuses (both intentionally and unintentionally) are needed. From these data, human exposure by skin contact, ingestion, and inhalation are estimated.[7]

6.3 *Hazard Identification*—Based on chemical structure, information on similar materials, efficacy, and available data on toxicity to animals, an initial assessment should be made of whether the material is biologically inactive or presents special concerns. In some cases, enough data on the toxicity of the material may be available to allow a good estimate of the concentrations likely to affect human beings adversely.

6.4 If the material(s) is subject to regulatory review by the U.S. Environmental Protection Agency or other federal or state agencies, the requirements of those regulations must be evaluated (see Appendix X2).

6.5 *Phase I Health Hazard Assessment*—By using information on the HECs and biological effects, the health hazard should be assessed as either minimal, potentially excessive, or uncertain.

6.5.1 *Minimal Health Hazard*—The health hazard to pesticide users and others can usually be judged minimal if one or more of the following conditions exists:

6.5.1.1 Use and distribution patterns are such that significant exposure to humans is very unlikely.

6.5.1.2 Existing evidence indicates that the material and its degradation products are toxicologically inactive to humans.

6.5.1.3 Toxicity is known for the material or materials of similar structure to the test material, and exposure information indicates that the exposure for humans is likely to be without an appreciable potential for deleterious effects. The data should include the results of acute, subchronic and, if available, chronic testing.

6.5.2 *Potentially Excessive Health Hazard*—The determination of a potentially excessive health hazard is usually appropriate if the HECs exceed the estimated MSCH. If there is continuing interest in the material, Phase II must be considered.

6.5.3 *Uncertain Health Hazard*—For most new materials, the available information will not be adequate to allow the

[4] *Condensed Chemical Dictionary*, Van Nostrand Reinhold Co., New York, NY (use latest edition).

[5] *The Merck Index: An Encyclopedia of Chemicals and Drugs*, Merck and Company, Rahway, NJ (use latest edition).

[6] *Handbook of Chemistry and Physics*, Chemical Rubber Company, Cleveland, OH (use latest edition).

[7] Hallenbeck, W. H. and Cunningham, K. M., Quantitative Risk Assessment and Occupational Health, Louis Publishers, Inc., Chelsea, MI, 1986.

conclusion of a minimal or potentially excessive health hazard. Thus, the health hazard will have to be judged uncertain. If there is continuing interest in the material, Phase II must be considered.

## 7. Phase II—Use of Medium-Cost Information

7.1 Whereas Phase I involves the collection and analysis of already available data, Phase II will require at least some medium-cost efforts to obtain new information on HECs and toxicity. An initial review of Phase I should indicate the most cost-effective starting point.

7.2 *Improved Estimates of Human Exposure Concentrations*—The HECs used in Phase I may have been obtained with only minimal information on release, and little or no information on biological, chemical, and physical properties that determine environmental fate. In Phase II, appropriate tests should be undertaken to obtain important data on biological, chemical, and physical properties which are not already available. If degradation is substantial, degradation products and their properties should be considered. Assumptions and data used to derive the HECs should be examined carefully to determine the confidence that should be placed in them. If the material is already in use, some environmental monitoring is appropriate; in addition, some field experience and work-place exposure data, if available, should be evaluated.

7.3 *Toxicity Testing*—Unless appropriate data are already available, acute and subchronic toxicity tests will normally be necessary to evaluate ingestion, skin penetration and irritation, eye irritation, and inhalation potential. Initial toxicity results on non-human mammals, such as the rat, mouse, rabbit, guinea pig, hamster, dog, or monkey, are often necessary to estimate the scope of the assessment process and to assist in defining chronic studies required in Phase III.

7.4 From these data, an improved estimate should be determined of the highest concentration of the test material which has no significant adverse effect on humans (MSCH).

7.5 *Phase II Health Hazard Assessment*:

7.5.1 *Minimal Health Hazard*—A judgment of *minimal* health hazard is appropriate if the following apply:

7.5.1.1 Toxicological data indicate that similar materials are biologically innocuous at the estimated or measured HECs.

7.5.1.2 Results of acute and subchronic toxicity tests with the test material yield an MSCH which is significantly above the HECs of the material.

7.5.2 *Potentially Excessive Health Hazard*—A judgment of *potentially excessive* health hazard is appropriate if acute and subchronic toxicity levels occur at concentrations near or below the HECs. If the health hazard is judged *potentially excessive* and there is continuing interest in the material, Phase III is necessary.

7.5.3 *Uncertain Health Hazard*—The health hazard should be judged *uncertain* if the following are true:

7.5.3.1 The MSCH from acute and subchronic testing is only several-fold above the HECs.

7.5.3.2 Experience with similar materials is limited or mixed, so that a definitive hazard assessment is lacking.

7.5.3.3 Human safety evaluations show unacceptable biological activity.

7.5.3.4 If the health hazard is judged *uncertain* and there is a continuing interest in the material, Phase III is necessary.

## 8. Phase III—Use of High-Cost Information

8.1 Because of the substantial increase in time, effort, and money required for tests considered in Phase III, it is particularly important in this phase that the health hazard assessment program be tailored to the individual material in order to obtain the most useful information in the least expensive, scientifically sound manner.

8.2 *Refined Estimates of Human Exposure Concentrations*—Unless it has already been conducted, a thorough modelling effort of the fate of the material should be performed using all available data. It is especially important to predict peak concentrations, concentrating mechanisms, and persistence. If the material of concern is already in use, field monitoring should be used to validate the model. Potential application misuses or accidents should be considered.

8.3 *Chronic Toxicity Testing*—Biological tests for mutagenicity, carcinogenicity, neurotoxicity, reproduction, teratogenicity, and inhalation should be conducted.

8.3.1 If the results of acute or subchronic toxicity tests present an unusual pattern or show large differences in sensitivity between species, chronic testing should probably include more than one species. The species used will depend on the hypothesis used to explain the unusual or unexpected differences.

8.3.2 Assessment of materials subject to regulatory review by the U.S. Environmental Protection Agency or other agencies will need to take into account species or test preferences indicated in agency guidelines.

8.4 *Phase III Health Hazard Assessment*:

8.4.1 *Minimal Health Hazard*—A judgment of *minimal* health hazard to applicators and consumers is probably appropriate if the MSCH is sufficiently greater than the HECs, so that the estimated confidence intervals do not overlap.

8.4.2 *Potentially Excessive Health Hazard*—A judgment of a *potentially excessive* health hazard is appropriate if the MSCH is below the HEC.

8.4.3 The health hazard may still be *uncertain* in some cases, or it may be known to be borderline. In such situations, small-scale field trials with chemical monitoring may be desirable to provide additional information on distribution and persistence, subchronic and chronic toxicity with non-rodent species, and field experience, if any have been evaluated.

## 9. Keywords

9.1 applicators; chemicals; environment; exposure; health hazard; humans; pesticides; toxicity

## APPENDIXES

**(Nonmandatory Information)**

### X1. SOURCES OF TOXICOLOGICAL INFORMATION

X1.1 *Bibliographic Databases:*

X1.1.1 Bibliographic Retrieval Services (BRS), Corporation Park, Scotia, NY. File Names: Agricola, BIOSOS Previews, CA Condensates, CA Search, Drug Information, Medlars, MEDOC, NTIS, Pollution Abstracts, Science Citation Index, and SSIE.

X1.1.2 DIALOG, Information Services Inc., Palo Alto, CA (part of Knight-Kidder Co.). File Names: Agricola, BIOSIS Prev. 1969–present, CA Condensates 1970–71, CA Search 1969–present, CHEMNAME, Conference Papers Index, Food Science and Technical Abstracts, Foods ADLIBRA, International Pharmaceutical Abstracts, NTIS, Pollution Abstracts, SCISEARCH 1974–present, and SSIE Current Research.

X1.1.3 SDC-Orbit, SDS Search Service, Pasadena, CA. File Names: Agricola, BIOCODES, BIOSIS/BIO6973, CAS6771/CAS7276, CAS77, Chemdex, Conference, Enviroline, Labordoc, NTIS, Pollution, and SSIE.

X1.1.4 Chemical Information System (CIS)—Chemical Information Systems, Inc., Baltimore, MD. File Names: Structure and Nomenclature System, Acute Toxicity (RTECS), Clinical Toxicology of Commercial Products, Oil and Hazardous Materials, and Technical Assistance Data System.

X1.1.5 National Library of Medicine, Public Health Service, National Institutes of Health, Bethesda, MD. File Names: Toxicology Data Bank (TDB), MEDLIN, TOXLINE, CANCERLIT, and RTECS.

X1.2 *Occupational Health Guidelines*—U.S. Department of Health and Human Services, Public Health Service, National Institute for Occupational Safety and Health, Bethesda, MD. The following documents are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC: *Registry of Toxic Effects of Chemical Substances* (RTECS), NIOSH Pub. No. 80-102; *Pocket Guide to Chemical Hazards*, NIOSH Pub. No. 78-210; *Occupational Health Guidelines*, NIOSH Pub. No. 81-123; and *The Industrial Environment—Its Evaluation and Control*, NIOSH Pub. No. 74-117.

X1.3 *Integrated Risk Information System (IRIS); Health Risk Assessment*—IRIS is an electronic on-line database of the U.S. Environmental Protection Agency that provides risk assessment and regulatory information on chemical substances. IRIS is available from: DIALCOM Inc., 500 Maryland Ave. SW, Suite 307, Washington, DC 20024.

X1.4 Manufacturers' and Trade/Professional data not listed in the other sources cited.

### X2. REFERENCES FOR ACUTE ANIMAL TOXICITY TESTING

X2.1 *Acute Oral Toxicity*—Consumer Product Safety Commission (CPSC) 16 CFR (Code of Federal Regulations) Part 1500.3; Department of Transportation (DOT) 49 CFR 173.343a1; Environmental Protection Agency, Toxic Substance Control Act (EPA-TSCA) 40 CFR 798.1175; and Occupational Safety and Health Administration (OSHA) 29 CFR 1910.1200, Appendix A, 3(a) and A, 6(a).

X2.2 *Acute Dermal Toxicity*—CPSC 16 CFR 1500.40; DOT 49 CFR 173.343a3; EPA-TSCA 40 CFR 798.1100; and OSHA 20 CFR 1910.1200, Appendix A, 3(b) and A, 6(b).

X2.3 *Acute Inhalation Toxicity*—CPSC 16 CFR part 1500.3; EPA-TSCA 40 CFR 798.1150; DOT 49 CFR 173.343a2; and OSHA 29 CFR 1910.1200, Appendix A, 3(c) and A, 6(c).

X2.4 *Eye Irritation*—CPSC 16 CFR 1500.42; EPA-TSCA 40 CFR 798.4500; and OSHA 29 CFR 1910.1200, Appendix A4.

X2.5 *Skin Irritation or Corrosion*—CPSC 16 CFR 1500.41 (Irritation); DOT 49 CFR Part 173, Appendix A (Corrosion); EPA-TSCA 40 CFR 798.4470; and OSHA 29 CFR 1910.1200, Appendix A, 4.

X2.6 *Skin Sensitization (40 CFR 798.4100)*—Freund's complete adjuvant test, guinea pig maximization test, split adjuvent technique, Buehler test, open epicutaneous test, Mauer optimization test, and footpad technique in guinea pigs.

X2.7 OSHA Hazard Communication Standard, 29 CFR 1910.1200.

X2.8 *Good Laboratory Practices*—(EPA-TSCA) 40 CFR 792, (EPA) 40 CFR 160, and (FDA) 21 CFR 58.

X2.9 Federal Hazardous Substances Act (CPSC), 16 CFR 1500.