Exposure and Risk Assessment, Health Monitoring, and Risk Management for Herbicide Applicators

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ABSTRACT

State departments of transportation across the country use herbicides in roadside vegetation management and insect control. Significant employee, public health, and environmental issues arise from such use. Issues of potential exposure, health risks, health monitoring, and risk management have assumed importance in design and maintenance of transport corridors. Programs that address these issues are described, including a numerical, relative hazard rating scale for ranking herbicides and pesticides. The state of Maine Department of Transportation has incorporated such programs into its decision making regarding use and restriction of herbicides. The programs, program results, and a critique of program capabilities and limitations are described. Critical issues facing prospective consumers and providers of such programs are analyzed.

Roadside vegetation management poses risks of applicator exposure to herbicides and risks of consequent adverse health effects for persons applying (applicators) these substances. Such occupational risks give rise to a need for employee health monitoring programs, as well as for risk management strategies. Such strategies must be simultaneously preventive (prospective) in their frequent ability to detect early warning signs of illness (such as reduced lung function) and flexibly responsive to the clinical findings of health monitoring programs (retrospective). Hence, four issues are identified:

1. Exposure potential,
2. Health risks,
3. Health monitoring, and
4. Risk management.

Two of the four issues have been addressed through provision of consulting services to the state of Maine Department of Transportation (MDOT). Specifically, MDOT has engaged Envirologic Data to perform health monitoring for MDOT employees, including herbicide applicators, and to assess potential health risks that may be associated with herbicides in use or considered for use by MDOT. In addition, the remaining two issues have been addressed through provision of services to other clients. Based on these experiences the purposes of this paper are to (a) describe appropriate service methodologies for exposure and health risk assessment, health monitoring, and risk management; (b) report program results and related activities in the state of Maine; and (c) discuss critical issues faced by both consumers and providers of the services described in this paper.

SCOPE

The four issues set forth correspond to distinguishable service programs that address the needs of potential users of herbicides. These programs are defined in the following paragraphs.

Exposure Assessment

Exposure assessment is the process of evaluating the potential for human or environmental contamination due to accidental or deliberate release of a substance, such as a herbicide. For herbicide applicators, the potential occupational exposures of concern primarily arise from two routes of exposure: inhalation and skin contact; ingestion is typically, but not always, of only secondary importance as a route of exposure.

Health Risk Assessment

Health risk assessment is the process of evaluating the potential adverse health effects that might occur following exposure to a particular hazard, such as a herbicide. [Terminology has been adopted consistent with the U.S. Congressional Office of Technology Assessment, in which a "hazard" is defined as a substance or exposure that harbors a "risk" to people (1). For example, a carcinogen is itself a hazard; risk is the probability of developing cancer as a result of exposure to the hazard.] For herbicide applicators, the health risks of concern may arise from chronic exposure (over a period of more than 3 months), from subchronic exposure (over a period of up to 3 months), or from acute, accidental exposure (on a single day). Adverse health effects may vary from acute poisoning which, though potentially fatal, is usually transient, to long-term effects such as cancer, mutations, and birth defects--or there may be no adverse health effects at all following exposure.

The likelihood of developing adverse health effects has been impossible to accurately quantify for most substances. Inability to quantify risk reflects the current, insufficiently advanced state of the art in toxicology and related sciences: quantitative risk assessment is more frequently undertaken than are its results believed by reasonable scientists. The difficulty primarily arises from the need to acquire experimental data by use of test animals exposed to high doses of a substance for only short

durations to produce high response rates (risks of 1/10 to 1/2). To quantify risk, it is then necessary to extrapolate to the human situation of relatively low doses for long durations with very low response rates (risks of 1/1,000,000 to 1/10,000 usually being regarded as acceptable). A numerical, relative risk assessment rating scale has been adopted that goes beyond qualitative risk assessment but avoids the current pitfalls of fully quantitative risk assessment.

Health Monitoring

Health monitoring is the process of clinically observing individuals to establish a baseline health picture for comparison with any future conditions that may arise. Health monitoring may also detect adverse health effects associated with particular hazards, such as herbicides. Health monitoring may continue beyond the clinical stage by means of periodic questionnaires aimed at detecting any new symptoms that might trigger further clinical observation or treatment. There are three objectives of employee health monitoring:

1. Establishment of a health baseline for protection of employers against liabilities for alleged job-related health damage to employees and former employees;
2. Protection of past and present employees by diagnosing and treating conditions revealed by health monitoring, whether related or unrelated to employment; and
3. Alleviating the fears and concerns of employees and families of employees who believe they may have been exposed to health hazards at their jobs, particularly when only insignificant changes are noted compared with any baseline health picture established earlier.

Risk Management

Assessment of exposure and health risk may raise the issue not only of health monitoring, but of risk management. The issue of risk management may also arise from the results of health monitoring, particularly if they reveal job-related pathology. Risk management is the process of developing strategies for maintaining risks at acceptable levels. Risks of exposure and of health damage associated with a particular hazard, such as a herbicide, may prove to be insignificant and unworthy of intensified management. However, at the opposite extreme, such risks may raise the issue of whether use of a particular substance should be continued. Most frequently, exposure and health risk assessment lead to effective as well as economical strategies of risk management.

EXPOSURE ASSESSMENT

Methodology

Although the state of Maine has recently expressed interest in exposure assessment, exposure assessments have not yet been performed for MDOT. The methodology described here is based on experience with other clients. Potential occupational exposure of applicators to herbicides would be regarded as a situation worthy of separate analysis. In performing such an analysis, assumptions would be made about the number of work days in each year, the number of work hours in each day, the percent of each work day during which exposure risk exists, as well as the efficacy of protective garments and breathing apparatus, and the concentration of the herbicide in the formulations being applied. Exposure estimates are then generated from the assumptions: consequently, the validity of exposure estimates depends entirely on the validity of the assumptions on which they were based.

Exposure assessments for herbicide applicators should be consistent with methodology established and approved by the U.S. Environmental Protection Agency (2). Moreover, much has been written to advance the field of exposure assessment [see, for example, Zervos and Fringer (3)], and such advances should be rapidly incorporated into standard methodologies as their use becomes feasible.

The environmental dynamics of a substance give rise to sources of exposure, such as air, drinking water, and food, which must be separately quantified. Ultimately, exposure is estimated by quantifying intake of the substance in air, drinking water, and food based on critical assumptions about inhalation rates, daily drinking volumes, and intake of various types of food. Exposure estimates are separately presented for adult males, females, children, and infants, as well as for any identified subpopulations at unusually high risk, either through excessive exposure or sensitivity to the substance.

Results

Exposure assessment can significantly complement employee health programs. MDOT has recently requested a proposal for services to review herbicide application operations and procedures to facilitate analysis of the potential for exposure of employees. In the past, in lieu of detailed exposure assessment, MDOT has used employee education and training programs supported by a detailed spray manual to reflect the assumption that exposure can occur and should be minimized through known and reasonable practices.

HEALTH RISK ASSESSMENT

Methodology

The health risk assessment process begins with an evaluation of the efficiency of absorption of the substance into the body by each potential route of exposure--that is, it begins where the exposure assessment ends. The health risk assessment process is divided into three tasks: (a) information search, (b) acquisition, and (c) analysis. Information search begins with in-house literature holdings and client-supplied documents. Initial search is followed by an on-line data base search using bibliographic retrieval services. This search generates a list of data sources from which a selection of relevant sources is made. Relevant sources of data are located among the most conveniently situated research libraries, and copies are acquired as expeditiously and economically as possible.

Once acquired, all literature is selectively distributed to appropriate specialists for summary and analysis. Specialists then synthesize the diverse information into the context of the risk assessment format specified in advance of each project. This format would typically include the following relevant information:

- General information, chemical and physical properties;
- Pharmacokinetics, including absorption into the body, distribution to various tissues and organs, metabolism, and excretion;

- Chronic, subchronic, and acute toxicity;
- Causation of cancer, mutations, birth defects, reproductive and other long-term effects;
- federal and state regulatory statutes and guidelines;
- Conclusions regarding adequacy of the data and specific research needs; and
- Literature citations and appendices.

Numerical, relative rating scales have been established for key health effect categories. Acute toxicity is rated on an ascending scale of 1 to 3, in which 1 corresponds to lowest toxicity [an oral LD_{50} (LD_{50} is the dose of a substance that is lethal within a specified time to 50 percent of a population of exposed test organisms) exceeding 5,000 ppm (parts per million, or milligrams per kilogram of body weight)]; 2 corresponds to an intermediate toxicity (oral LD_{50} of 50 to 5,000 ppm); and 3 corresponds to the highest acute toxicity (oral LD_{50} of less than 50 ppm). Long-term health effects [carcinogenicity (causation of cancer), mutagenicity (causation of mutations), teratogenicity (causation of birth defects) and reproductive effects (reduction in fertility, potency, or other measure of reproductive competency)] are rated on a scale of 0 to 3, in which 0 corresponds to no adverse health effects, 1 corresponds to insufficient or conflicting evidence of effect, and 2 and 3 correspond to increasing potency or evidence of potency of the substance of interest. The specific criteria for numerical ratings are listed in the Appendix.

Results

The state of Maine, via the Maine Board of Pesticides Control (MBPC) and the MDOT, has incorporated health risk assessment into its regulatory and policy making procedures. Health risk assessment services are procured by a three-step process: (a) publication of a request for proposals (RFP) fulfilling specified health risk assessment service requirements, (b) evaluation of competing proposals, and (c) negotiation of a 1-year contract with the private consultant whose proposal was deemed most appropriate relative to the needs of the state.

In Maine the Commissioner of Agriculture and the MBPC are responsible for regulating herbicides. Herbicides that are shown to pose significant public health hazards through the risk assessment process are reviewed through public hearings to allow full consideration of economic and health concerns before regulation. MDOT has the additional concern and responsibility for employees who apply herbicides and has shared costs of herbicide risk assessments with MBPC since early 1984. MDOT management then makes judgments regarding the hazards of the various herbicides from an occupational perspective. Such judgments are made independently of MBPC regulatory responsibility relating to the overall public health and welfare of the citizens of Maine.

Several pesticides and herbicides have been examined through public hearings sponsored by MBPC because of the hazard potential. At the hearings, the methodology used for risk assessment was critically examined and found to have scientific validity. Because of the health data brought to light by risk assessment, the Commissioner of Agriculture applied additional restrictions on the use and application of herbicides in the state.

Envirologic Data has, since its inception, provided all of MDOT's health risk assessment services. The following herbicides have been assessed:

- Fosamine ammonium (trade name, Krenite™);
- Glyphosate (trade name, Roundup™);
- Dicamba (trade name, Banvel™);
- Triclopyr (trade name, Garlon™);
- Dalapon (trade name, Dowpon™);
- Diuron (trade name, Karmex™); and
- Bromacil (trade name, Hyvar™).

MDOT has reviewed the risk assessments of herbicides to determine which pose the least threat to employee health. Decisions are made as to which herbicides should be used for the various spray program needs throughout the growing season. Eventually, with health risk assessments for each herbicide, detailed comparisons can be performed to identify the least hazardous herbicides for use.

HEALTH MONITORING

Methodology

An ongoing health monitoring program for employees potentially at risk is an important tool in evaluating the effects of chronic, low-level exposure or acute exposures related to accidents in handling or application of herbicides. Although acute toxicity is usually readily recognized and medically manageable via established treatment procedures, chronic or long-term toxicity is neither manifested quickly nor easily recognized. Thus, an employee health monitoring program must be comprehensive in scope and include indicators of subclinical disease and exposure. Specifically, laboratory testing capable of detecting biochemical or physiological changes that may be precursors of overt disease is a necessity.

The health monitoring program should include the following components:

- Review of herbicide use and principal health effects of herbicides;
- Review of nonoccupational (avocational) exposures to chemicals;
- Medical screening;
- Data analysis and reporting; and
- Periodic monitoring.

A review of herbicides used in a spraying program is important in identifying relationships between exposures and possible health effects. With a knowledge of principal health effects, interpretation of results of laboratory tests and other medical screening is possible. Ideally, information from the health risk assessment provides definitive information regarding possible human health effects. Where such data are lacking, results of animal testing and other research methodologies may be used to reflect the potential for effects in humans.

The initial medical screening program establishes a baseline medical profile for comparison with test values to be derived from future periodic monitoring. Initial screening also identifies medical problems that may place the employee at above-normal risk in relation to occupation. The following constitutes a broad-based initial screening:

- History and physical examination. The employee's past medical and occupational histories are ascertained via the Milcom Health History Questionnaire and interview with the physician. The physical examination includes a detailed evaluation of body organ systems that are most likely to be affected by herbicide exposure.
- Laboratory evaluation. An extensive battery of laboratory tests complements the history and physical examination. Acute exposure to toxic sub-

stances is generally recognized and medically manageable based on established procedures and manifested symptoms. However, because chronic exposure to low levels of potentially toxic materials may not produce obvious signs and symptoms of illness, detailed laboratory assessment is necessary to detect changes in biochemical and physiological parameters. The battery of laboratory tests performed allows evaluation of blood composition, electrolyte balance, enzyme levels, organ function, the immunological system, and pulmonary function.

Data analysis and reporting involve compilation of the initial medical screening data to allow statistical comparisons of individual test results with group norms, and group norms with general population norms. For large groups, this is facilitated by using computer data base management software. Data analysis may detect deviations from acceptable normal limits, group trends, and identifiable symptoms possibly related to exposure. Medical concerns unrelated to occupational exposures are reported to individuals for followup with their personal physicians. Results relating to possible occupational exposure are reported for consideration by management.

Periodic reexamination of employees involved in the program is important for monitoring current health status and for comparing followup results with the baseline values originally established. Recommendations for ongoing monitoring should be based on initial test results and the degree of potential exposure, among other criteria.

Results

A health monitoring program for MDOT was initiated in May 1984. Initial program results for more than 30 employees have been reported (4) and include findings of abnormalities that may or may not be related to occupational causes.

Nonoccupation-related problems were reported directly to monitored individuals; four, in particular, were treated as special cases in that early medical treatment of existing conditions was indicated. Several other individuals were advised to follow up on potential medical problems such as lung disease, liver inflammation, lipid disorders, high blood pressure, anemia, diabetes mellitus, and nonhemolytic jaundice. Single cases of possible atherosclerotic vascular disease, carpal tunnel syndrome, early rheumatoid arthritis, connective tissue disorder, gastrointestinal blood loss, urinary tract infection, eczema, and tinea were discovered.

No definitive findings of occupational illnesses have yet been made. However, based on statistical comparison of individual test results with group norms, several individuals were identified who may possibly be responding to occupational exposures and who require further testing. In particular, tests for liver enzyme activity and cholinesterase levels in plasma and red blood cells revealed marginally abnormal results for several individuals. The liver enzyme levels were slightly to moderately elevated, whereas the cholinesterase values were slightly depressed compared with statistical norms. These test results may indicate exposures to herbicides used in MDOT's spray programs; however, the same results can be caused by other substances commonly encountered in our highly technological society--or they may be unrelated to exposures to particular substances. If it were deemed important to establish a causal relationship as a condition for corrective action, further testing for specific substances would be necessary.

It is important to emphasize that these results do not indicate the presence of herbicide-induced disease, nor do they indicate that occupational exposures have occurred. An alternative possibility is that, for some or all of these individuals, nonoccupational medical effects may have been detected. Additional testing and analysis are required to define the causes of the abnormal test values. These results demonstrate the importance of ongoing monitoring. Through reexamination and specific evaluations, and repeating key tests, trends can be delineated or suggestive findings can be confirmed.

RISK MANAGEMENT

Methodology

Risk management, when necessary, is the responsibility of the client; moreover, the issue of acceptable risk levels that would trigger risk management action can only be determined by the client. Nevertheless, options for addressing this question can be proposed. In general, if risks are perceived to be sufficiently great to trigger health monitoring, simple risk management strategies should, at a minimum, be developed.

Risk management strategies must be implemented when exposure to a particular substance exceeds regulatory exposure guidelines. Such strategies may be simple and economical. The greatest expense for risk management is, of course, justified when the required degree of risk abatement is greatest, and this situation typically arises most urgently in the unusual event that health monitoring reveals job-related pathology.

The methodology for determining whether a disease is job-related is most difficult when the disease is common in the general population, and easiest when it is rare except in association with a particular occupation (clustered). Clustering of health effects can arise from on-the-job experiences or from off-hours experiences shared by an occupational group, such as social activities. Determining job-relatedness of disease is accomplished by statistically comparing the observed incidence (frequency) of cases of the disease among employees with the expected incidence among the general population. As a rule, the more commonly a disease occurs in the general population, the more of an excess of disease cases among employees would be necessary to document its job-relatedness. Moreover, some evidence is necessary that the disease can, at least potentially, be causally related to the substance(s) to which employees are known to be exposed.

What does risk management mean for herbicide applicators? It may mean no change in operations, if there is no evidence of occupational illness. On the other hand, it may mean substituting safer herbicides; using less volume, lower concentrations, or alternate formulations of a given herbicide; applying the herbicide under more restrictive weather conditions or over shorter periods of the growing season; or wearing protective garments or breathing apparatus. In any case, employee training programs must be designed to educate employees about the importance of adhering to appropriate risk management strategies and numerous other standard operating procedures.

Results

MDOT's risk management program is currently implemented in-house rather than via procuring private risk management services. MDOT's in-house program

emphasizes careful herbicide selection and exposure control. To date, Envirologic Data's work for MDOT has only involved making recommendations regarding health monitoring results and the proposal for re-examination. After confirmation is obtained for the cause of the abnormal values discovered in the baseline testing, specific actions may be recommended to MDOT management for incorporation into the existing risk management policies and procedures. This complements well the current use of the health risk assessment data the department uses for selection of herbicides.

DISCUSSION OF CRITICAL ISSUES

By incorporating several of the program elements described in this paper into its approach to regulating and managing use of toxic substances, MDOT has assumed an aggressive posture in protecting the public health and the health of state employees who apply or otherwise encounter such substances. Herbicides will continue to be used in maintaining transportation corridors. Developing and establishing the means to assess and manage risks incurred through such use is the only rational approach to the complex environmental and health issues posed.

Exposure Assessment

Potential exposure to a particular hazard generally varies in proportion to the production volume of the hazard. This potential for exposure assumes, in the worst case, that all of the substance that has been produced is released into the environment. The realistic case is then determined by evaluating the actual practices that are designed to prevent fugitive releases during production, distribution, use, and disposal. Hence, the substance of interest may spread progressively over a geographically wider area, but its concentration would diminish rapidly in the process in proportion to the effectiveness of control measures.

In addition to possible geographic spread there is a time dimension, that is, the substance exhibits a degree of stability or instability that determines its half-life (time required for half of an initial amount of the substance to degrade) in each environment. The half-life is, more specifically, determined by the ability of the substance to withstand physical, chemical, and biological degradation processes acting on it in varying proportions in terrestrial, aquatic, atmospheric, and other environments. A substance that exhibits a low water solubility and high vapor pressure may rapidly move from the aquatic to the atmospheric environment through strictly physical transformations of state. A substance that hydrolyzes readily might be chemically stable in dry soil, but unstable in aquatic environments. The issue of whether instability of the substance corresponds to detoxification must be addressed via examination of the breakdown products.

The accuracy of exposure assessment depends on the realism of the assumptions on which it is based. Decisions by MDOT regarding herbicide use must frequently be made before experience has been accumulated in the state. Consequently, realistic exposure assumptions are more difficult to formulate.

Providers of exposure assessment services should prominently set forth the exposure assumptions that underlie their estimates. Moreover, they should convey some sense of the degree of uncertainty, statistically or otherwise, attending their estimates and assumptions. When these practices are followed, the reward for undertaking exposure assessment is likely to be increased protection of potentially exposed populations and environments, as well as--in the longer term--less need for stringent regulatory action for protection.

The advantages of exposure assessment, cited earlier, can be simultaneously achieved because, in the absence of exposure assessment, worst-case assumptions should properly be adopted by decision makers. Such assumptions protect workers and the public to the maximum extent possible. The role of exposure assessment is not to relax that high level of protection; rather, it is to identify the routes of exposure that contribute most to overall risk, and thereby to suggest the most cost-effective means of exposure risk management. Thus, exposure assessment contributes to definition of controls that must be imposed on use of substances such as herbicides. Controlled use usually constitutes safe use, as well as a viable alternative to prohibition of use.

Health Risk Assessment

A critical issue in assessing health risks is the proprietary nature of some of the most useful data. The degree of disclosure required of manufacturers by law (by the Federal Insecticide, Fungicide and Rodenticide Act and its amendments, as well as by other statutes, including administrative law) is in flux; however, proprietary information is frequently voluntarily made available under constraints of a nondisclosure agreement signed by the consulting firm and, possibly, the client firm. Nondisclosure may be interpreted in many ways, but any such agreement should permit the use of company data for drawing conclusions regarding exposure and health risk, though limits may be placed on the freedom of the consultant or client to cite or otherwise reveal company data in support of consulting or decision documents.

A second critical issue involves the appropriate scope of the consultant's health risk assessment services. For example, a criterion of risk is persistence of the hazard in natural and agricultural ecosystems. Persistence is measured by the half-life of the substance, but half-life of the substance may be very different from half-life of toxicity. Consequently, the question arises of whether the consultant's scope of work should include evaluating intermediate breakdown products. This can be of critical significance in cases where the breakdown products are themselves persistent and/or toxic. If breakdown products are excluded from the consultant's scope of work, the possibly erroneous impression may be conveyed that a risk is transient, when what is meant is that a substance is transient.

A third critical issue is the consultant's willingness and ability to examine and interpret data that might be ambiguous, complex, or controversial. One error that consultants may make is to conclude that a particular adverse health effect, for example cancer, is not caused by a substance when in fact it might be. The error may easily arise from the consultant's acceptance and misinterpretation of an investigator's conclusion that the substance was not carcinogenic in a test organism, or in any number of tests. Tests for carcinogenicity frequently involve small numbers of test animals, severely limiting the power of the test to detect cancer causation except when a very high proportion of the animals develop it. Hence, carcinogenicity tests tend to be one-sided; negative results should not signify absence of carcinogenic risk. The maxim holds that "absence of evidence is not evidence of absence".

Health Monitoring

The primary objective of the health monitoring program is to detect adverse health effects that may

be associated with occupational exposure to herbicides. However, because of the frequently comprehensive nature of medical screening, abnormalities not associated with occupational exposures may be found. Such findings should be reported to the affected individuals for followup with their personal physicians. Therefore, the results of a program normally are reported as either related or not related to occupation.

An issue of confidentiality is raised in connection with findings of nonoccupation-related disease. Such medical screening results must remain confidential in keeping with the normal patient-doctor relationship. These results are reported only to the monitored individuals. However, the issue of confidentiality is again raised in cases of abnormal findings which, though unrelated to occupation, may be exacerbated by particular job assignments. As a resolution of this issue, the service provider may inform the employee, who then seeks reassignment to an alternative job compatible with his or her medical condition. Alternatively, the service provider may seek permission of the employee to confer with management regarding any medical conditions constraining the employee's position assignment.

Risk Management

The most critical issue is that of acceptable risk, that is, deciding on an acceptable target for risk management strategies. As a general rule, costs increase with increasing management and decreasing risks. The consultant should, if possible, set forth several risk management options, ranked by expected risk reduction efficacy. The client or the consultant can supply the cost estimates corresponding to each option. Implementation by the client typically begins with the option that reduces the most risk at the least cost, and proceeds by selection of each best-remaining risk reduction option. The process typically ends when either the acceptable risk target or the budget endpoint is reached.

Determination of acceptable risk by budget is not recommended from a toxicological viewpoint and, in some situations, may be illegal. However, there are rarely guidelines for determining acceptable risk with regard to exposure to the many hazards for which regulatory standards are nonexistent. Traditionally, but for no toxicologically justifiable reason, occupational risks regarded as acceptable have been higher than acceptable risk levels to the general population. Typically acceptable general population risks, based on historical U.S. Environmental Protection Agency (EPA) regulatory actions, have been on the order of 10^{-6}, that is, one additional death associated with a regulated substance per million individuals over a lifetime. Occupational risks of 10^{-4} (one in 10,000) and even greater have been tolerated. Recent trends have resulted in toleration of higher risks (5) and, at least among workers, to expressions of concern about risk (6).

A corollary of acceptable health risk is acceptable liability, that is, liability for health damage that can be linked to occupational causation. Liability includes Workmens' Compensation insurance, toxic tort law settlements and awards, as well as victims' compensation legislation, which may be on the horizon. The implication of the emerging toxic tort, victims' compensation, and acceptable liability issues is that risk management must increasingly adopt a prospective philosophy. This means making essentially speculative investments in risk reduction when uncertainty about health risk exists. The services described in this paper, taken together, aim at "fine-tuning" to avoid both health damage and associated liabilities, but the state of the art in toxicology is insufficiently advanced to fully accomplish this mission. Nevertheless, the client can make effective decisions with regard to selection of highly qualified consultants and application of stringent risk management standards today to avert potential problems tomorrow.

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Appendix

Envirologic Data Digital Relative Rating Scale and Rating Criteria

Acute Toxicity

1 LD_{50} >5,000 ppm
2 LD_{50} 50-5,000 ppm
3 LD_{50} <50 ppm

Teratogenicity

0 = Studies show substance to be nonteratogenic
1 = No data available or data inconclusive
2 = Teratogenic in nonmammalian species or
Teratogenic in one mammalian species
3 = Positive in human epidemiological study or
Teratogenic in two or more mammalian species or
Teratogenic in one mammalian species with teratogenicity in nonmammalian species

Carcinogenicity

0 = Studies show substance to be noncarcinogenic
1 = No data or data inconclusive
2 = Positive in short-term carcinogenicity tests or
Positive in long-term carcinogenicity bioassay in one mammalian species without corroboration
3 = Positive in human epidemiological study, or
Positive in long-term carcinogenicity bioassay in two or more mammalian species, or
Positive in long-term carcinogenicity bioassay in one mammalian species with corroboration by replication and short-term carcinogenicity tests

Mutagenicity (Sample short- and long-term mutagenicity tests are included at end of this Appendix.)

0 = Studies show substance to be non-mutagenic
1 = No data available or data inconclusive
2 = Positive in short-term mutagenicity tests or
Positive in long-term mutagenicity bioassay without corroboration
3 = Positive in human epidemiological study or
Positive in two or more long-term mutagenicity bioassays or
Positive in long-term mutagenicity bioassay with corroboration by short-term mutagenicity tests

Persistence

0 = Half-life of less than 24 hr
1 = Half-life of 24 hr to one week
2 = Half-life of one week to one month
3 = Half-life of one month or greater

Reproductive Rating Scale

Female

0 = Substance shows no reproductive effects
1 = No data or
Data inconclusive or
Uterine weight change in animals or
Hormonal pattern change
2 = Decrease weight of offspring < 15 to 20 percent
3 = Human uterine weight change or
Follicular failure [Note follicular failure: destruction, change in maturation, depletion, corpus luteum.] or
Anovulation (interruption--temporary or permanent) or
Decrease number of offspring (litter per year, number per litter) or
Fetal resorption due to maternal effects or
Decrease weight of offspring > 15 to 20 percent or
Positive human epidemiological study

Male

0 = Substance shows no reproductive effects
1 = No data or
Data inconclusive or
Prostate weight change or
Alteration of prostate secretions
2 = Decrease sperm count is greater than level for fertility [Note fertility level: at least 16 to 20 million sperm/ml.; 50 percent should have rapid motility and mature oval heads; accept 30 percent abnormal forms.]
3 = Decrease in sperm count is less than level for fertility or
Arrested spermatogenesis or
Testicular atrophy or
Positive human epidemiological study

Examples of Short-Term and Long-Term Tests Used in Mutagenicity Rating

Short-Term Tests

Ames salmonella/microsome test
Mitotic recombination and gene conversion in S. cerevisiae
Transformation in cell culture
Chromosome aberrations in cell culture
Unscheduled DNA synthesis
Sister chromatid exchange
Microbial host mediated assay
Experiments with Drosophila
Bird studies
Relative toxicity test

Long-Term Tests

Dominant lethal test in rodents
Heritable translocation assay
Specific mutation assay
Mouse micronucleus assay
In vitro human chromosome breakage