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GUIDANCE MANUAL FOR ASSESSING HUMAN HEALTH RISKS FROM CHEMICALLY CONTAMINATED FISH AND SHELLFISH

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INTRODUCTION

Contamination of aquatic resources by toxic chemicals is a well recognized problem in many parts of the U.S. High concentrations of potentially toxic chemicals have been found in sediments and in aquatic organisms from Puget Sound, the Southern California Bight, northeast Atlantic coastal waters, the Hudson River, the Great Lakes, and elsewhere (Malins et al. 1984; Tetra Tech 1985b,d, 1986c; Brown et al. 1985; DeVault et al. 1986; Rideout and Bender 1986). Heavy consumption of contaminated fisheries products by humans may pose a substantial health risk (e.g., Sonzogni and Swain 1984; Swain 1986; Capuzzo et al. 1987). This concern has prompted recent studies of catch and consumption patterns for recreational fisheries and associated health risks (e.g., Puffer et al. 1982; Conner 1984; Landolt et al. 1985, 1987; Versar 1985; Swain 1986).

To protect the health of consumers of fish and shellfish, information is needed on relative health risks associated with various edible aquatic species, geographic locations, and consumption rates. In the past, diverse models have been used to estimate human health risks from exposure to toxic substances in food [e.g., Cordle et al. 1978; U.S. Office of Technology Assessment 1979; U.S. Environmental Protection Agency (EPA) 1980b; Food Safety Council 1980, 1982; Connor 1984; Tollefson and Cordle 1986]. For consistency among EPA regions and programs, a standardized procedure is recommended here for assessing human health risks from consumption of chemically contaminated fish and shellfish.

OBJECTIVES

The purpose of this manual is to provide guidance for health risk assessment related to chemically contaminated fisheries based on EPA approaches (e.g., U.S. EPA 1980b, 1986a-e, 1987a). The objectives of the guidance manual are to:

- Describe the steps of a health risk assessment procedure for consumption of contaminated fish and shellfish
- Provide guidance on presentation of risk assessment results
- Summarize assumptions and uncertainties of the recommended procedure for risk assessment
- Summarize standard model variables (e.g., Carcinogenic Potency Factors or Reference Doses for chemicals) and criteria [e.g., U.S. Food and Drug Administration (FDA) action levels] related to risk assessment, and information sources for updating these values.

The guidance provided in this manual is directed primarily at risk assessment related to recreational fisheries. Although assessment of human health risks from commercial fisheries products is not addressed specifically in the examples provided herein, many of the concepts discussed throughout the manual are relevant to risk analysis of commercial fisheries.

This manual provides guidance only, and does not constitute a regulatory requirement of any kind. The technical content is entirely consistent with approved EPA procedures for risk assessment, as published in the Federal Register (U.S. EPA 1986a-e). The relationship between these procedures and risk assessment approaches used by FDA is described briefly in the background section below.

ORGANIZATION

Background information on available health risk assessment guidance and use of this manual is provided in the remainder of this introduction. An overview of risk assessment is provided in the following section, including a discussion of the distinction between risk assessment and risk management, and a review of their possible uses. The major steps of the risk assessment process recommended herein are described in subsequent sections. Guidance is provided on mathematical models used to estimate chemical exposure and risk. Sources of information on toxic chemicals and model variables are noted. Finally, suggestions for presentation of risk assessment results are provided. Uncertainties and assumptions of the assessment approach described in this manual are summarized.

BACKGROUND

Risk analysis encompasses both risk assessment and risk management. Risk assessment is a scientifically based procedure to estimate the probability of adverse health effects from a specific exposure to a toxic agent. Risk assessment differs from risk management, although both are elements of regulatory decision-making (National Research Council 1983). Risk assessment provides the scientific basis for public policy and action. In risk management, risks are interpreted in light of legislative, socioeconomic, technical, and political factors, and appropriate controls are determined. Risk management often involves defining an acceptable risk level, i.e., the maximum risk considered tolerable. Risk management often involves evaluation of risks in light of potential benefits associated with an activity. For example, a risk manager might weigh the risks associated with chemical contamination of fish and shellfish against the health benefits (e.g., decreased risk of heart disease) associated with consumption of fish and shellfish in place of red meat.

In September 1986, EPA published final guidelines for assessing health risks related to environmental pollutants. The guidelines are in five parts (U.S. EPA 1986a-e):

- Carcinogen Risk Assessment
- Exposure Assessment
- Mutagenicity Risk Assessment
- Health Assessment of Suspect Developmental Toxicants
- Health Risk Assessment of Chemical Mixtures.

These guidelines pertain to health risk assessment for all environmental exposures [e.g., air exposure; ingestion of water or environmentally contaminated foods; and other direct human contact with contaminated soils, water, sediments, or other materials (FR51 No. 185, p. 34049)]. The guidelines were developed through a 2-year process that included contributions and review by the larger scientific community; full Agency consideration of public comments in response to proposed guidelines on November 23, 1984; and review and approval by the EPA Science Advisory Board (FR51 No. 185, p. 33992).

This guidance is in the form of a policy statement and does not constitute a regulatory requirement. The guidance is intended simply to describe what EPA believes to be the most scientifically defensible methods for assessing environmental health risks, and to inform the public that these are the methods EPA will use in conducting the health risk assessments required in its statutorily mandated programs.

While U.S. EPA's (1986a-e) risk assessment guidelines apply to all exposure routes, they do not contain detailed information on application of the basic principles for each exposure route. This guidance manual provides such step-by-step assistance for assessing health risks from exposure through consumption of chemically contaminated aquatic organisms. The guidance is applicable to freshwater, brackish water, and saltwater fish and shellfish. It is based entirely on the principles set forth in U.S. EPA (1986a-e).

As described in a recent report by EPA's Risk Assessment Council and FDA (U.S. EPA and U.S. FDA 1987), FDA, EPA, and the states have somewhat differing roles in assessing and managing risks from fish consumption. These roles are summarized below.

FDA has the lead responsibility for risk management of foods in interstate commerce or other products of national importance including fish and shellfish. For some chemicals in foods (specifically pesticides), EPA assists FDA in performing the technical risk assessments that support risk management decisions. The federal government is not directly responsible for managing risks to individuals who consume unusually large amounts of foods not in interstate commerce or foods harvested from locally contaminated areas (e.g., some recreational fisheries). Environmental agencies and health departments at the state and local levels have responsibility for protecting consumers of local fisheries products. These agencies are responsible for issuing public health advisories and regulations related to local fisheries.

Only the FDA has federal responsibility for setting action levels and tolerances for concentrations of specific chemicals in fish or other foodstuffs that constitute sufficient health hazards to the general public to require that the foodstuffs be removed from interstate commerce. Action levels are established and revised according to criteria in the code of Federal Regulations (21 CFR 109 and 509). An action level is revoked when a formal tolerance for the same substance is established. In developing action levels and tolerances, FDA takes into account both the magnitude of the health risks to consumers and the economic impacts of banning a foodstuff from a particular source. FDA sets limits on chemical contaminants in fisheries products to achieve an optimal balance of health protection and minimization of economic impacts on food-producing and harvesting industries (e.g., commercial fisheries and fish marketers).

All action levels and tolerances to date have been developed to be protective nationally, rather than on a regional or local basis. These national standards protect

the average consumer of a foodstuff, assuming the consumer eats foods from a typical "national market basket" (U.S. FDA 1984). For these reasons, it has been stated by FDA that action levels and tolerances are not intended to protect certain consumers of local fish and shellfish, such as local recreational fishermen whose consumption of fish from a given water body may exceed the national average (Taylor, J., October 1986, personal communication).

EPA and FDA recognized the need to coordinate their activities and guidance in assessing health risks from contaminated fish and shellfish. A formal interagency mechanism is being created to resolve potential differences in risk assessment calculations for specific chemicals or specific exposure situations. U.S. EPA and U.S. FDA (1987) provides a detailed discussion of the evolving FDA/EPA coordination and procedures whereby states can obtain further information or assistance pertaining to risk management in specific local situations.

Applicability of this Guidance Manual

EPA's nonregulatory technical guidance, including this manual and the 1986 final guidelines for risk assessment (U.S. EPA 1986a-e), is available to state and local governments responsible for fisheries management. This manual is intended for use as a handbook by state and local agencies responsible for assessing potential risks from local fish or shellfish consumption. For example, it may be useful in assessing risks to highly exposed regional populations (e.g., certain fishermen or families who may eat unusually large amounts of fish) and in cases where a national action level or tolerance has not been defined for a chemical that is a local pollution problem. This manual does not provide guidance on policy issues that are beyond the scope of the technical risk assessment process (e.g., selection of acceptable risk levels, and methods for performing local cost-benefit analyses). Such risk management decisions at state and local levels are not ordinarily within the scope of federal regulatory authority.

For specific technical assistance in applying the risk assessment methods described in this manual, users may call the EPA Office of Water (see Appendix A) for updated information on regional EPA facilities that can provide on-site assistance in applying risk assessment techniques.

Relationship of this Manual to Other EPA Documents

This manual is not intended as an exhaustive, technically-detailed guide to all aspects of sampling, statistical design, laboratory analysis, exposure assessment, and toxicological risk analysis. Citations are provided to references that provide details on these topics. In addition, several other EPA documents are available that provide relevant information:

- U.S. EPA (1987a) Integrated Risk Information System (IRIS) Manual - A regularly updated electronic database on the toxicity and carcinogenicity of individual chemicals (see Appendix B herein)

- Contaminants in Fish: The Regulation and Control of Residues for Human Safety [Report by the EPA Risk Assessment Council Subcommittee on Fish Residue Issues (U.S. EPA and U.S. FDA 1987)]. This report includes a discussion of the relationships of EPA, FDA, and state responsibilities for risk assessment and risk management.

- General guidelines on exposure and risk assessment (U.S. EPA 1986a-e) discussed earlier.

- Guidance documents on risk assessment approaches for specific chemicals [e.g., dioxins and dibenzofurans (Bellin and Barnes 1986)].

- Superfund Risk Assessment Information Directory (U.S. EPA 1986g).

- Risk Assessment, Management, Communication: A Guide to Selected Sources (U.S. EPA 1987b) - A general bibliography which is updated periodically.

Relationship of Fisheries Risk Assessment to Water Quality Criteria and Standards

The Criteria and Standards Division of EPA's Office of Water Regulations and Standards is responsible for developing water quality criteria for the protection of aquatic life and human health. Section 304(a) of the Clean Water Act requires EPA to develop recommendations for criteria to be used by the states in setting water quality standards. These criteria are summarized in "Quality Criteria for Water - 1986" (U.S. EPA 1986h). The technical procedures for deriving human health criteria for water are described in "Water Quality Criteria Documents; Availability" (U.S. EPA 1980b).

Water quality criteria and standards are established as guidelines or legal measures for acceptable concentrations of contaminants in water. State agencies and EPA use water quality criteria and standards to regulate discharges of contaminants to surface waters. In contrast, the risk assessment approach described in this document may be used to develop guidelines on concentrations of chemical contaminants in tissues of fish and shellfish. Data on tissue concentrations of contaminants are often used by state health departments in regulating human exposure to contaminated fish and shellfish, or in developing health risk advisories that allow sport fishermen and other frequent fish eaters to adjust their own consumption rates. The risk assessment methods described in this manual are consistent with those used by EPA to develop water quality criteria. Moreover, the toxicological and epidemiological data used to establish guidelines for concentrations of contaminants in fish and shellfish are the same as those used to develop acceptable levels in water. In developing water quality criteria, U.S. EPA (1980b, 1986h) considered human health risks from consumption of chemically contaminated fish and shellfish. For each chemical, a bioconcentration factor was used to establish the relationship between contaminant concentrations in fish and shellfish associated with three "reference" (i.e., benchmark) levels of health risk (10^{-5}, 10^{-6}, 10^{-7}) and corresponding concentrations of contaminants in water. A bioconcentration factor is an empirically derived measure of the potential for a chemical to accumulate in tissues

of aquatic organisms. Bioconcentration factors are usually expressed simply as the ratio of the chemical concentration in tissue to the concentration in water.

Relationship of EPA Risk Assessment Methods to FDA Risk Assessment Methods

Because of differences in legislative and regulatory responsibilities among EPA, FDA, and state and local governments, these entities have developed differing procedures for risk assessment and risk management. As an EPA guidance manual, this document presumes the use of standard EPA risk assessment procedures. However, certain procedures recommended in this manual can be modified to make the risk assessment compatible with alternative approaches used by FDA and some states. This section explains how conversion factors can be used to make risk assessment procedures recommended herein compatible with certain assumptions used in FDA risk assessments.

A major difference between EPA and FDA risk assessment approaches concerns the methods for extrapolating the toxic potency of chemicals in small experimental animals (e.g., rats and mice) to estimate potential effects in humans. U.S. EPA (1986a) pointed out several species-specific factors that may influence the response to a carcinogen, including life span, body size, genetic variability, concurrent diseases, and the rates and products of metabolism and excretion. To account for at least some of the differences between experimental animals and humans, the estimate of exposure in laboratory animals is multiplied by a scaling factor to obtain an estimate of equivalent dosage in humans. EPA uses the ratio of animal-to-human surface area, whereas FDA uses a corresponding ratio of body weights as a scaling factor. Thus, EPA uses mg of carcinogen per m^2 body surface area per day as a standardized scale for expressing dosages, whereas FDA uses mg carcinogen per kg body weight per day. This difference in interspecies extrapolation factors results in approximately a five- to ten-fold difference in estimates of carcinogenic potency (and risk) derived by the two agencies.

In recognition of the difficulties that differences in interspecies extrapolation procedures between EPA and FDA may pose for state agencies and others who rely on federal guidance on risk assessment, EPA's Risk Assessment Council and FDA reviewed the pros and cons of their respective methods for dosage scaling. They concluded that the most appropriate method for interspecies dosage extrapolation may vary depending on exposure conditions. For example, one procedure may be more realistic for lipophilic chemicals, whereas the other would be more appropriate for hydrophilic chemicals. Differences in target organs (i.e., primary site of toxicity) among carcinogens also affects the preferred extrapolation procedure.

Because the EPA extrapolation procedure results in a higher estimate of risk than the FDA procedure (by approximately an order of magnitude), the former is considered more protective. For most EPA assessments, the surface-area based extrapolation is appropriate. The technical basis for EPA's approach relies primarily on a demonstrated relationship between pharmacological effects (e.g., balance of rates of metabolism and excretion) and body surface area (Pinkel 1958; Freireich et al. 1966; Dedrick 1973). If state or local policymakers decide that the body-weight based extrapolation is more appropriate for local risk management needs, then procedures recommended in this manual can be modified by converting EPA's dose-response data using a ratio of human body weight to surface area. This would allow the risk assessor to use carcinogenic potency factors in EPA's computerized database, IRIS (U.S. EPA 1987a). IRIS is a database maintained by EPA to provide regularly updated toxicological data for use in

risk assessment. The use of IRIS would greatly increase the ability of a state to perform risk assessments for chemicals of local concern.

Although the conversion of EPA estimates of toxic potency to estimates based on equivalent dosage scales related to body weight is not technically complex, the modified procedure should preferably be carried out only by experienced toxicologists. The conversion factor will vary depending on whether the dose-response data were derived from rats or from mice. Thus the original data set must be reviewed to determine an appropriate conversion factor. In general, an EPA estimate of carcinogenic potency would be multiplied by a factor equal to the ratio of surface area per unit body weight (m^2/kg) of the laboratory animal to that of humans. For example, if the EPA carcinogenic potency factor is C and the surface area per unit body weight is X for the laboratory animal and Y for humans, the corresponding potency factor based on dosage scaled to body weight is C multiplied by X divided by Y. Because specific data on surface area are often unavailable, the body weight to the two-thirds power is typically used as an estimate of surface area. Note that some EPA carcinogenic potency factors are derived from epidemiological studies and therefore do not require conversion.

Other steps in the process to estimate carcinogenic potencies may vary somewhat among regulatory agencies. For example, different agencies may choose different data sets to derive a carcinogenic potency factor for the same chemical. The mathematical expression used to model the dose-response relationship may also differ among agencies. Hogan and Hoel (1982) and Cothern et al. (1986) discuss various models for extrapolating data from high doses used in laboratory experiments to the low doses of concern in carcinogenic risk assessment. At low doses corresponding to risks of 10^{-2} to 10^{-6} or less, different models may produce results that vary by as much as several orders of magnitude. Nevertheless, the linearized multistage procedure used by EPA (U.S. EPA 1986a; also see below, Dose-Response Assessment) yields results that correspond approximately (within a factor of two) to those produced by the linear model used by FDA. The interagency Subcommittee on Fish Residue Issues of the EPA Risk Assessment Council, which includes representatives from FDA, concluded that the differences in procedures for modeling dose-response relationships between EPA and FDA were small relative to the uncertainties in other steps of a risk assessment. Therefore, U.S. EPA (1987b) does not discuss procedures to reconcile these differences.

A final distinction between EPA's risk assessment procedures and other potential approaches is that EPA does not yet provide a standardized approach for assessing carcinogenic effects on children and fetuses. Information on peri-natal carcinogenicity is presently being developed by EPA and others.

OVERVIEW OF RISK ASSESSMENT AND RISK MANAGEMENT

As defined earlier, the objective of risk assessment is to estimate the probability of adverse health effects from exposure to a toxic agent. The elements of risk assessment and their relationship to risk management are shown in Figure 1. The following sections provide an overview of the steps in risk assessment, the need for risk assessment, and the potential uses of risk assessment of chemically contaminated fisheries. The general format for risk assessment and all definitions of terms used in this report are consistent with those provided by National Research Council (1983) and U.S. EPA (1984a-e, 1987a). Background information on food safety evaluation by federal and state agencies is provided by U.S. Office of Technology Assessment (1979) and Food Safety Council (1980, 1982). Examples of approaches used by FDA to assess human health risks from toxic chemical exposures are described in Cordle et al. (1978) and Flamm and Winbush (1984).

MAJOR STEPS IN RISK ASSESSMENT

A complete risk assessment includes the following steps:

- **Hazard identification**: Qualitative evaluation of the potential for a substance to cause adverse health effects (e.g., birth defects, cancer) in animals or in humans

- **Dose-response assessment**: Quantitative estimation of the relationship between the dose of a substance and the probability of an adverse health effect

- **Exposure assessment**: Characterization of the populations exposed to the toxic chemicals of concern; the environmental transport and fate pathways; and the magnitude, frequency, and duration of exposure

- **Risk characterization**: Integration of qualitative and quantitative information from the first three steps, leading to an estimate of risk for the health effect of concern.

Because uncertainties are pervasive in risk assessment, uncertainty analysis is a key element of each stage of the assessment process. Assumptions and uncertainties are summarized in the risk characterization step. The risk characterization includes a balanced discussion of the strengths and weaknesses of the data presented.

NEED FOR RISK ASSESSMENT APPROACH

Direct measurement of human health risks is possible in certain limited circumstances. Such circumstances generally involve a single high exposure or repeated moderate exposures of humans to a specific chemical with a clear adverse effect. For example, direct measurement of the incidence of chloracne (a skin disorder) might be

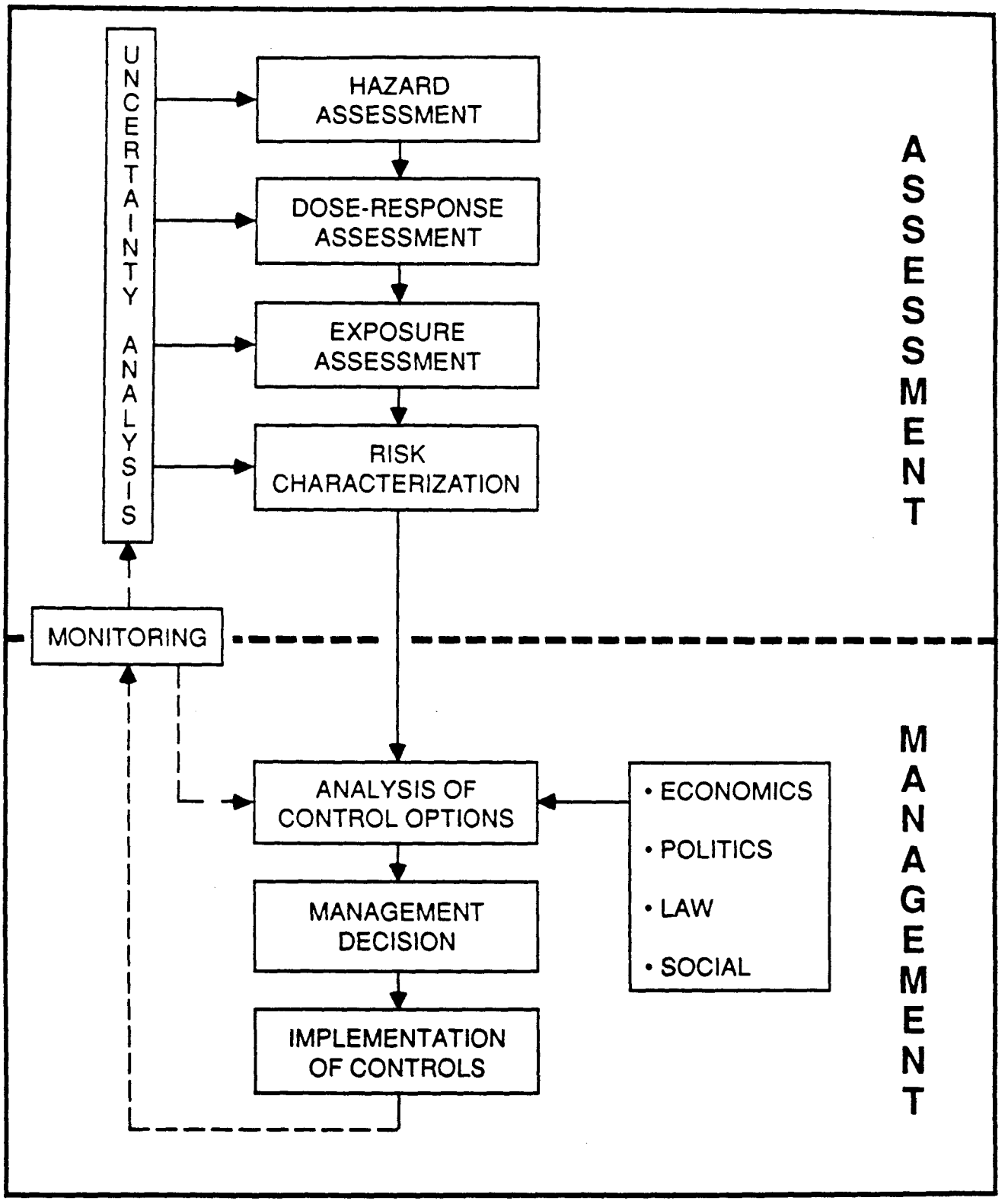


Figure 1. Overview of risk assessment and risk management

possible in a population of workers exposed to a polychlorinated biphenyl (PCB) spill. In contrast, it is virtually impossible to directly measure the incidence of cancer associated with consumption of chemically contaminated fish or shellfish. The long latency period for cancer, the potential for contamination of fisheries by multiple chemicals, and confounding exposures through other routes would complicate the interpretation of such data. Mathematical models are therefore used by EPA, FDA, the Agency for Toxic Substances and Disease Registry, states and, other regulatory agencies to estimate human health risks from exposure information. Risk assessment procedures discussed in this manual focus on estimating potential health risks from long-term exposure to relatively low levels of contamination. This prospective approach is also useful for developing regulations to prevent exposure to toxic chemicals and associated risks.

Scientific knowledge of the effects of toxic chemicals on humans is still rudimentary. Much of the present information is extrapolated from results of laboratory tests on animals (e.g., rats and mice). Animal test data are used to estimate levels of chemical exposure that are unlikely to cause toxic effects in human populations. Toxicologists are thus faced with many uncertainties when estimating the potential for human health risks associated with intake of toxic chemicals. Despite these uncertainties, regulatory decisions must be made. Many assumptions and subjective judgments may enter into an evaluation of human health risk. The risk assessment approach provides a framework for consistent, systematic estimation of health risks, with clear statements of assumptions and uncertainties.

The risk assessment framework offers an alternative to some common approaches to evaluation of data on chemical residues in fish and shellfish. As noted by Kneip (1983) and Peddicord (1984), many investigators have evaluated chemical residue data in light of human health concerns simply by comparing tissue concentrations of selected chemicals to action levels or tolerances established by U.S. FDA (1982, 1984). This approach is limited for the following reasons:

- FDA limits are available for only a few chemicals (mercury and approximately 13 organic compounds).
- FDA has not established regulatory limits for some of the most potent suspected human carcinogens (e.g., 2,3,7,8-tetrachlorodibenzodioxin) or for some of the common contaminants in surface waters (e.g., polynuclear aromatic hydrocarbons and most heavy metals).
- Action levels and tolerances were intended to be used only for regulation of interstate commerce of food products.
- When setting regulatory limits, FDA considers economic impacts of food regulation as well as the potential human health risks on a national basis (U.S. FDA 1984). When using FDA limits to interpret bioaccumulation data, investigators implicitly adopt economic policies of FDA. Thus, risk management issues are not clearly separated from risk assessments.

Use of regulatory limits on toxic chemicals in food products established by other countries (Nauen 1983) would suffer from many of the limitations listed above for FDA values. Moreover, a concise review of the basis for each of these limits is not available.

USES OF RISK ASSESSMENT

Risk assessment may be applied to data on chemical residues in fish and shellfish for the following purposes:

- Identify and rank toxic chemical problems in specific locations
- Develop environmental criteria or guidelines at the national, state, regional, or local level
- Develop public information and advisories.

The first two applications fall within the general category of regulatory decision-making. In this context, one goal of EPA is to define, identify, and set priorities for reducing unacceptable risks. Risk assessment and management provide a framework for balanced analysis of environmental problems and consistent policies for reducing health risks (e.g., through reduction of toxic pollutant discharges and cleanup of polluted areas).

Risk assessment can be used to identify and rank environmental problems in several ways. First, contaminated sites can be ranked according to the relative risks associated with consuming fish and shellfish harvested nearby (e.g., Versar 1985). Site rankings may be used to establish priorities for investigation of contaminant sources and for cleanup. Maps of chemical residue data or risk estimates provide a geographic overview of the condition of harvested resources. Second, priority chemicals can be identified according to associated health risks (e.g., Ames et al. 1987). Finally, various fishery species and weight classes within species can be ranked according to relative risks.

Risk assessment is an important analytical tool for developing environmental criteria and guidelines. For example, water quality criteria derived by U.S. EPA (1980b) are based in part on human health risk assessment. FDA uses quantitative risk assessment to estimate potential human health risks, which are considered together with economic factors in developing action levels for chemical contaminants in fishery products (U.S. FDA 1984). Risk assessment models can be used to develop guidelines on maximum advisable contaminant concentrations in recreationally harvested species. Such guidelines can contribute to development of target cleanup criteria established to develop remedial actions for contaminated sites.

The results of risk assessments may be used to inform the public about the relative health risks of various fishery species and geographic locations. Providing the recreational public with such information allows for individual choice in determining harvest area, target species, consumption rates, and other factors based on relative risk. Furthermore, risk assessment may contribute to management decisions by federal, state, and local agencies, which may include:

- Investigating sources of pollution
- Reducing exposure potential by implementing pollution controls
- Restricting fishery harvests by geographic area or by species
- Issuing public advisories or controls to limit:
  - Geographic area of harvesting
  - Harvest season
  - Harvest methods
  - Species harvested
  - Catch number
  - Size range harvested
  - Consumption rate.

Further information on the relationship between risk assessment and risk management may be found in U.S. EPA (1984), Ames et al. (1987), Lave (1987), Russell and Gruber (1987), and Travis et al. (1987).

HAZARD IDENTIFICATION

The first step in the risk assessment process is to define toxicological hazards posed by the chemical contaminants in samples of fish and shellfish. These hazards are summarized in a toxicity profile or IRIS chemical file for each contaminant of concern. The results of the hazard assessment influence the nature and extent of subsequent steps in risk analysis. For example, the endpoint of concern in dose-response assessment may be selected based on the most severe adverse effect identified in the hazard assessment. In the absence of quantitative data for other steps in the risk assessment process, the hazard assessment constitutes the final product for a qualitative evaluation of risk.

CONTAMINANTS OF CONCERN

The contaminants of concern to be included in a particular risk assessment should be selected based on the following criteria:

- High persistence in the aquatic environment
- High bioaccumulation potential
- High toxicity to humans (or suspected high toxicity to humans based on mammalian bioassays)
- Known sources of contaminant in areas of interest
- High concentrations in previous samples of fish or shellfish from areas of interest.

General information on persistence, bioaccumulation potential, and toxicity may be obtained from references such as Lyman et al. (1982) and Callahan et al. (1979). Other key sources that are periodically updated are the Registry of Toxic Effects of Chemical Substances (e.g., Tatken and Lewis 1983) and the Annual Report on Carcinogens (e.g., National Toxicology Program 1982). Specific information that is directly useful in risk assessment should be obtained from IRIS (see below, Sources of Information and Appendix B).

Recommendations regarding specific contaminants of concern are beyond the scope of this guidance manual. A general list of contaminants with available EPA toxicological indices [Reference Dose (RfD) or Carcinogenic Potency Factor] listed in IRIS is provided in Appendix B. The procedures for quantitative risk assessment outlined in this manual are designed for use only with chemicals having toxicological indices. The bioaccumulation potential of various chemicals is a key consideration in selecting contaminants of concern. EPA priority-pollutant organic chemicals and selected pesticides are listed in Table 1 in descending order of bioaccumulation potential, according to their octanol-water partition coefficients (Tetra Tech 1985a). Note that organic compounds with a log octanol-water partition coefficient greater than or equal to 2.3 were recommended

TABLE 1. ORGANIC PRIORITY POLLUTANTS AND 301(h) PESTICIDES RANKED ACCORDING TO OCTANOL-WATER PARTITION COEFFICIENTS (K_{ow})
(updated from Callahan et al. 1979)

Priority Pollutant No.	Substance	log(K_{ow})	Reference
69	di-n-octyl phthalate	8.06	m
83	indeno(1,2,3-cd)pyrene	7.66	
89	aldrin	7.40	o
79	benzo(ghi)perylene	7.05	i
111	PCB-1260	6.91	d
--[r]	mirex	6.89	b
75	benzo(k)fluoranthene	6.85	
74	benzo(b)fluoranthene	6.60	
82	dibenzo(a,h)anthracene	6.50	k
107	PCB-1254	6.48	d
73	benzo(a)pyrene	6.42	i
91	chlordane	6.42	i
92	4,4'-DDT	6.36	n
90	dieldrin	6.20	o
110	PCB-1248	6.11	d
129	TCDD (dioxin)	6.10	i
94	4,4'-DDD	6.02	i
106	PCB-1242	6.00	a
72	benzo(a)anthracene	5.91	j
112	PCB-1016	5.88	d
76	chrysene	5.79	j
93	4,4'-DDE	5.69	h
99	endrin aldehyde	5.60	
53	hexachlorocyclopentadiene	5.51	d
9	hexachlorobenzene	5.47	k
100	heptachlor	5.44	d
101	heptachlor expoxide	5.40	d
39	fluoranthene	5.22	j
84	pyrene	5.18	h
41	4-bromophenyl phenyl ether	5.08	g
64	pentachlorophenol	5.00	d
40	4-chlorophenyl phenyl ether	4.92	g
20	2-chloronaphthalene	4.72	g
81	phenanthrene	4.57	h
98	endrin	4.56	d
78	anthracene	4.54	h
109	PCB-1232	4.48	
80	fluorene	4.38	d
--[r]	methoxychlor	4.30	b
52	hexachlorobutadiene	4.28	f
66	bis(2-ethylhexyl)phthalate	4.20	d
68	di-n-butyl phthalate	4.13	m

TABLE 1. (Continued)

77	acenaphthylene	4.07	
67	butyl benzyl phthalate	4.05	b
108	PCB-1221	4.00	
8	1,2,4-trichlorobenzene	3.98	k
12	hexachloroethane	3.93	b
1	acenaphthene	3.92	b
102	alpha-HCH	3.85	p
103	beta-HCH	3.85	p
104	delta-hexachlorocyclohexane	3.85	h
--[g]	parathion	3.81	e
7	chlorobenzene	3.79	d
105	gamma-HCH	3.72	h
21	2,4,6-trichlorophenol	3.69	c
95	alpha-endosulfan	3.60	
96	beta-endosulfan	3.60	
97	endosulfan sulfate	3.60	
49	fluorotrichloromethane (removed)	3.53	c
26	1,3-dichlorobenzene	3.48	k
25	1,2-dichlorobenzene	3.38	k
27	1,4-dichlorobenzene	3.38	k
55	naphthalene	3.36	h
113	toxaphene	3.30	
38	ethylbenzene	3.15	
62	N-nitrosodiphenylamine	3.13	b
22	para-chloro-meta cresol	3.10	a
31	2,4-dichlorophenol	3.08	a
28	3,3'-dichlorobenzidine	3.02	
37	1,2-diphenylhydrazine	2.94	g
58	4-nitrophenol	2.91	d
--[g]	malathion	2.89	e
60	4,6-dinitro-o-cresol	2.85	
6	tetrachloromethane	2.64	d
42	bis(2-chloroisopropyl)ether	2.58	g
85	tetrachloroethene	2.53	b
11	1,1,1-trichloroethane	2.47	b
34	2,4-dimethylphenol	2.42	b
87	trichloroethene	2.42	b
15	1,1,2,2-tetrachloroethane	2.39	b
47	bromoform	2.30	
32	1,2-dichloropropane	2.28	
86	toluene	2.21	b
--[g]	guthion	2.18	
14	1,1,2-trichloroethane	2.18	
24	2-chlorophenol	2.16	b
50	dichlorodifluoromethane (removed)	2.16	c
4	benzene	2.11	d
51	chlorodibromomethane	2.08	
35	2,4-dinitrotoluene	2.00	
36	2,6-dinitrotoluene	2.00	
33	1,3-dichloropropene	1.98	
30	1,2-trans-dichloroethene	1.97	c

TABLE 1. (Continued)

--[s]	demeton	1.93	
23	chloroform	1.90	b
48	dichlorobromomethane	1.88	
56	nitrobenzene	1.83	b
5	benzidine	1.81	g
13	1,1-dichloroethane	1.78	
57	2-nitrophenol	1.77	
54	isophorone	1.67	b
71	dimethyl phthalate	1.61	b
16	chloroethane	1.54	
59	2,4-dinitrophenol	1.53	
29	1,1-dichloroethene	1.48	
65	phenol	1.46	a
10	1,2-dichloroethane	1.45	b
70	diethyl phthalate	1.40	b
63	N-nitrosodipropylamine	1.31	
44	dichloromethane	1.30	
19	2-chloroethylvinylether	1.28	g
43	bis(2-chloroethoxy)methane	1.26	g
3	acrylonitrile	1.20	b
18	bis(2-chloroethyl)ether	1.12	b
46	bromomethane	1.00	
2	acrolein	0.90	b
45	chloromethane	0.90	
88	vinyl chloride	0.60	
61	N-nitrosodimethylamine	-0.58	g

[a] Veith et al. (1979a).
[b] Veith et al. (1980).
[c] Gossett et al. (1983).
[d] Veith et al. (1979b).
[e] Kenaga and Goring (1980).
[f] Leo, A., 20 November 1984, personal communication.
[g] U.S. EPA (1980).
[h] Karickhoff (1981).
[i] Rapport and Eisenreich (1984).
[j] Miller et al. (1985).
[k] Means et al. (1980).
[l] Miller et al. (1984).
[m] McDuffie (1981).
[n] Chiou et al. (1981).
[o] Briggs (1981).
[p] Solubilities of the various isomers of HCH indicate that they will have similar $\log(K_{ow})$ values.
[q] Estimated according to the procedure described by Chiou et al. (1982).
[r] Chlorinated 301(h) pesticides that are not on the priority pollutant list.
[s] Organophosphorus 301(h) pesticides that are not on the priority pollutant list.
NA = not applicable.

by Tetra Tech (1985a) for inclusion in EPA Section 301(h) monitoring programs. EPA priority-pollutant metals are listed in Table 2 in descending order of bioaccumulation potential, according to bioconcentration factor (Tetra Tech 1985a).

Screening of potential contaminants of concern should be done on a case-by-case basis during preparation of risk assessments. When data on concentrations of contaminants in edible tissues of fishery organisms are available, preliminary calculations of potential risks may be made to rank chemicals by relative priority for detailed evaluation. If contaminant concentration data are available for soils, air, and water (at a hazardous waste site, for example), U.S. EPA (1986f) methods for selecting indicator chemicals for public health evaluations at Superfund sites may be used to gain perspective on contaminants of concern. For potential carcinogens, the qualitative weight of evidence for carcinogenicity should be considered. Those chemicals with sufficient evidence of carcinogenicity in humans should generally be considered as contaminants of concern.

TOXICITY PROFILES

Toxicity profiles are summaries of the following information for the selected chemicals of concern:

- Physical-chemical properties (e.g., vapor pressure, octanol-water partition coefficients)
- Metabolic and pharmacokinetic properties (e.g., metabolic degradation products, depuration kinetics)
- Toxicological effects (e.g., target organs, cytotoxicity, carcinogenicity, mutagenicity) according to specific uptake route of concern (i.e., ingestion).

A toxicity profile may consist of an IRIS chemical file. An example file taken from IRIS is provided in Appendix B.

The key elements of a hazard identification should be summarized in a concise tabular format. The examples shown in Table 3 and in the first two sections of the IRIS file (Chronic Systemic Toxicity; Risk Estimates for Carcinogens) in Appendix B illustrate the kinds of information used to evaluate toxicological hazards. Neither toxicity profile in Table 3 is intended to be comprehensive.

Information in a toxicity profile is used to support the weight of evidence classification for the likelihood of a chemical causing a given health effect. The endpoints considered should include noncarcinogenic as well as carcinogenic effects. EPA has developed a weight-of-evidence classification scheme which indicates the potential carcinogenicity of chemicals (U.S. EPA 1986a; 1987a). It includes the following categories:

- **Group A - Human Carcinogen:** This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer.
- **Group B - Probable Human Carcinogen:** This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited." It also includes agents for which the

ALPHABETIC LISTING OF CHEMICALS ON IRIS (03/31/87)

67-64-1	Acetone
79-10-7	Acrylic Acid
15972-60-8	Alachlor
116-06-3	Aldicarb
309-00-2	Aldrin
107-18-6	Allyl Alcohol
20859-73-8	Aluminum Phosphide
7773-06-0	Ammonium Sulfamate
7440-36-0	Antimony
74115-24-5	Apollo
7440-39-3	Barium
542-62-1	Barium Cyanide
43121-43-3	Bayleton
68359-37-5	Baythroid
1861-40-1	Benefin
17804-35-2	Benomyl
25057-89-0	Bentazon
92-87-5	Benzidine
50-32-8	Benzo[a]pyrene (BaP)
7440-41-7	Beryllium
92-52-4	1,1-Biphenyl
117-81-7	Bis(2-ethylhexyl)phthlate (BEHP)
111-44-4	Bis(chloroethyl)ether (BCEE)
74-83-9	Bromomethane
1689-99-2	Bromoxynil Octanoate
106-99-0	1,3-Butadiene
71-36-3	n-Butanol
85-70-1	Butylphthalyl Butylglycolate (BPBG)
7440-43-9	Cadmium
592-01-8	Calcium Cyanide
133-06-2	Captan
63-25-2	Carbaryl
56-23-5	Carbon Tetrachloride
55285-14-8	Carbosulfan
5234-68-4	Carboxin
133-90-4	Chloramben
57-74-9	Chlordane
506-77-4	Chlorine Cyanide
67-66-3	Chloroform
1897-45-6	Chlorothalonil
2921-88-2	Chlorpyrifos
64902-72-3	Chlorsulfuron
16065-83-1	Chromium(III)
7440-47-3	Chromium(VI)
544-92-3	Copper Cyanide
21725-46-2	Cyanazine
57-12-5	Cyanide, free
460-19-5	Cyanogen
127-20-8	Dalapon
39515-41-8	Danitol
94-82-6	2,4-DB
50-29-3	DDT
1163-19-5	Decabromodiphenyl Ether (DBDPE)
8065-48-3	Demeton
106-37-6	1,4-Dibromobenzene
84-74-2	Dibutyl Phthalate
924-16-3	Dibutylnitrosamine
75-71-8	Dichlorodifluoromethane
107-06-2	1,2-Dichloroethane
75-35-4	1,1-Dichloroethylene
120-83-2	2,4-Dichlorophenol
94-75-7	2,4,-Dichlorophenoxyacetic acid (2,4-D)
62-73-7	Dichlorvos
55-18-5	Diethylnitrosamine
55290-64-7	Dimethipin
60-51-5	Dimethoate
120-61-6	Dimethyl Terephthalate
98765-43-2	Dimethyldoorknob (DMDK)
62-75-9	Dimethylnitrosamine
12345-67-8	Dinitrochickenwire (DNCW)
51-28-5	2,4-Dinitrophenol
88-85-7	Dinoseb
127-39-4	Diphenylamine
122-66-7	1,2-Diphenylhydrazine
85-00-7	Diquat
298-04-4	Disulfoton
145-73-3	Endothall
106-89-8	Epichlorohydrin
563-12-2	Ethion
141-78-6	Ethyl Acetate
100-41-4	Ethylbenzene
84-72-0	Ethylphthalyl Ethylglycolate (EPEG)
16984-48-8	Fluoride
59756-60-4	Fluridone
944-22-9	Fonofos
64-18-6	Formic Acid
39148-24-8	Fosetyl-Al
110-00-9	Furan
1071-83-6	Glyphosate
1024-57-3	Heptachlor Epoxide
87-82-1	Hexabromobenzene
87-68-3	Hexachlorobutadiene
319-84-6	alpha-Hexachlorocyclohexane (alpha-HCH)
319-86-8	delta-Hexachlorocyclohexane (delta-HCH)
6108-10-7	epsilon-Hexachlorocyclohexane (epsilon-HCH)
no CAS No.	Hexachlorocyclohexane, technical (t-HCH)
77-47-4	Hexachlorocyclopentadiene (HCCPD)
19408-74-3	Hexachlorodibenzo-p-dioxin (HxCDD)
67-72-1	Hexachloroethane
74-90-8	Hydrogen Cyanide
7783-06-4	Hydrogen Sulfide
35554-44-0	Imazalil
81335-37-7	Imazaquin
78-83-1	Isobutyl Alcohol
78-59-1	Isophorone
33820-53-0	Isopropalin
58-89-9	Lindane
330-55-2	Linuron
no CAS No.	Londax
123-33-1	Maleic Hydrazide
94-74-6	MCPA
93-65-2	MCPP
57837-19-1	Metalaxyl
16752-77-5	Methomyl
75-09-2	Methylene Chloride
78-93-3	Methyl Ethyl Ketone (MEK)
108-10-1	Methyl Isobutyl Ketone (MIBK)
22967-92-6	Methyl Mercury
298-00-0	Methyl Parathion
51218-45-2	Metolachlor
21087-64-9	Metribuzin
300-76-5	Naled
1929-82-4	Nitrapyrin
14797-55-8	Nitrate
10102-43-9	Nitric Oxide
14797-65-0	Nitrite
98-95-3	Nitrobenzene
10102-44-0	Nitrogen Dioxide
86-30-6	N-Nitrosodiphenylamine
621-64-7	N-Nitrosodi-N-propylamine
10595-95-6	N-Nitrosomethylethylamine
930-55-2	N-Nitrosopyrrolidine
27314-13-2	Norflurazon
32536-52-0	Octabromodiphenyl ether
19044-88-3	Oryzalin
23135-22-0	Oxamyl
42874-03-3	Oxyfluorfen
76738-62-0	Paclobutrazol
1910-42-5	Paraquat
32534-81-9	Pentabromodiphenyl ether
608-93-5	Pentachlorobenzene
87-86-5	Pentachlorophenol
52645-53-1	Permethrin
108-95-2	Phenol
108-45-2	m-Phenylenediamine
62-38-4	Phenyl Mercuric Acetate
732-11-6	Phosmet
7803-51-2	Phosphine
151-50-8	Potassium Cyanide
506-61-6	Potassium Silver Cyanide
1610-18-0	Prometon
23950-58-5	Pronamide
1918-16-7	Propachlor
709-98-8	Propanil
139-40-2	Propazine
51630-58-1	Pydrin
13593-03-8	Quinalphos
7783-00-8	Selenious Acid
630-10-4	Selenourea
74051-80-2	Sethoxydim
7440-22-4	Silver
506-64-9	Silver Cyanide
26628-22-8	Sodium Azide
143-33-9	Sodium Cyanide
148-18-5	Sodium Diethyldithiocarbamate (Dithiocarb)
57-24-9	Strychnine

TABLE 2. INORGANIC PRIORITY POLLUTANTS RANKED ACCORDING TO BIOCONCENTRATION FACTOR (BCF)

Priority Pollutant No.	Substance	Log BCF[a]
115	arsenic	2.544
118	cadmium	2.513
119	chromium VI	2.190
119	chromium III	2.104
123	mercury	2.000
124	nickel	1.699
127	thallium	1.176
114	antimony	ND
117	beryllium	ND
121	cyanide	ND
124	nickel (subsulfide, refinery dust)	ND
125	selenium	ND
126	silver	ND

[a] BCF = Bioconcentraction Factor (U.S. EPA 1980b; Tetra Tech 1985a).

ND = No data.

TABLE 3. TOXICITY PROFILE FOR MERCURY AND PCBs[a]

Property	Mercury[b]	PCBs[c]
CAS Number	7439-97-6	1336-36-3
Physical-Chemical		
Molecular Weight	200.6-318.7	154.2-498.7
Vapor Pressure (mm Hg)	0.012-0.028	2.8×10^{-9} - 7.6×10^{-5}
Solubility (mg/L)	0.056-400,000	<0.001-5.9
Log K_{ow}[d]	N/A[e]	4.0-6.9
Log Bioconcentration Factor[d]	2.0-4.6	1.9-5.2
Carcinogenic Status	Noncarcinogen	Probable human carcinogen[f] Group B2 -- Sufficient animal evidence -- Inadequate human evidence
Acute Toxicity		
Human (mg/kg body wt) LD_{50}	29[g]	--
Mammal (mg/kg body wt) LD_{50}	1.0-40.9	1,010-16,000
Aquatic (mg/L) LC_{50}	0.015-32.0	0.001-61.0
Chronic Toxicological Effects		
Humans	Motor and sensory impairment leading to paralysis, loss of vision and hearing, and death. Kidney dysfunction.	Skin lesions, liver dysfunctions, and sensory neuropathy.
Mammals	Reproductive impairment and teratogenic effects.	Hepatotoxicity, fetotoxicity, skin lesions, and hepatocellular carcinoma
Aquatic Organisms	Developmental and structural anomalies, suppression of growth and reproduction, impairment of behavior.	Reproductive and developmental impairment.
Critical end point for risk assessment	Central nervous system effects (e.g., ataxia and parathesia)[h]	Hepatocellular carcinoma[f]

TABLE 3. (Continued)

[a] This is an example toxicity profile and is not intended to be comprehensive.

[b] Mercury may occur in its elemental form, as inorganic salts, or as organic complexes. Consequently, the chemical and toxicological properties vary tremendously depending on the degree of complexation or metal speciation.

[c] Physical-chemical properties and toxicity vary according to the degree of chlorine substitution, the number of adjacent unsubstituted carbons and steric configuration.

[d] Tetra Tech (1985a).

[e] N/A = not applicable.

[f] EPA (1980a,b 1985a); IARC (1978).

[g] For mercury (II) choride via oral route of exposure (Tatken and Lewis 1983). Relevance to consumption of mercury (primarily methylated) in fish is questionable.

[h] Clarkson et al. (1973).

weight of evidence of carcinogenicity based on animal studies is "sufficient." The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient" evidence of carcinogenicity in animals as presenting a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate" evidence or "no data" from epidemiologic studies would usually be categorized under Group B2.

- **Group C - Possible Human Carcinogen**: This group is used for agents with limited evidence of carcinogenicity in animals in the absence of data on humans. It includes a wide variety of evidence; e.g., (a) a malignant tumor response in a single, well-conducted experiment that does not meet conditions for sufficient evidence; (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting; (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity; and (d) response of marginal statistical significance in a tissue known to have a high or variable background rate.

- **Group D - Not Classifiable as to Human Carcinogenicity**: This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.

- **Group E - Evidence of Noncarcinogenicity for Humans**: This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies. The classification of an agent in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent is not a carcinogen under any circumstances.

The above descriptions for the categories were taken from U.S. EPA (1986a). At present, a weight-of-evidence classification for carcinogenicity is available in IRIS for each chemical assigned a Carcinogenic Potency Factor.

SOURCES OF INFORMATION

In many cases, EPA regions and others may rely on toxicity profiles generated previously. IRIS is a key source of chemical toxicity data, including information from critical studies and weight-of-evidence classifications for carcinogens. The first step in a hazard assessment should be to consult IRIS chemical files for potential contaminants of concern. IRIS chemical files will be available for approximately 270 chemicals by November 1987. Further information on IRIS is provided in Appendix B.

The primary sources of toxicity profiles are the EPA Office of Waste Programs Enforcement and Office of Health and Environmental Assessment (e.g., Appendix C, Table C-1). EPA toxicity profiles are available for approximately 195 chemicals. Additional sources are shown in Appendix C, Table C-2. Under the Superfund Amendments and Reauthorization Act of 1986, EPA and the Agency for Toxic Substances and Disease

Registry are preparing toxicity profiles for 100 hazardous substances considered as high priority contaminants at Superfund sites.

Supplementary information on the toxicity of contaminants of concern may be obtained from bibliographic or chemical/toxicological databases. DIALOG, a comprehensive bibliographic database system (Dialog Information Services, Inc., 3460 Hillview Avenue, Palo Alto, CA 94304), offers access to databases such as Pollution Abstracts, National Technical Information Service, and ENVIROLINE. Chemical and toxicological information can be obtained from the databases listed in Appendix C, Table C-3.

DOSE-RESPONSE ASSESSMENT

After the potential hazard associated with each contaminant of concern is characterized, the relationship between dose of a substance and its biological effect is determined. Dose-response data are used to determine the toxicological potency of a substance, a quantitative measure of its potential to cause a specified biological effect. The concepts of exposure, dose, dose-response relationship, and toxicological potency are discussed in the following sections.

EXPOSURE AND DOSE

The concepts of exposure and dose, as defined below, are central to risk assessment:

- **Exposure**: Contact by an organism with a chemical or physical agent
- **Dose**: The amount of chemical uptake by an organism over a specified time as a consequence of exposure.

The "ingested dose," or amount of chemical ingested, is distinct from the "absorbed dose." For the oral route of exposure, the absorbed dose is the amount of chemical assimilated by absorption across the lining of the gastrointestinal system. Exposure level or exposure concentration is used to denote the concentration (mg/kg wet weight) of contaminant in edible tissue of fish or shellfish. As shown below, the absorbed dose is estimated from food consumption rate, the exposure concentration, and an absorption coefficient (see Exposure Assessment).

DOSE-RESPONSE RELATIONSHIPS

The form of the dose-response relationship for carcinogens is assumed to be fundamentally different from that for noncarcinogens (U.S. Office of Science and Technology Policy 1985). Examples of general dose-response relationships are shown in Figure 2. The lack of a demonstrated threshold in dose-response relationships for carcinogens (U.S. EPA 1980b, 1986a; U.S. Office of Science and Technology Policy 1985) implies a finite risk of cancer even at very low doses of the carcinogen.
For noncarcinogenic effects, there is usually a threshold dose, i.e., a dose below which no adverse biological effects are observed in the animal bioassay. The threshold dose is termed the No-Observed-Adverse-Effect-Level (NOAEL), as shown in Figure 2. Note that a nonzero mean response may be a NOAEL if that mean response is not significantly different from zero as determined by a statistical test. The Lowest-Observed-Adverse-Effect-Level (LOAEL) is the lowest concentration that results in a statistically significant health effect in the test population.

A measure of toxicological potency is derived from an empirical dose-response relationship for the chemical of interest. Toxicological potency indices for two broad categories of toxicants are defined as follows:

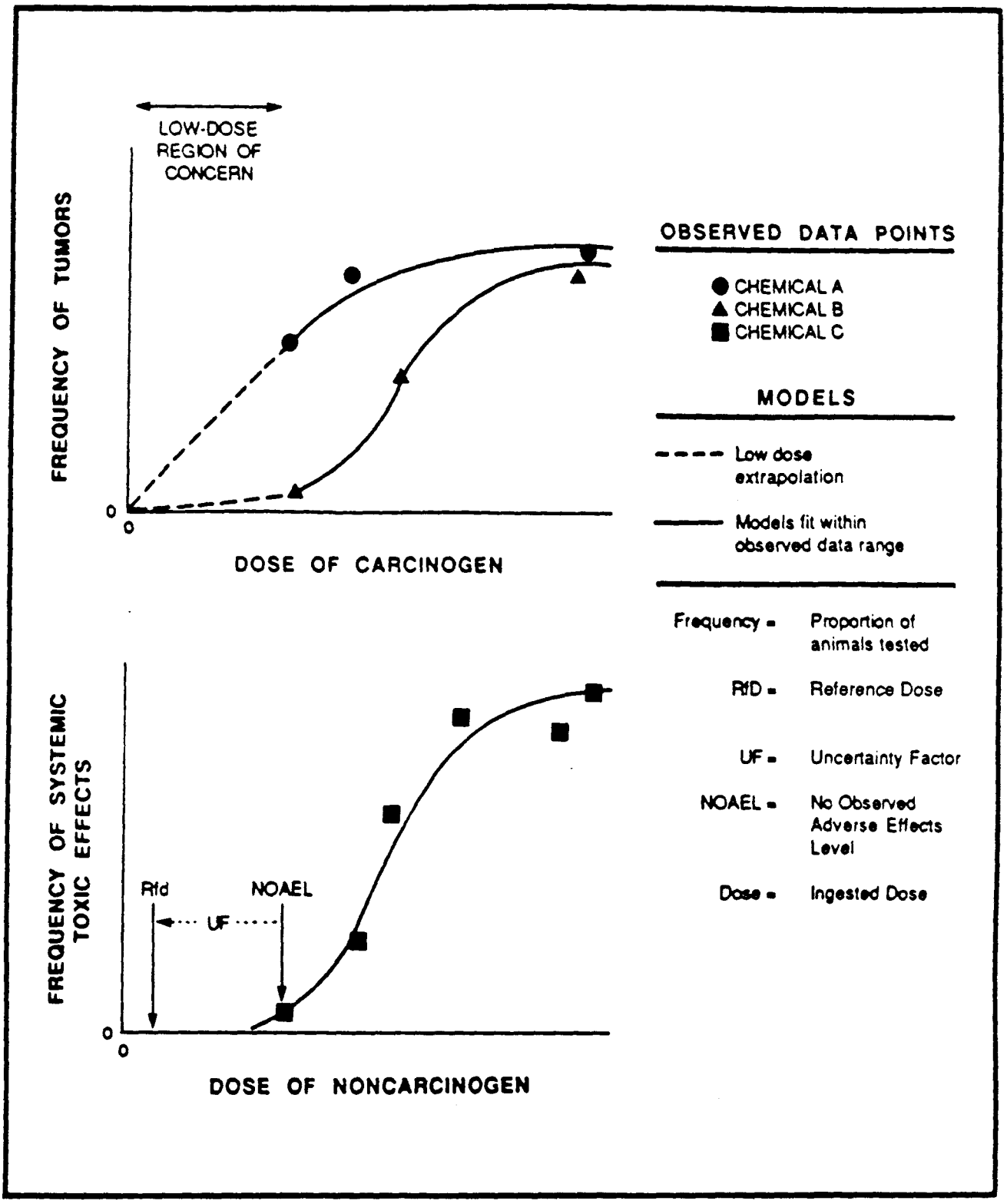


Figure 2 Hypothetical example of dose-response curves for a carcinogen and a noncarcinogen.

- **Carcinogens** are individually characterized by a **Carcinogenic Potency Factor**, a measure of the cancer-causing potential of a substance estimated by the upper 95 percent confidence limit of the slope of a straight line calculated by the linearized multistage procedure or another appropriate model

- **Noncarcinogens** are individually characterized by an RfD, an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subpopulations) that is unlikely to produce an appreciable risk of adverse health effects during a lifetime.

Carcinogenic Potency Factors are also referred to as Slope Factors. RfDs are conceptually similar to Acceptable Daily Intakes (U.S. EPA 1987a).

The data set used to define toxicological indices is determined by the quality of available data, its relevance to modes of human exposure, the similarity of the species to humans, and other technical factors. Adequate data from clinical or epidemiological studies of humans are preferred over animal data. If adequate human data are not available, a data set for the animal species most similar to humans or for the most sensitive species is used in the dose-response assessment. Data are evaluated by EPA to ensure high quality (e.g., U.S. EPA 1980b, 1985a).

The main source of dose-response data for deriving Carcinogenic Potency Factors and RfDs is lifetime cancer bioassays performed on rats or mice. Because most of these experiments are designed to be cost-effective, doses in bioassays may be orders of magnitude above those encountered in the human environment. High doses are used in laboratory bioassays for several reasons: 1) to reduce the time required to produce a response and thus overcome problems related to latency period (i.e., length of time between exposure and appearance of health effects), 2) to obtain sufficient statistical power to detect health effects, and 3) to decrease the absolute number of animals required and thereby reduce costs. Doses in animal bioassays for oral uptake of contaminants are usually the administered (ingested) dose, not the absorbed dose (i.e., uptake across the lining of the gastrointestinal system).

Carcinogenic Potency Factors and RfD values derived by EPA are listed in the IRIS database. At present, values for these toxicological indices are being standardized for agency-wide use. A brief overview of methods by which these indices are derived is presented below.

CARCINOGENIC POTENCY FACTORS

The Carcinogen Assessment Group of EPA currently uses the linearized multistage procedure to derive Carcinogenic Potency Factors (U.S. EPA 1980b, 1985a, 1986a, 1987a). The multistage model assumes that carcinogenesis results from a series of interactions between the carcinogenic chemical and DNA, with the rate of interactions linearly related to dose. For example, a chemical may induce a mutation in the DNA of a cell to initiate carcinogenesis. However, a series of further interactions between DNA and the same chemical (or another one) may be necessary to promote carcinogenesis and induce a tumor. The multistage model is the model most frequently used by EPA when there is no convincing biological evidence to support application of an

alternative model. Other models include the logit, probit, single-hit, and Weibull models (Food Safety Council 1980, 1982; Hogan and Hoel 1982; Cothern et al. 1986). At high doses (corresponding to lifetime risks greater than about 10^{-2}), all currently used models yield generally similar risk estimates. Below risks on the order of 10^{-2}, the models diverge increasingly as dose declines. In the low-dose range, the linearized multistage model generally predicts risks similar to the single-hit (i.e., linear) model. For many data sets, both of these models yield higher estimates of low-dose risk than do other models (U.S. EPA 1980b; Hogan and Hoel 1982; U.S. Office of Science and Technology Policy 1985). The mathematical form of the multistage model for a specified carcinogen is:

$$R(d) = 1 - \exp\left[-(q_1 d + q_2 d^2 + \ldots + q_k d^k)\right] \quad (1)$$

where:

$R(d)$ = Excess lifetime risk of cancer (over background at dose d) (dimensionless)
q_i values = Coefficients [kg day mg^{-1} (i.e., the inverse of dose units)]
d = Dose (mg kg^{-1} day^{-1})
k = Degree of the polynomial used in the multistage model.

U.S. EPA (1987a) described the linearized multistage procedure as follows:

- The multistage model is fitted to the data on tumor incidence vs. dose
- The maximum linear term consistent with the dose-response data is calculated, which essentially defines the linear portion of the dose-response function at low doses
- The coefficient of the maximum linear term, designated as q_1^*, is set equal to the slope of the dose-response function at low doses
- The resulting estimate of q_1^* is used as an upper-bound estimate of the Carcinogenic Potency Factor (termed Slope Factor in U.S. EPA 1987a)

q_1^* is usually calculated as the upper 95 percent confidence limit of the estimate of the coefficient q_1 in Equation 1. Because the slope of the dose-response function at high doses could be different from that at low doses, the use of q_1^* as an upper-bound estimate of potency is not valid at high exposures. In general, q_1^* should not be used as the upper-bound estimate of potency at exposures corresponding to excess lifetime risks greater than approximately 10^{-2} per individual (i.e., one excess tumor per 100 exposed individuals).

The model commonly used to estimate plausible-upper-limit risk for low levels of exposure over a lifetime is therefore:

$$R^*(d) = q_1^* d \quad (2)$$

where:

$R^*(d)$ = Upper-bound estimate of excess lifetime risk of cancer (dimensionless)
q_1^* = Upper-bound estimate of carcinogenic potency (kg day mg^{-1})
d = Dose (mg kg^{-1} day^{-1}).

Equation 2 represents a linear approximation of the multistage model.

If a potency factor is derived from nonhuman data, as is usually the case, it must be extrapolated to humans. Before being applied to humans, Carcinogenic Potency Factors derived from animal data are corrected using surface-area differences between bioassay animals and humans (U.S. EPA 1980b, 1986a). The rationale for using surface-area extrapolations is detailed in Mantel and Schneiderman (1975). The relationship between surface-area extrapolation and body-weight extrapolation approaches is discussed in the Introduction above (see Background, Relationship of EPA Risk Assessment Methods to FDA Risk Assessment Methods).

REFERENCE DOSES

Current methods for predicting human health effects from exposure to noncarcinogenic chemicals rely primarily on the concept of an RfD (U.S. EPA 1987a). The RfD is derived from an observed threshold dose (e.g., NOAEL or LOAEL if the NOAEL is indeterminate) in a chronic animal bioassay by applying an uncertainty factor, which usually ranges from 1 to 1,000 (Dourson and Stara 1983). The relationship between the NOAEL, the RfD, and the uncertainty factor are illustrated in Figure 2 above. The uncertainty factor accounts for differences in threshold doses among species, among intraspecies groups differing in sensitivity, and among toxicity experiments of different duration. Dourson and Stara (1983) and U.S. EPA (1987a) discuss the methods for deriving RfDs and the criteria for selecting uncertainty factors. In brief, an uncertainty factor of 1000 is based on combining a factor of 10 to account for animal-to-human extrapolation, a factor of 10 to protect sensitive individuals, and a factor of 10 to account for use of a LOAEL in place of a NOAEL.

SOURCES OF INFORMATION

In many cases, EPA regions and other agencies will be able to rely on dose-response assessments generated previously. Current values for Carcinogenic Potency Factors and RfDs are given in IRIS (U.S. EPA 1987a; e.g., see Appendix B). Before using these values, investigators should consult the IRIS database and current EPA health assessment documents for information on their derivation and uncertainties for each chemical. Contacts for information on specific chemicals are listed in IRIS Chemical Files.

Carcinogenic Potency Factors

The Carcinogenic Potency Factors calculated by the EPA Carcinogen Assessment Group are published in IRIS and in each health assessment document produced by the Office of Health and Environmental Assessment (e.g., U.S. EPA 1985a). The EPA Carcinogen Assessment Group determines these carcinogenic potency values and updates

them periodically. Before being entered into IRIS, Carcinogenic Potency Factors and supporting documentation are reviewed by the Carcinogen Risk Assessment Verification Endeavor (CRAVE) work group. The list of Carcinogenic Potency Factors published in each health assessment document is intended only to provide comparative information for various chemicals. IRIS should be used as the primary source of Carcinogenic Potency Factors for risk assessment.

Reference Doses

IRIS is the primary source of RfD values. An example of an IRIS data sheet for the pesticide lindane is shown in Appendix B. The data sheet provides information on the RfD, the endpoints (biological effects) of concern, experimental data sets, doses, uncertainty factors, additional modifying factors, confidence in the RfD, reference documentation, and dates of agency RfD reviews.

Individual program offices within EPA may need to be consulted for information on chemicals not yet incorporated into IRIS. For example, the Office of Drinking Water is a source of RfDs for selected chemicals. In May 1987, the Office of Drinking Water released draft Health Advisories containing RfDs and guidelines for short-term effects for 16 pesticides: alachlor, chlordane, 1,2-dibromo-3-chloropropane (DBCP), 2,4-dichlorophenoxyacetic acid (2,4-D), 1,2-dichloropropane, endrin, ethylene dibromide (EDB), heptachlor and heptachlor epoxide, lindane, methoxychlor, oxymyl, pentachlorophenol, toxaphene, and 2,4,5-trichlorophenoxypropionic acid (2,4,5-TP). Office of Drinking Water Health Advisories will eventually be incorporated into IRIS.

EXPOSURE ASSESSMENT

Exposure assessment is the process of characterizing the human populations exposed to the chemicals of concern, the environmental transport and fate pathways of those chemicals, and the frequency, magnitude, and duration of the exposure dose (U.S. EPA 1986b). For exposure assessment of contaminated fish and shellfish, the following factors should be considered:

- Concentrations of contaminants in aquatic biota of concern
- Potential environmental transfer of contaminants from sources through aquatic species to humans
- Fisheries harvest activities, diet, and other characteristics of exposed human populations
- Numerical variables (e.g., food consumption rate, contaminant absorption efficiency) used in models to estimate exposure
- Purpose of the exposure assessment (e.g., assessment of potential closure of sport or commercial fishery; documentation of health risk from local contaminant sources such as hazardous waste site or wastewater discharges; development of sportfish consumption advisories).

Information on contaminant concentrations and the exposed population is combined to construct an exposure profile, which includes estimates of average rates of contaminant intake by exposed individuals. Key stages of an exposure assessment for contaminated fish and shellfish are discussed in the following sections.

TISSUE CONCENTRATIONS OF CONTAMINANTS

Guidance on development of study designs to measure concentrations of toxic substances in edible tissues of fish and shellfish is provided in this section. The guidance provided below focuses primarily on field surveys or monitoring programs involving the collection of samples directly from aquatic environments, or from harvesters when the specific geographic origin of samples is known. Such guidance is directly relevant to analysis of recreational fisheries. The present document does not specifically address approaches to marketplace sampling of commercial fisheries products, although some of the concepts discussed below apply to marketplace surveys. Sampling designs for collection of fisheries products from the marketplace are available in FDA Compliance Program Guidance Manuals (e.g., U.S. FDA 1986). Sampling of commercial fisheries directly at the source is preferred over marketplace sampling because the former often allows documentation of the sampling location.

If the exposure assessment is designed to include contaminant intake from consumption of commercial fish and shellfish, samples may be obtained in two ways. First, samples of target species can be obtained directly from commercial fishermen. In this case, a

strict quality assurance/quality control (QA/QC) program should be implemented to ensure proper handling, storage, and documentation of samples. Documentation should include sampling location, species name, size (length, carapace width, or shell height/width), weight, sex, reproductive condition, time and date of sampling, and preservation technique. In most cases, a technician or observer should be on board the fishing vessel to maintain proper sample handling and documentation. Alternatively, samples may be collected by monitoring program personnel using vessels other than commercial fishing boats. In this case, samples should be collected in a way that simulates commercial fishing practices as closely as possible (e.g., same species, size classes, season, fishing area, sampling method, and water depth). Regardless of the general approach to sampling, the organisms collected should be placed directly in temporary storage on board the sampling vessel. Upon return to shore, resection of samples should be accomplished as quickly as possible using an adequate clean-room. If an extended sampling cruise necessitates resectioning on board, an adequate clean-space should be set aside to ensure that samples are not contaminated.

Analysis of chemical residues in tissue to support an exposure assessment is one kind of bioaccumulation study. Bioaccumulation is defined here as the uptake and retention of a contaminant (e.g., a potentially toxic substance) by an organism. The term bioconcentration refers to any case of bioaccumulation wherein the concentration of contaminant in tissue exceeds its concentration in the surrounding medium (i.e., water or sediment). The phrase "bioaccumulation survey" will be used below to refer to measurement of chemical residues in tissue samples from fish and shellfish collected in the field.

The elements of a study design for analysis of chemical residues in tissue include:

- Objectives
- Target species and size (age) class
- Sampling station locations
- Target contaminants
- Sampling times
- Kind of sample (e.g., composite vs. grab, cooked vs. raw; fillet vs. whole organism)
- Sample replication strategy
- Analytical protocols, including detection limits
- Statistical treatment of data.

Because the complexity and specific features of a sampling design will depend on the objectives of the exposure assessment, no single design can be recommended here. Nevertheless, some basic steps in the study design process can be summarized as follows:

- Define concise objectives of the study and any hypotheses to be tested.

- Define spatial and temporal characteristics of fisheries relative to harvesting activities (e.g., seasonality, catch or consumption rates, species composition, size ranges, demersal vs. pelagic species).

- Define harvesting activities and methods of preparing food for consumption that potentially affect exposure to contaminants.

- Define kinds of samples to be collected (species, type of tissue, mode of preparation) and variables to be measured, based on a preliminary exposure analysis.

- Evaluate alternative statistical models for testing hypotheses about spatial and temporal changes in measured variables. Select an appropriate model.

- When possible, use stratified random sampling for each fish and shellfish species, where the different strata represent different habitat types or kinds of harvest areas that may influence the degree of tissue contamination.

- When practical, specify equal numbers of randomly allocated samples for each stratum/treatment combination (e.g., habitat type in combination with species or season).

- Include samples from a relatively uncontaminated reference or control area to help define local contamination problems.

- Perform preliminary sampling or analyze available data to evaluate the adequacy of alternative sampling strategies (e.g., composite samples vs. tissue from individual organisms) and statistical power as a function of the number of replicate samples.

- Develop a QA/QC program that covers: sample collection and handling; chain of custody; data quality specifications; analytical methods and detection limits; data coding; data QA/QC steps to assess precision, accuracy, and completeness; database management specifications; data reporting requirements; and performance audits.

- Define data analysis steps, including statistical tests, data plots, summary tables, and uncertainty analysis.

Note that the second and third steps above depend on information developed as part of the characterization of the exposed population (see Exposed Population Analysis below). Also, practical limitations of field sampling may dictate compromises in the sampling design. For example, use of equal sample sizes is generally recommended because statistical analysis of data sets with unequal sample sizes may be difficult or unnecessarily complex. However, collection of equal numbers of replicate samples for each treatment (or stratum) may be undesirable if both dominant and rare species are to be sampled at a series of harvest locations with a broad range of harvest yields. Depending on the specific objectives and corresponding study design, a series of statistical analyses rather than a single test may be appropriate.

Detailed guidance on sampling strategies is provided by Phillips (1980), Green (1979), Tetra Tech (1985b,c; 1986b), Phillips and Segar (1986), and Gilbert (1987). Much of the guidance provided in the following sections incorporates the suggestions of these authors.

The statement of objectives is a critical step in the study design process, since specification of other design elements depends on the survey objectives. The study objectives must in turn relate to the objectives of the exposure assessment in which the data will be used. The relationships between study objectives and general features of a sampling design are addressed in the next section.

Study Objectives and General Sampling Design

Specific objectives of a chemical residue study should be defined to ensure collection of appropriate data for the exposure assessment. Different objectives may require radically different sampling designs. Although the primary objective of a field study may be to estimate the mean concentrations of specified chemical contaminants in edible tissues of harvested species, it may be necessary to specify additional objectives to meet the needs of exposure assessment or risk management. For instance, statistical discrimination among mean contaminant concentrations in samples from different harvest areas, seasons, or species may be desired. Such information might be needed to manage relative risks among harvest areas and to impose fisheries closures on a site-specific basis.

Example Objectives--

Some examples of objectives for exposure assessments paired with appropriate bioaccumulation survey objectives are given below. These objectives are provided to illustrate the ways in which the elements of a bioaccumulation study design depend on the exposure assessment objectives. They are not intended to be recommended objectives for an actual exposure assessment. In these examples, the bioaccumulation study design involves specifically the measurement of chemical residues in edible tissues of fishery species. Information on the exposed population, including an analysis of their dietary habits (e.g., fisheries species consumed, food preparation method, and consumption rate), is discussed later (see Exposed Population Analysis). Such information may influence the objectives of the exposure assessment and the bioaccumulation survey.

Example 1:

- Exposure Assessment: Estimate the worst-case exposure for a wide range of contaminants over a predefined geographical area.

- Bioaccumulation Design: Estimate mean concentrations of contaminants in edible tissues of a selected narrow size range of individuals of the most contaminated species during the season of peak contaminant concentrations.

Example 1 represents a screening survey to evaluate the need for further work. Edible portions of a limited number (e.g., 3-5) of individual organisms or composite samples would be analyzed for a large number of compounds and the risk assessment

conducted assuming moderate or high (but plausible) consumption rates. The species and size range selected would be the ones most likely to accumulate high concentrations of contaminants. Typically, the target species for a screening survey would be the largest individuals of a bottom dwelling species associated with soft sediments.

Example 2:

- Exposure Assessment: Estimate the long-term average exposure to each of the contaminants A, B, and C through consumption of aquatic species L, M, N, and O combined from harvest area Z for the average person in the exposed human population.

- Bioaccumulation Design: Estimate the mean concentrations of contaminants A, B, and C in edible tissues of aquatic species L, M, N, and O combined from harvest area Z over an annual period.

Example 2 illustrates a simple case involving the consumption of multiple species from a single harvest location. Individual or composite samples of each species would be analyzed separately during different seasons or during a single season expected to represent the annual average. If samples are analyzed separately during different seasons (e.g., see discussion of Example 4 below), the mean annual exposure for all species could still be calculated from the seasonal data. In general, highly composited samples are not recommended because information on different factors (e.g., species, seasons) that affect contaminant concentrations is lost.

Example 3:

- Exposure Assessment: Estimate a plausible-upper-limit of exposure to each of the contaminants A, B, and C through consumption of aquatic species L, M, N, and O combined from harvest area Z for a seasonal harvester in the exposed population.

- Bioaccumulation Design: Estimate the upper bound of the 95 percent confidence interval of the mean concentration for each of the contaminants A, B, and C in edible tissues of aquatic species L, M, N, and O combined from harvest area Z during the season of highest contamination.

The general sampling design for the objectives of Example 3 would require replicate composite samples to estimate upper bounds of 95 percent confidence intervals for the mean concentrations of contaminants across species. To meet these objectives, samples could be composited across species, although this is generally not recommended. Multispecies composites would not provide data for assessing exposures corresponding to different dietary habits. To obtain an upper-limit estimate of exposure, it might be sufficient to analyze samples from only one season if available information on seasonal variation was sufficient to select one season as the expected worst case.

Example 4:

- Exposure Assessment: Estimate the probability distribution of exposure to each of the contaminants A, B, and C through consumption of each of aquatic species L, M, N, and O from harvest area Z for various

segments of an exposed population (e.g., ethnic groups) over an annual period.

- Bioaccumulation Design: Estimate the probability distribution of concentrations of contaminants A, B, and C in edible tissues of each of aquatic species L, M, N, and O from harvest area Z over an annual period.

To accomplish the objectives of Example 4, extensive seasonal data on the dietary composition of several subgroups of the exposed population must be available. Separate replicate composite samples of each harvested species could be analyzed for each season. During each season, the species analyzed would correspond to those represented to a significant extent in the diet. Probability (frequency) distributions and means of contaminant concentrations would be derived for each species during each season. By combining data from different species, the probability distribution of exposure and the mean exposure weighted by species representation in the diet could be calculated for each population segment. Note that data to support the analyses required by Example 4 are seldom available before a specially designed study is conducted.

Example 5:

- Exposure Assessment: Estimate an average and a plausible-upper-limit of exposure to each of the contaminants A, B, and C through consumption of each of aquatic species L, M, N, and O from each of the harvest areas X, Y, and Z over an annual period.

- Bioaccumulation Design: Estimate the mean concentration and the upper bound of the 95 percent confidence interval of the mean concentration for each of the contaminants A, B, and C in edible tissues of each of species L, M, N, and O from each of the harvest areas X, Y, and Z during each of the harvest seasons.

The sampling strategy appropriate for Example 5 is complicated by the occurrence of discrete harvest areas. Replicate composite samples of a given species would generally be required for each season and area in which the species is harvested. Because the characteristics of the exposed population may differ among harvest areas, it may be appropriate to divide the exposed population into segments corresponding to geographic areas, ethnic groups, age classes or other factors. The seasonal and total annual exposure for each segment of the exposed population would be calculated for each species as in Example 4 above.

Influence of Environmental and Population Factors--

The four examples just given illustrate the variety of general study designs that may be needed to meet diverse objectives. The specific design of a chemical residue study will depend on the interplay between dietary patterns of the exposed population and environmental factors that influence concentrations of contaminants in tissues of aquatic organisms. Some of the important environmental factors are:

- Conventional water quality (i.e., hardness, salinity, temperature, suspended solids)
- Habitat location, depth, proximity to contaminant sources
- Contaminant concentrations in water
- Contaminant concentrations in sediments
- Species available for harvest and migratory cycles
- Organism activity pattern, food habits, and habitat
- Seasonal biological cycles (e.g., stage of sexual cycle) in relation to the frequency and seasonality of contaminant inputs (e.g., industrial discharges, waste dumps, dredging)
- Organism size (or weight), age, and sex
- Lipid content of tissue analyzed (where lipophilic organic contaminants are of concern).

Examples of the interaction between these factors and parameters of the exposed population are given in Figure 3.

Seasonal variation in environmental factors or activities of the exposed population may correlate with contaminant concentrations in consumed fish and shellfish. Therefore, at least general knowledge of seasonal changes in contaminant concentrations and human consumption patterns may be needed to design an appropriate sampling approach for estimating long-term exposure. Two extreme examples of contamination and diet patterns are provided below:

Homogeneous Diet and Contamination:

- Each of the species is present in the harvest area all year
- There is no seasonal variation in contaminant concentrations
- Contaminant concentrations do not vary among species
- Species are equally represented in the diet.

Heterogeneous Diet and Contamination:

- Some species are absent from the harvest area during one or more seasons
- Contaminant concentrations vary among species and among seasons
- Some species are eaten more than others, and diet composition varies seasonally.

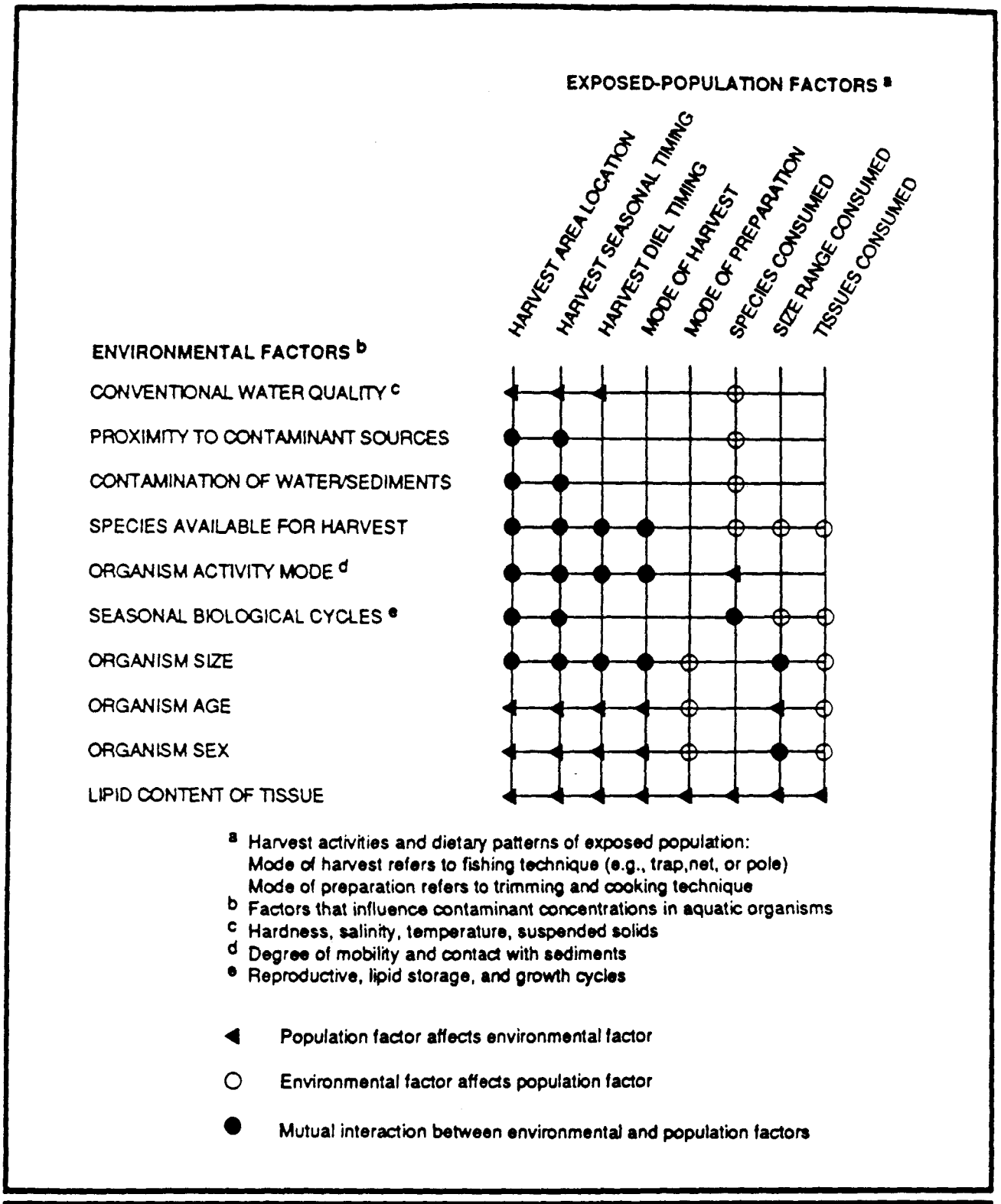


Figure 3 Interaction between environmental factors and exposed population factors.

In the first case above (homogeneous diet and contamination), the study design could be relatively simple. Mean contaminant concentrations could be estimated from analyses of a single composite sample of one of the species collected at one time of year from each harvest area. If previous data were available to verify the lack of variation in chemical concentrations among species and among seasons, it would be appropriate to extrapolate the results from a single composite sample to the entire diet composed of several species. However, this is an unrealistic case. It is more likely that both contaminant concentration and diet composition will vary seasonally, and that contaminant concentrations will vary among species. Analyses of contaminant concentrations in each species during different seasons is generally recommended here to meet the diverse objectives of a typical exposure assessment.

Selection of Target Species and Size Classes

Ideally, the set of species selected for contaminant analysis would include all harvested species. Because available data and funds for collecting new data are often limited, only one or a few target species may be used for human health risk assessment. The particular species selected for an exposure assessment will depend on the study objectives. Examples of approaches and guidance on selection of target species are given below.

Four alternative objectives that affect the choice of target species are:

- Perform a comprehensive analysis of harvested species
- Characterize the typical exposure case represented by the dominant harvested species
- Characterize exposure for the worst-case species (e.g., heavily consumed species expected to be highly contaminated)
- Characterize the spatial distribution of contamination using an indicator species.

The criteria for selecting species for chemical analyses to meet each of these objectives are shown in Table 4. For the first objective (comprehensive species analysis), all of the harvested species do not necessarily need to be analyzed, but some criterion is required to select species for analysis (e.g., the most important species in the harvest that together comprise greater than 95 percent of the catch by weight). For the second objective (typical exposure), a few of the dominant species (by weight) in the harvest may be selected to represent a typical exposure level. However, this approach has the major disadvantage that highly contaminated species may be overlooked (see Dominant Harvested Species below). For the third objective (worst-case species analysis), the target species should be among the most contaminated species in the harvest. If the worst-case assessment is species-specific (i.e., the consumption rate for a single species is used to estimate exposure), then the target species should also be one of the dominant species in the harvest. When the dominant component of the diet differs among subpopulations of concern, then specific dietary information for subpopulations should be used to select the worst-case target species. The target species may be the most contaminated species regardless of its status in the diet of the entire exposed population. For the last objective (site-specific analyses of the spatial distribution of contamination), an

TABLE 4. CRITERIA FOR SELECTING TARGET SPECIES[a]

Species Characteristics	Alternative Design Objectives[b] Comprehensive Species Analysis	Typical Exposure Case	Worst-Case Species	Spatial Pattern Indicator Specie
Harvest ranking	**Species forming ≥95% of catch**	**Dominant species in catch**	**Dominant species in catch**	Variable
Home range size	Variable	Variable	Variable	**Small**
Contamination level	Variable	Variable	**High**	**High**

[a] Criteria for selecting target species to meet a given objective are shown in **bold**.

[b] A full statement of each objective is given in the text.

indicator species with a small home range that is expected to have high concentrations of contaminants in edible tissue would be selected. Note that an indicator species could be a species that is relatively rare in the harvest. Although home range size and degree of contamination of species may not constrain the selection of species to meet the first two objectives listed above, selecting species without regard to contamination levels will not necessarily ensure that the overall purpose of performing an exposure assessment will be met.

Dominant Harvested Species--

If available, data on fisheries catches or consumption from field surveys (e.g., Finch 1973; Puffer et al. 1982; Landolt et al. 1987; McCallum 1985) can be used to select species for analysis that are dominant members of the catch on a wet-weight basis. The advantages of choosing the dominant harvested species for exposure assessment are that:

- Exposure estimates will be based on realistic conditions in terms of relative contribution of species to the diet, providing that catch data reflect consumption patterns or that consumption data are used for the selection of species
- Adequate numbers of organisms for chemical analyses should be relatively easy to obtain.

The disadvantages of this approach are that:

- Species that are minor components of the diet by weight but that are highly contaminated may be overlooked
- Exposure of human subpopulations that consume species other than the dominant component of the diet overall may not be protected
- Which species are dominant often varies spatially, making it difficult to compare risk estimates for different sites
- Extensive species-specific data on catch, consumption, and contamination patterns are needed to select target species (these data are costly to obtain if not already available)
- If samples are obtained directly from harvesters, a major component of the catch may be unidentifiable because the catch is sometimes cleaned before being surveyed.

Indicator Species--

The use of selected indicator species is an alternative to the use of dominant harvested species. Indicator species can be chosen to represent the average (or maximum) contamination levels in the harvest, as determined from available data or from a pilot survey. Use of indicator species may be appropriate for investigations with multiple objectives (e.g., assessment of bioaccumulation in fishery species and human health

risks for specific areas within a water body). Indicator species may include both highly mobile and relatively sedentary species. If small-scale discrimination of spatial patterns of contamination is a concern, indicator species should include nonmigratory biota or species that exhibit minimal movement within the aquatic habitat (e.g., bivalve molluscs and English sole in nearshore marine areas; mussels and sculpins in streams).

The use of a few indicator species for exposure assessment is appropriate for initial screening of geographic areas before more detailed exposure assessments are conducted. If no potential health problems are identified in an initial risk analysis, further data collection may not be warranted, unless long-term monitoring is desired. If, on the other hand, analysis of tissues from indicator species reveals substantial health risks, further field surveys may be needed to perform a detailed exposure assessment, using consumption patterns and contaminant concentrations for a wider variety of harvested species.

The use of indicator species for exposure assessment offers the following advantages:

- Field surveys based on indicator species are cost-effective because efforts can be focused on collecting large sample sizes of one or a few species rather than minimally adequate sample sizes of many species
- Background information on the distribution, abundance, and contamination of indicator species may be available
- Indicator species can be selected to represent the average or maximum level of contamination expected for all harvested species (assuming background or pilot data are available)
- Because the indicator species does not have to be a dominant species in the harvest, extensive data on catch and consumption patterns may not be needed.

The disadvantages of the indicator species approach are that:

- The exposure estimate may be biased if the indicator species does not truly represent the case of interest (e.g., average- or worst-case concentrations of contaminants)
- The selected species may be a good indicator for some contaminants of concern but not for others
- If the selected indicator species are not major components of the harvest, the exposure assessment may appear unrealistic
- Background data on the distribution, abundance, and contamination of the harvested species are usually needed to select appropriate indicator species.

Phillips (1980), Tetra Tech (1985b), and Phillips and Segar (1986) provide criteria for selecting target species for bioaccumulation surveys. Important criteria to consider when choosing indicator species for an exposure assessment are listed below. The target species should be:

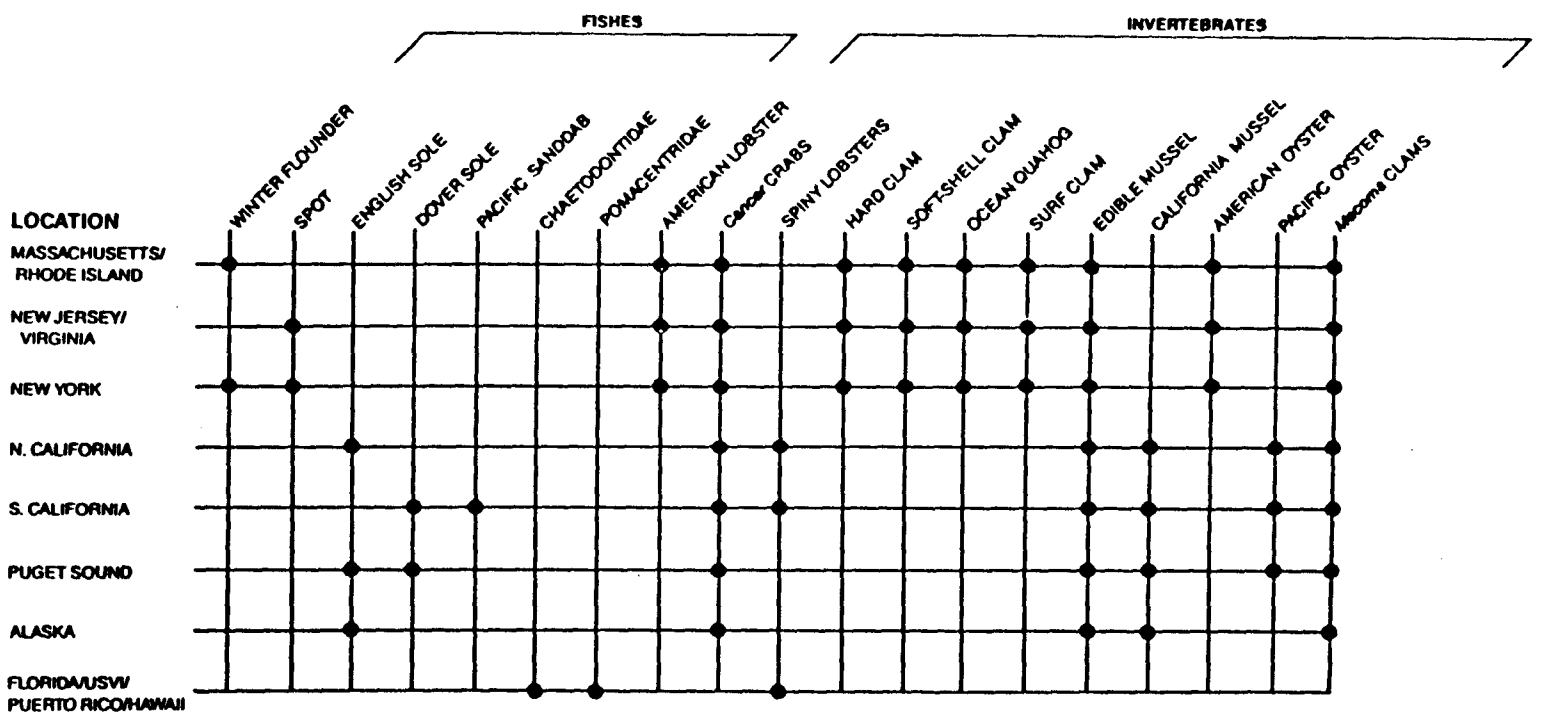
- Harvested by the exposed population or be representative of the contamination levels in the primary harvested species
- Relatively sedentary to be representative of a specific study area
- Easy to sample and abundant enough to obtain adequate samples
- Large enough to yield an adequate sample size for chemical analysis.

Some additional criteria for target species to be used as indicators of contaminant concentrations in the environment are:

- Contaminant concentrations in the target organisms should be related to those in the environment
- Metabolic regulation of contaminant concentrations by the target species should be absent or weak
- Contaminant interactions should not greatly diminish the usefulness of the target species as a site-specific indicator when contaminant composition is expected to differ among sites
- Target species should integrate the effects of contaminant uptake over time.

A summary of indicator species recommended by Tetra Tech (1985b) for monitoring of chemical residues in marine and estuarine species is shown in Figure 4. Many of the recommended indicator species are associated with soft-sediment substrates. Contact with sediments by such species may lead to body burdens of contaminants that are high relative to those in pelagic organisms of similar lipid content and size. However, the relationship of contaminant concentrations in demersal (bottom-dwelling) vs. pelagic (open-water) organisms is difficult to predict without extensive data. As shown by Tetra Tech (1986c), English sole may be used as an indicator of the order-of-magnitude contaminant concentrations that would be expected in edible tissues of pelagic fish species in Puget Sound, WA. However, relative contamination among species may vary among bays within Puget Sound. For example, in Commencement Bay, the average PCB concentration in muscle of English sole was about twice that in recreationally harvested pelagic species (Pacific cod, Pacific hake, Pacific tomcod, rockfish, walleye pollock, and white-spotted greenling; based on data from Gahler et al. 1982). In Elliott Bay, the average PCB concentration in angler-caught English sole was about 0.4 times that in harvested pelagic species (sablefish, squid, Pacific cod, Pacific hake, Pacific tomcod, rock sole, and rockfish; based on data from Landolt et al. 1985). Site-specific data are needed to evaluate contamination of potential indicator species relative to contamination in other species of interest.

Apparently, no comprehensive review of target species for bioaccumulation studies in lakes and streams has been conducted. However, it is clear that salmon and trout (Salmonidae), perch (Percidae), and sunfish (Centrarchidae) species will be preferred for tissue analysis in many cases because they constitute the bulk of the fisheries harvest. Freshwater mussels, especially Anadonta spp. and Corbicula spp., crayfish, sculpins



Note: See Appendix Table D-1 for scientific names of recommended target species.

Reference: Tetra Tech (1985b)

Figure 4 Summary of recommended marine and estuarine indicator species.

(Cottidae), and catfishes (Ictaluridae) may be preferred as target species for site-specific analyses.

Size Classes--

A study design for analysis of chemical residues should incorporate stratified random sampling of a selected size class or various size classes within each target species. Stratification by size is extremely important, since both lipid content and contaminant concentrations can vary greatly among different sized organisms of the same species (Phillips 1980). Moreover, the nature of the relationship between body size and contaminant concentration varies among chemicals, among species, and possibly among sampling stations and seasons (Phillips 1980; Strong and Luoma 1981; Sloan et al. 1985; Johnson 1987). The size classes of each species selected for analysis should be representative of those in the diet of the potentially exposed human population. For persistent chlorinated organic compounds and organic mercury complexes, the largest (i.e., oldest) individuals within an aquatic species are expected to be the most contaminated. If organic compounds are of concern and a limited analysis is planned, the study should focus on the largest individuals likely to be harvested by the exposed human population.

Sampling Station Locations

Two general approaches to field sampling are possible. First, the investigator can obtain samples directly from harvesters. This approach has the advantage that the sampled population is the population of direct interest for the exposure and risk assessments. However, one drawback of this approach is the potential for contamination or degradation of samples due to handling of the samples by the harvesters. Moreover, the precise sampling locations may be unknown if samples are collected at dockside from recreational or commercial fishing boats. The second approach is to obtain samples independent of the normal harvesting efforts, allowing standard sample handling practices to be implemented. Independent sampling also facilitates the collection of adequate samples for stratification by organism size, habitat, or some other variable. The remainder of this section addresses a sampling effort that is independent of normal harvesting activities.

Sampling stations should generally be located in known harvest areas. However, additional stations in relatively uncontaminated reference or control areas should also be sampled. By comparing results among harvest areas and between each harvest area and the reference station, one can establish not only the degree of spatial heterogeneity but also the magnitude of elevation above reference of contaminant concentrations (and corresponding health risks) at each harvest area. Because sampling depth or vertical position on the shore may influence contaminant concentration in aquatic organisms, reference station characteristics should be closely matched to those for the harvest areas.

Sampling stations may be located within a study area according to one of several probability sampling designs (Figure 5). Gilbert (1987) provides a concise summary of conditions under which each sampling design is preferred.

Simple random sampling implies that each individual organism within a species has an equal chance of being selected for measurement and that selection of one individual does not influence selection of others. A simple random sampling strategy is appro-

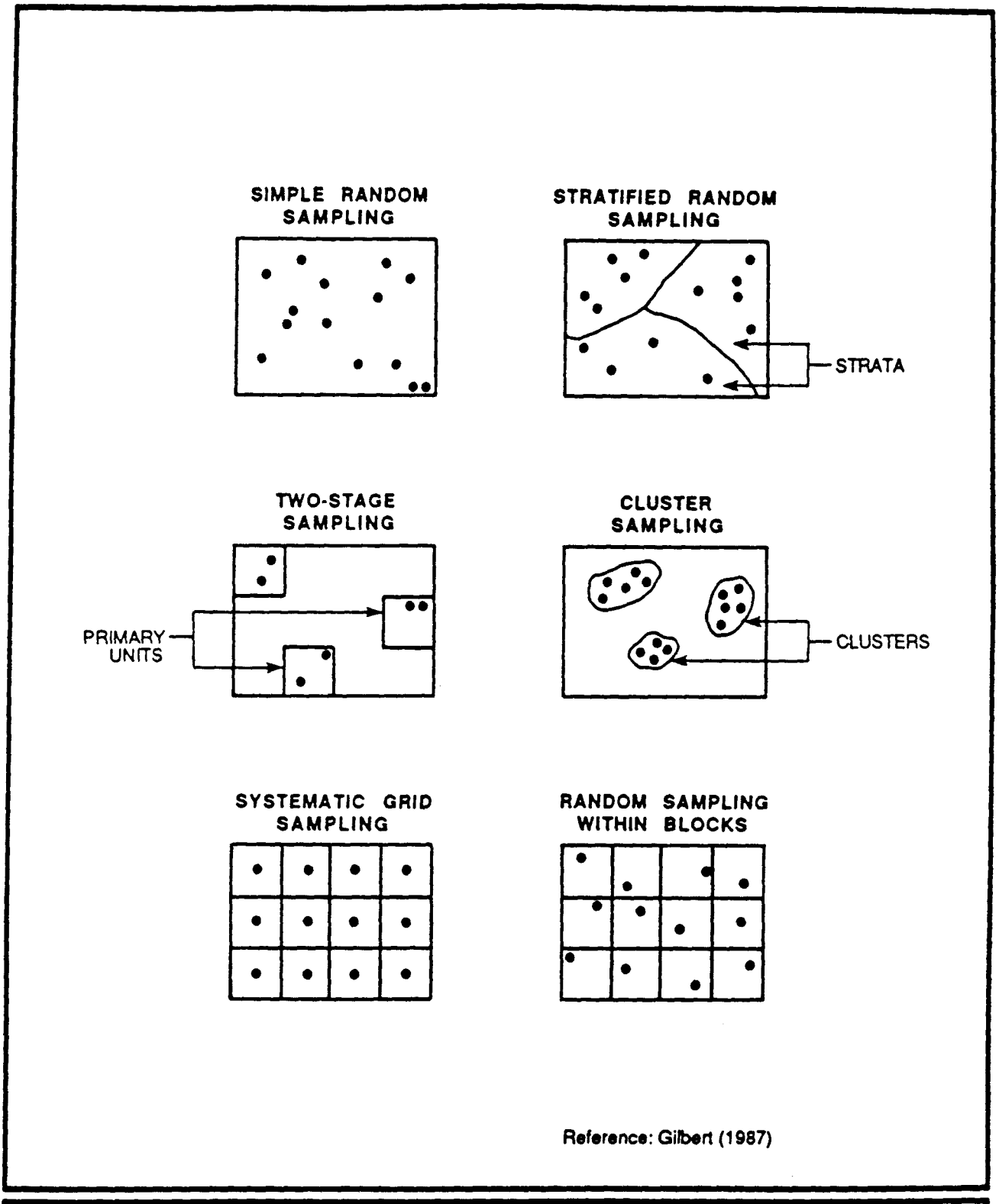


Figure 5 General sampling station layouts for probability sampling in two dimensions.

priate if there are no major trends or patterns of contamination in the study area. Note that sampling of fish or shellfish with sampling gear (e.g., hook and line, nets) will always be nonrandom to some extent because of the selective nature of the gear.

Stratified random sampling involves random sampling within nonoverlapping strata of a population (e.g., subareas based on concentrations of fishing effort). This sampling approach is appropriate when geographic areas within a harvest region are heterogeneous relative to the kind or degree of contamination.

Two-stage sampling involves random or systematic subsampling of primary units selected by a random sampling technique. For example, fish could be collected randomly from a given stream reach. In the second stage of sampling, subsamples of fillet from each fish could be selected randomly for chemical analyses. Multistage sampling is an extension of two-stage sampling.

Cluster sampling involves choosing groups of individual organisms at random, then measuring contaminant concentrations in all individuals within each cluster. Cluster sampling is sometimes used to estimate means if clusters of sampling units (e.g., individual organisms in a clump) can be selected randomly more easily than can individual units.

Systematic sampling consists of sampling at locations and/or times according to a pattern. For example, samples may be collected at equidistant points on a spatial grid or at equally spaced time intervals. Systematic sampling is generally preferred for mapping patterns of contamination. As such, it is more appropriate for soil or sediment sampling than for bioaccumulation studies. The random-sampling-within-blocks strategy shown in Figure 5 combines systematic and random sampling. Such procedures produce more uniform coverage than does simple random sampling.

Gilbert (1987) describes systematic sampling approaches for locating "hot spots" or highly contaminated local areas. He addresses the following questions:

- "What grid spacing is needed to hit a hot spot with specified confidence?"
- "For a given grid spacing, what is the probability of hitting a hot spot of specified size?"
- "What is the probability that a hot spot exists when no hot spots were found by sampling on a grid?"

If grid sampling is to be applied to a bioaccumulation study, the target species must exhibit limited mobility. Grid sampling can also be applied to collection of aquatic sediment samples. Gilbert (1987) provides guidance on spacing of grid samples.

Grid sampling is especially appropriate for identifying environmental contamination associated with discrete sources of pollution such as industrial discharges, storm drains, and combined sewer overflows. The use of caged mussels is a promising approach for identifying sources through chemical residue analysis. As part of the Long Island Sound Estuary Program, EPA Region I is using caged mussels to monitor chemical contaminants entering the Sound from tributaries. The California mussel watch program (e.g., Ladd et al. 1984), the U.S mussel watch (Goldberg et al. 1978, 1983; Farrington et al. 1983), and the NOAA status and trends program (Boehm 1984) illustrate the use of both resident and caged transplant mussels to monitor bioaccumulation of toxic chemicals

over space and time. Toxic chemical residues in mussels are excellent indicators of point source discharges as well as pollution gradients (Phillips 1976; Popham et al. 1980; Phelps et al. 1981). U.S. EPA (1982) described recommended protocols for caged mussel studies.

A combination of two-stage and stratified- random (or stratified-grid) sampling is recommended here for most studies of fisheries contamination to support exposure assessment. The two stages correspond to an individual organism and edible tissue. Samples of individual organisms may or may not be composited depending on specific study objectives (see below, Kinds of Samples, Composite Sampling). Sampling strata may include harvest area, species, and size classes. Other sampling strategies may be either too simple or inappropriate to meet the typical objectives of exposure assessment studies.

Time of Sampling

The timing of bioaccumulation surveys should be based on the temporal distribution of harvest seasons and inherent biological cycles of target species. The timing of harvest periods depends on the availability of fishery resources, which may be influenced by the migratory patterns and feeding cycles of target species. Biological cycles that influence an organism's susceptibility to bioaccumulation should also be considered when choosing a sampling period. The most important of these is the reproductive cycle, which is discussed further below. In crustaceans (e.g., crab and shrimp), the molting cycle also determines the potential for bioaccumulation of toxic chemicals. The rate of uptake of contaminants by crustaceans is highest just after molting, before hardening of the integument limits its permeability.

The reproductive cycles of aquatic organisms may exert a major influence on tissue concentrations of many contaminants, especially organic compounds (Phillips 1980). If a worst-case analysis is desired, the target species should be sampled at a time during the harvest period when tissue contaminant concentrations are expected to be at their highest levels. An effort should be made to sample at or just before the peak of reproductive ripeness, before gametes or offspring are released. At this stage of the reproductive cycle for a given species, lipid content and concentrations of organic contaminants in tissues should be at their highest levels. Because the time of sampling should be tailored to the reproductive characteristics of the target species, sampling periods may vary among species. However, once a sampling period is chosen, it should remain constant over time if an ongoing monitoring program is planned.

An alternative approach is to sample throughout the harvest season for each target species. In this way, representative values can be obtained for estimating means within sampling periods and for detecting seasonal or long-term trends. In most cases, exposure assessments will be performed over relatively short periods of time (e.g., a year), and multiyear sampling may not be required. Within a harvest season, however, sufficient samples should be collected to estimate the mean concentrations of contaminants during the harvest period. To estimate temporal variation or to obtain worst-case estimates, replicate samples will be needed at several times within the harvest season. The frequency of sampling should be related to the expected rate of change in tissue concentrations of contaminants. For an extensive review of temporal changes in bioaccumulation and body burdens of contaminants in aquatic organisms, the reader should consult Phillips (1980).

Kinds of Samples

The kind of tissue sampled and the sampling unit (i.e., individual organisms vs. composites of several organisms) greatly influence the sensitivity, precision, and representativeness of an exposure assessment. The issues of composite sampling and sample preparation techniques are addressed in the following sections.

Composite Sampling--

An alternative to the analysis of tissue from individual organisms is the analysis of composite samples. Composite tissue sampling consists of mixing tissue samples, each called a subsample, from two or more individual organisms typically of a single species collected at a particular site and time period. The mixture is then analyzed as a single sample. The analysis of a composite sample therefore provides an estimate of an average tissue concentration for the individual organisms that make up the composite sample. Composite sampling is a cost-effective strategy when the individual chemical analyses are expensive but the cost of collecting individual samples is relatively small. The collection of composite samples is required in cases where the tissue mass of an individual organism is insufficient for the analytical protocol.

Bioaccumulation surveys designed to support exposure assessments may use a composite sampling strategy. Current risk assessment models used by EPA are based on estimates of long-term average exposure. Estimates of the mean concentrations of contaminants in edible tissue samples from harvested organisms are used as estimates of the exposure concentrations for human consumers of fish and shellfish. Composite sampling of the tissue from selected organisms is a method for preparing a sample that will represent an average concentration. The collection of replicate composite tissue samples at specified sampling locations will result in a more efficient estimate of the mean (i.e., the variance of the mean obtained with replicate composite samples is smaller than that obtained with the collection of replicate samples of individual organisms).

One major disadvantage of composite sampling is the inability to directly estimate the range and the variance of the underlying population of individual samples. Such information is extremely useful in bioaccumulation monitoring programs as an early warning signal of increasing levels of contamination. For example, only a few individuals within a sample may contain high contaminant concentrations. Mixing these individuals with less contaminated organisms in a composite sample at a given station may dilute the contaminants and mask a potential problem. In exposure assessment, the patchy distribution of highly contaminated fish or shellfish may indicate the spatial distribution of sources of contaminants. Also, a lack of data on individual samples may mask the potential for short-term health effects (e.g., learning disabilities, neurological malfunctions) in sensitive individuals or in those who consume excessive amounts of highly contaminated organisms over a short period of time. In some cases, however, preliminary exposure and risk assessment calculations could be performed to justify focusing on chronic effects (e.g., carcinogenesis).

The benefits of compositing individual samples from a single station within a given sampling period often outweigh the disadvantages just discussed. In such cases, Rohde (1976) and Tetra Tech (1986b) provide a method for calculating the variance of

the underlying population of individual samples when the variance of the composite samples is known:

$$\text{Var } X = n \text{ (Var } Z) \tag{3}$$

where:

Var X = variance of the mean of individual samples
Var Z = variance of the mean of composite samples
n = number of subsamples constituting the composite sample.

This equation assumes that replicate observations from individual and composite samples are normally distributed. Also, the composites must each consist of subsamples of equal mass (i.e., the same mass of tissue is taken from each organism). For unequal proportions of composite subsamples (i.e., tissue mass), the variance of the series of composite samples increases and, in extreme cases, exceeds the variance of grab samples. Thus, it is recommended here that the same mass of tissue be taken from each organism contributing to a composite sample of a single species. For the analyses presented below, it was assumed that the composite samples consist of subsamples of equal proportions.

Two special cases of composite sampling are "space-bulking" and "time-bulking" (cf. Phillips and Segar 1986). Space-bulking involves sampling of individual organisms from several locations and combining tissue samples into one or more composite samples for analysis. Time-bulking involves taking multiple samples over time from a single location and compositing these samples. Time-bulking over a harvest season is especially appropriate where short-term variations in contaminant concentrations in tissue samples are significant and budget constraints preclude repeated analyses over time.

The adoption of space-bulking or time-bulking strategies ultimately relates to the objectives of the exposure assessment. Because exposure concentrations are typically averaged over time in risk assessment models, time-bulking may be more justified than space-bulking. In any case, one should use these strategies with extreme caution since significant information on spatial and temporal heterogeneity may be lost. Selection of space-bulking or time-bulking techniques should be supported by analyses of available data or data from preliminary sampling. Tiered analyses of samples can also be used to evaluate the appropriateness of compositing strategies. For example, individual samples may be stored separately over the entire harvest season. At the end of sample collection, preliminary analyses of individual tissue samples from a selected series of sites and times could be performed to evaluate temporal and spatial heterogeneity and to devise an appropriate compositing strategy.

Tetra Tech (1986b) evaluated the effects of composite sampling on the statistical power of a sampling design (see Appendix D). Their results demonstrate that the confidence in the estimate of the mean concentration of contaminant in tissue increases as the number of individual samples in the composite increases. The statistical power (i.e., the probability of detecting a specified minimum difference among treatments) increases dramatically with the number of individual samples in each replicate composite sample. However, the benefit of adding more individual samples to each composite eventually decreases with each successive increase in the number of individual samples per composite. For moderate levels of variability in chemical residue data, 6-10 individual samples within each of 5 replicate composite samples may be adequate to detect a treatment difference equal to 100 percent of the overall mean among treatments.

Rohde (1976), Schaeffer et al. (1980), Brumelle et al. (1984), and Gilbert (1987) also discuss statistical aspects of composite sampling.

Sample Preparation--

Tissue samples should be removed from target organisms and prepared for analysis according to a well-defined protocol. Tissue preparation methods can greatly affect the results of bioaccumulation analyses (Smith et al. 1973; Skea et al. 1981; Puffer and Gossett 1983; Landolt et al. 1987). In specifying a tissue preparation protocol, the following issues should be addressed:

- Type of tissue (e.g., muscle fillet, whole body, internal organs)
- Location of tissue in organisms' body
- Removal of any or all of shells, scales, skin, and subcutaneous fat
- Raw vs. cooked samples and cooking method
- Homogenization method
- Minimum sample mass for each kind of analysis.

The kind and location of tissue analyzed may influence the realism of the exposure assessment. For example, most humans consume only fillets of fish, not internal organs or whole fish. Because internal organs are often more contaminated by toxic chemicals than are fillets, exposure estimates based on chemical analyses of organs or whole fish could be unrealistically high. Removal of skin and subcutaneous fat from samples before chemical analysis generally reduces the mean concentrations of chlorinated organic compounds. However, this practice may also reduce the variance of measurements, allowing more sensitive discrimination among statistical treatments (e.g., species or sampling locations). Even within the fillet tissue, contaminant concentrations may vary depending on the original location of the sample on the fish's body. Cooking of fillets before chemical analysis may result in a 2-64 percent decrease in the concentration of PCBs relative to the uncooked sample, but the results vary greatly with species and cooking method (Smith et al. 1973; Skea et al. 1981). However, cooking may also activate or transform chemicals to create carcinogens (e.g., creation of benzo(a)pyrene during char-broiling). Finally, adequate homogenization of samples before they are analyzed is necessary to obtain representative results.

Because information on the effects of tissue preparation methods on the results of chemical residue analyses is limited, it is recommended that a pilot survey be performed to establish consistent, reliable methods. Relevant protocols for sample storage and preparation are available in a bioaccumulation monitoring guidance document issued by the EPA 301(h) program (Tetra Tech 1986e) and in the EPA Interim Methods for the Sampling and Analysis of Priority Pollutants in Sediments and Fish Tissue (U.S. EPA 1981). Because many decisions about sample preparation depend on the specific objectives of the study, no single protocol for sample preparation covers all of the possible approaches. For example, samples are usually blotted dry before being weighed to obtain an estimate of wet weight. However, when bivalve molluscs are being prepared for analysis, it may be desirable to retain excess water for later analysis.

Analysis of raw edible tissues is recommended to provide data on the concentrations of contaminants initially present in tissues that are normally consumed. Eventually, it may be possible to mathematically account for cooking effects in the exposure assessment. At present, however, data on cooking effects are highly variable.

Sample Replication

Replicated measurements of contaminant concentrations in tissue samples are needed to perform uncertainty analysis (e.g., characterizing the precision of the estimates of mean contaminant concentrations). Replicated data are also needed for many statistical tests of spatial and temporal trends. Sample replication is recommended here for all bioaccumulation measurements to be used in exposure assessments. Guidance on selection of a sample replication scheme is provided in Appendix E. In most cases, at least five replicate samples of individual fish (or shellfish) are required to provide minimal statistical power (e.g., ability to discriminate a treatment difference equal to 200 percent of the overall mean among treatments). Increases in sample replication beyond about 10 individual replicates clearly do not provide sufficient benefits in statistical power to justify added costs of sampling and analysis (Appendix E). Greater power can be achieved in a cost-effective manner by composite sampling if information on contamination of individual organisms is not needed (Appendix D).

Selection of Analytical Detection Limits and Protocols

Criteria for selection of method detection limits for analytical protocols may be based on risk assessment models explained below (see Risk Characterization). For example, the analytical chemistry methods may be chosen to enable detection of a chemical concentration associated with a specified minimum risk level defined as acceptable by risk managers. Other factors may dictate choice of a lower detection limit. For example, routine analytical methods may attain much lower limits than required by the specified minimum detectable risk level. Also, lower detection limits may be desired if an objective of the study is to develop baseline bioaccumulation data as well as health risk data. In some cases (e.g., 2,3,7,8-tetrachlorodibenzo-p-dioxin, benzidine, dieldrin, N-nitrosodimethylamine), the minimum detection limit that can be achieved with current technologies corresponds to a plausible-upper-limit risk that is substantially above risk levels of potential concern (e.g., 10^{-5} to 10^{-6}). Tetra Tech (1985c) provides further guidance on detection limits for bioaccumulation surveys.

Approved routine EPA methods for sampling and full-scan analysis of chemical contaminants in tissues are not available. U.S. EPA (1981) published interim methods for sampling and analysis of priority pollutants in tissues. EPA-approved protocols for chemical analysis of water samples were adapted for application to tissue samples as part of the Section 301(h) marine discharge waiver program of the Office of Marine and Estuarine Protection [see Tetra Tech 1986e for 301(h) sampling and analysis protocols]. Specifically, 301(h) analytical methods for extractable organic compounds were adapted from Method 1625 Revision B (U.S. EPA 1984a) and additional guidance from the EPA Contract Laboratory Program for Organic Analysis (U.S. EPA 1984c). When applicable, the 301(h) protocols incorporate established EPA advisory limits for precision, accuracy, and method performance (U.S. EPA 1984c). The EPA Office of Acid Deposition, Environ-

mental Monitoring, and Quality Assurance is developing further guidance on sampling and analysis methods to support exposure assessments.

Other available methods for analysis of chemical contaminants in tissue samples include those used by U.S. FDA (1978), NOAA (MacLeod et al. 1984), and Ozretich and Schroeder (1985). These analytical protocols are designed to apply to specific subsets of the EPA priority pollutants. U.S. FDA (1978) methods, as described in the Pesticide Analysis Manual, include variations in procedures for tissues differing in lipid content.

The choice of an analytical protocol may be influenced by available financial resources. Chemical analysis of samples is often the most costly portion of a sampling and analysis program. Higher analytical costs may be required to achieve greater sensitivity (i.e., lower detection limits). Examples of analytical costs are shown in Table 5. At a given level of sensitivity, a wide range of precision is encountered among diverse organic compounds. For example, the low end of the range of variation shown for extractable compounds in Table 5 can usually be achieved for hydrocarbon analyses, whereas substantially more variability is common for analyses of phthalates and some organic acid compounds. A wide range of analytical costs is also encountered at a given level of sensitivity (Table 5). Differences in analytical techniques, laboratory experience with these techniques, and pricing policies of laboratories account largely for the wide variation in cost.

QA/QC Program

An adequate QA/QC program is essential for any sampling and analysis effort to support exposure assessment. U.S. EPA (1984c, 1985c) provides guidance on QA/QC for chemical analysis. Tetra Tech (1986f) describes QA/QC procedures for field and laboratory methods used by the Section 301(h) program. Horwitz et al. (1980) provide guidance on QA/QC in the analysis of foods for trace contaminants. Brown et al. (1985) describe QA guidelines followed by NOAA for chemical analysis of aquatic environmental samples.

A QA/QC plan should be developed as part of the study design for sampling and analysis of chemical residues. The QA/QC plan should include the following information:

- Project objectives
- Project organization and personnel
- QA objectives for precision, accuracy, and completeness for each kind of measurement
- Summary of sampling procedures, including sample containers, preparation, and preservation
- Forms for documenting sample custody, station locations, sample characteristics, sample analysis request, and sample tracking during laboratory analysis
- Detailed description of analytical methods
- Calibration procedures for chemical measurements

TABLE 5. APPROXIMATE RANGE OF COST PER SAMPLE FOR ANALYSES OF EPA PRIORITY POLLUTANTS IN TISSUES AS A FUNCTION OF DETECTION LIMITS AND PRECISION[a]

EPA Priority Pollutant Group	Approximate Detection Limit	Typical Precision	Approximate Cost Range[b]
Extractable acid/base/neutrals/ PCBs/pesticides	<1-20 ppb	<±5% - >±100%	$900->$2,000
Volatiles	<5-20 ppb	<±10% - >±100%	$250-$350
Metals	100 ppb	<±10% - >±30%	$250-$300

[a] NOTE: Range of per sample cost is based on multiple quotes compiled in 1986 for specific applications and >5 samples. The actual costs may vary from the range shown. This information is provided solely for perspective on relative differences in cost and should not be interpreted as a recommendation of appropriate costs for any given circumstance.

[b] Each cost range is mainly the result of laboratory differences in technique and pricing, NOT the range in precision or detection limits shown.

- Internal QC checks for analytical laboratories
- Performance and system audits for sampling and analysis operations
- Preventive maintenance for equipment
- Procedures for data management, data QA review, and data reporting for each kind of measurement
- Corrective actions
- Procedures for QA/QC reporting and responsible federal and state QA officers
- Mechanisms for approval of alterations to the monitoring program, for suspending sample analyses, and for stopping sample analyses within a tiered design.

Relevant portions of the QA plan should be incorporated in the statement of work for each contract laboratory involved in sample analyses.

Documentation and QA Review of Chemical Data

Adequate documentation of the results of chemical analyses are needed to ensure proper interpretation of the data. If a contract laboratory is performing the sample analyses, such documentation should be specified in the original statement of work. The documentation listed below is recommended for chemical residue data:

- A cover letter discussing analytical problems (if any) and referencing or describing the procedure used
- Reconstructed ion chromatograms for GC/MS analyses for each sample
- Mass spectra of detected target compounds (GC/MS) for each sample
- GC/ECD and/or GC/FID chromatograms for each sample
- Raw data quantification reports for each sample
- A calibration data summary reporting calibration range used (and DFTPP and BFB spectra and quantification report for GC/MS analyses)
- Final dilution volumes, sample size, wet-to-dry ratios, and instrument detection limit
- Analyte concentrations with reporting units identified (to two significant figures unless otherwise justified)

- Quantification of all analytes in method blanks (ng/sample)
- Method blanks associated with each sample
- Tentatively identified compounds (if requested) and methods of quantification (include spectra)
- Recovery assessments and a replicate sample summary (laboratories should report all surrogate spike recovery data for each sample; a statement of the range of recoveries should be included in reports using these data)
- Data qualification codes and their definitions.

The data reporting forms for the EPA Contract Laboratory Program illustrate an appropriate format for documentation of chemical data.

All contaminant concentration data to be used in a risk assessment should undergo a thorough QA review by a qualified chemist independent of the laboratory that analyzed the samples. In some cases, the analytical laboratory may provide a QA review that is simply checked by an independent chemist. The purpose of the QA review is to evaluate the data relative to data quality objectives (e.g., precision and accuracy) and performance limits established in the QA plan. In many cases, qualifiers are necessary for selected data values. These qualifiers should be added to the database. A summary of data limitations should always be included in the risk characterization (see below, Risk Characterization). The EPA Office of Acid Deposition, Environmental Monitoring, and Quality Assurance is developing guidelines for quality assurance of chemical data to support exposure assessments.

Statistical Treatment of Data

Statistical analyses of data will depend on specific study objectives. For each species, statistical summaries of tissue concentration data should include sample size, estimates of arithmetic mean concentration, range, and a measure of variance (standard error or 95 percent confidence limits). Geometric mean concentrations are appropriate measures of central tendency when only estimates of tissue burden of contaminants or exposure dose are desired. However, arithmetic means are needed to compare exposure estimates with RfDs and to calculate health risk for chronic effects because long-term consumption is an averaging process. Mean tissue concentrations and variances may be calculated for mixed-species diets if data are available on the proportion of each species in the diet.

The one-way ANOVA model discussed earlier or multifactor ANOVA models are appropriate for testing for differences in mean contaminant concentrations among species, among sampling stations, or among time periods (Schmitt 1981; also see Tetra Tech 1986b,d). For small sample sizes and data that do not satisfy the assumptions of ANOVA, nonparametric tests such as the Wilcoxon rank sum test for two treatments or the Kruskal-Wallis test for multiple comparisons are recommended. These tests have the added advantage of being relatively insensitive to a few missing data points or undetected observations (Gilbert 1987). Long-term data sets may be tested for trends by time series analysis (for reviews, see Montgomery and Reckhow 1985 and Gilbert

1987). Examples of trend analysis for chemical contaminants in fish are provided by Brown et al. (1985) for PCBs in striped bass of the Hudson River and by DeVault et al. (1986) for PCBs and DDT in lake trout from the upper Great Lakes.

Data on concentrations of contaminants of concern in tissue samples will often contain observations below detection limits. Means and variances for tissue concentrations should be calculated twice: once using detection limits for undetected observations and once using 0 for undetected observations. Although alternative approaches are possible (e.g., using one-half the detection limit), the approach recommended here yields more accurate, complete results by quantifying the range of the estimated values. According to the EPA Exposure Assessment Group, calculations of plausible-upper-limit risk estimates based on detection limits should generally be avoided. However, risk estimates based on detection limits may occasionally be useful to indicate that particular chemicals, species, or geographic locations are not problems, even assuming undetected contaminants are present at concentrations just below their respective detection limits.

The choice of contaminant concentration values to use in subsequent calculations to estimate exposure (and ultimately risk) is partly a risk management decision. Exposure estimates are commonly based on arithmetic mean concentrations of contaminants in edible tissue of fish or shellfish. Use of the upper 90 or 95 percent confidence limit in place of the mean would provide a conservatively high estimate of exposure. Calculation of conservative estimates for exposure is an appropriate step in uncertainty analysis. However, U.S. EPA (1986b) guidelines on exposure assessment discourage the use of worst-case assessments. Use of upper confidence limits for chemical concentrations in combination with a plausible-upper-limit estimate for the Carcinogenic Potency Factor may lead to an unrealistic (i.e., highly unlikely) estimate of upper-bound risk, especially if a conservatively high estimate of fish consumption is also adopted. In most cases, the best estimate of exposure based on mean contaminant concentrations should be used to develop risk estimates. If upper confidence limits for chemical concentrations are used to develop risk estimates, the effects of compounding conservative assumptions should be evaluated.

ANALYSIS OF SOURCES, TRANSPORT, AND FATE OF CONTAMINANTS

Exposure pathways and routes are potential mechanisms for transfer of contaminants from a source to a target human population or subpopulation. The sources, transport, and fate of chemicals in the environment are analyzed to evaluate exposure pathways and routes. To compensate for a limited database, this analysis often includes mathematical modeling of contaminant transport and fate. The modeling of exposure pathways focuses on transfer of contaminants from source to target fishery species, since the transfer step from fishery to humans can be based on knowledge of fishery harvest activities (see below, Exposed Population Analysis). When extensive data on contamination of a fishery is available and source-tracing is not an objective, modeling of chemical transport and fate may be unnecessary.

Although the specific uses of modeling in exposure assessment are diverse, several broad objectives may be outlined as follows:

- Estimate the spatial and temporal distribution of concentrations of chemical contaminants in edible tissues of fish and shellfish
- Identify potential sources of contaminants
- Evaluate alternative source controls or remedial actions.

Estimation of contaminant concentrations in fish and shellfish by mathematical modeling is especially useful when available data on tissue contaminants are limited. If the distribution of contaminants in sediments or water can be estimated from available data or model predictions, estimates of chemical residues in fishery species can be based on relationships of tissue contamination to environmental contamination (e.g., laboratory-derived bioconcentration factors). Spatial characterization is important for identifying areas of high contamination resulting from heterogeneous transport and deposition of contaminants. Temporal characterization is important for defining time-dependent changes in contaminant concentrations that may mitigate future exposure and risk.

Predictions of spatial trends in chemical residues may also aid in identifying and controlling sources of pollutants. For example, when data on sources, sediments, and tissues are available, modeling of chemical transport and transformation processes may help to link the patterns of chemical contaminants observed in the environment with specific individual sources. Information on differential degradation of contaminants and compositional relationships for complex mixtures can be used to support the model analysis (e.g., calibration and validation). Finally, modeling of contaminant releases in combination with chemical residues in fisheries may aid in evaluating alternative source controls or remedial actions for waste sites. The results of modeling can indicate the level of source control or remedial action needed to achieve a desired level of environmental quality.

In the exposure assessment guidelines, U.S. EPA (1986b) describes general approaches for characterizing sources, exposure pathways, and environmental fate of chemicals. Analysis of chemical transport and fate is a major endeavor, which cannot be addressed in detail here. For additional information, the interested reader should consult Callahan et al. (1979), Burns et al. (1981), Jensen et al. (1982), Mills et al. (1983), Games (1983), Connor (1984b), Thomann and Connolly (1984), Onishi (1985a,b), U.S. EPA (1986b), Pastorok (1986), and references therein.

EXPOSED POPULATION ANALYSIS

The second stage of the exposure assessment, analysis of exposed populations, includes the following steps:

- Identify potentially exposed human populations and map locations of fisheries harvest areas
- Characterize potentially exposed populations
  - Subpopulations by age, sex, and ethnic composition
  - Population abundance by subpopulation

- Analyze population activities

  - Harvest trip frequency
  - Seasonal and diel patterns of harvest trips
  - Time per harvest trip
  - General activity (e.g., clamming, crabbing, fishing)

- Analyze catch/consumption patterns by total exposed population and subpopulation

  - Proportion of successful trips
  - Catch by numbers and weight according to species
  - Time since last meal of locally harvested organisms
  - Number of consumers sharing catch
  - Parts of organisms eaten
  - Method of food preparation (e.g., raw, broiled, baked)

- Estimate arithmetic average consumption rate by species and by total catch for the total exposed population and for subpopulations. For seasonal fisheries, consumption rates may be estimated on an annual and a seasonal basis.

Only selected steps may be performed in a given exposure assessment, depending on data availability, study objectives, and funding limitations. Note that many of the steps to characterize harvest activities and consumption rates apply only to analyses of recreational fisheries. When estimating consumption of fish and shellfish of commercial origin, harvest activities are irrelevant. Also, the specific geographic origin of commercial fisheries products is often unknown.

Two approaches to estimating consumption rates are outlined below. In the first approach, a comprehensive analysis of a recreational fishery is performed based on extensive catch/consumption data for the exposed population. In the second approach, estimates of consumption rates are based on available values for the U.S. population (or subpopulations) or other assumed values. Most of the available estimates were derived from recall or diary studies (Lindsey 1986) and include commercial fisheries products. It is recommended here that local or regional assessments of fishery consumption be performed whenever possible to avoid possible errors inherent in extrapolating standard values for the U.S. population to distinct subpopulations. Moreover, extrapolation of standard consumption estimates that include commercial fisheries products to recreational fisheries should generally be avoided.

In developing a profile of the exposed population, there is no single "correct" estimate of consumption rate. Because consumption rates are highly variable, use of a range of values or a probability distribution for consumption rate estimates is recommended. This approach may also be followed when estimating consumption rates for subpopulations of interest.

An alternative to the typical practice of basing risk estimates on selected consumption rates involves presenting risk estimates graphically for a wide range of consumption rates that essentially includes all possible realistic values (see below, Presentation and Interpretation of Results). For example, plots of estimated risk vs. consumption rate are useful for public advisories on recreational fishery resources. In this case, each

individual may evaluate risks by selecting a consumption value based on his or her diet. Use of this approach avoids having to collect extensive data on the exposed population. A similar approach involves selecting an "acceptable" risk level and providing advice on levels of consumption, such that the "acceptable" risk is not exceeded. The advantage of both of these approaches is that consumption rates need not be determined or assumed. While both may provide excellent formats for advising sports fishermen, they may not be appropriate in cases where involuntary exposures are likely (e.g., commercial fisheries).

Comprehensive Catch/Consumption Analysis

Appropriate field survey forms, data analyses, and format for presentation of results for a comprehensive catch/consumption analysis of fisheries are provided by Landolt et al. (1985), McCallum (1985), and National Marine Fisheries Service (1986). Details of methods will not be presented here, except to emphasize some important considerations for calculating consumption rates. Examples analyses of catch/consumption data can be found in Puffer et al. (1982) for coastal waters of southern California, in Landolt et al. 1985, 1987) for Puget Sound, in Belton et al. (1986) for New York Bay and Newark Bay, and in National Marine Fisheries Service (1986) and companion documents for other areas of the U.S.

Lindsay (1986) reviewed alternatives to field survey methods, including use of food diaries and dietary recall. Gartrell et al. (1986a,b) described methods used by FDA in their total diet studies to estimate rates of consumption of various foods. However, the results of the FDA total diet studies are of limited use in the present context because fish are grouped with meat and poultry. Estimates of seafood consumption used by FDA to calculate average intake of methylmercury for exposed portions of the U.S. population were based on a diary survey sponsored by the Tuna Research Foundation (Tollefson and Cordle 1986). Supplementary information on analysis of fisheries consumption data can be found in SRI (1980).

The average rate of consumption of fish or shellfish is the key exposure variable for use in subsequent steps of risk assessment. Consumption rates should be expressed in terms of g/day and meals/yr [meals/yr may be calculated from g/day by assuming an average meal of fish or shellfish equals about 150 g (0.33 lb) if the average meal size is unknown]. Average consumption rate for each harvest species is calculated from field data according to the following steps:

- For each successful angler trip, calculate the weight of harvest by species based on number and total weight harvested per household
- Calculate mean harvest weight consumed per person per time by
  - Dividing the total harvest weight for each species by the number of consumers in household and by the days elapsed since last meal from the same area

- Multiplying the value obtained in the preceding computation by a factor to account for the proportion of cleaned weight to total weight [according to Landolt et al. (1985), this factor equals about 0.5 for squid and crabs, 0.3 for fish, and 1.0 for shucked clams; these estimates should be verified or replaced by local data]

- Calculate mean consumption rate per person by geographic harvest area, by subpopulation, and by total exposed population.

Note that the above method (cf. Landolt et al. 1985, 1987) may provide a biased estimate of average consumption rate due to its dependence on a short-term observation (i.e., time since last meal). Averaging of data over a longer time period might be preferable, but such data may be more susceptible to biases from inaccurate recall of consumers (interviewees). Harvest weights should generally be determined directly rather than from length measurements. However, for shellfish and crabs, it may be necessary to establish tissue weights from weight-length regression analysis.

The model for calculating mean daily consumption rate (I_{ijk}) for fishery species i, human subpopulation j, and area k is therefore:

$$I_{ijk} = \frac{1}{N_{ijk}} \sum_{l} I_{ijkl} = \frac{1}{N_{ijk}} \sum_{l} \frac{w_{ijkl}\, p_i}{H_{jkl}\, T_{jkl}} \qquad (4)$$

where:

I_{ijkl} = Mean daily consumption rate of species i for subpopulation j, area k, and household l (kg/day)
N_{ijk} = Number of households (successful harvest trips) for species i, subpopulation j, and area k
w_{ijkl} = Weight of species i harvested by household l of subpopulation j in area k (kg)
p_i = Proportion of cleaned edible weight of species i to total harvested weight
H_{jkl} = Number of people in household l of subpopulation j in area k
T_{jkl} = Time elapsed since last meal by household l of subpopulation j in area k (days).

When consumption rates (I_{ijkl}) are log-normally distributed, a geometric mean consumption rate may be calculated by log-transforming the data before applying Equation 4 to calculate a mean consumption rate.

Consumption rate data may be summarized further by calculating means across species, subpopulations, and areas. However, it should be recognized that means of I_{ijk} across species do not represent actual diet patterns for consumers of mixed-species diets. To calculate mean consumption rates for mixed-species diets, all I_{ijkl} should be summed across species within a household before determining mean consumption rates across households (I_{jk}):

$$I_{jk} = \sum_{l} \frac{I_{jkl}}{N_{jk}} = \sum_{l} \sum_{i} \frac{I_{ijkl}}{N_{ijk}} \qquad (5)$$

Where:

I_{jkl} = Mean daily consumption rate of all fishery species for household l, subpopulation j, and area k (kg/day)
N_{jk} = Number of households in subpopulation j and area k

and other terms are defined above.

Landolt et al. (1985) summarized the assumptions involved in calculating mean consumption rates (I_{ijkl}) by household as follows:

- Consumption
  - p_i values are assumed as noted above
  - Catch was distributed evenly among consumers in house- hold
  - People in household actually ate the entire cleaned catch
  - Personal harvest consumption was distributed evenly over the time interval since the last successful trip
- Fishing interval
  - Fishing frequency (days) is related to seasonal fisheries; that is, interviewees did not report average time interval for entire year but only for recent past. Therefore, calculated consumption rates cannot be directly extrapolated to a yearly basis. Fishing interval was set to 1 day if unreported (Landolt et al. 1985).

Despite the limitation noted in the last item above, calculated consumption rates can be extrapolated to an annual average rate by multiplying the I_{ijkl} by 365 days and by a species-specific factor equal to the fraction of the year a fishery is available. Determination of this species-specific factor is somewhat subjective because of large seasonal fluctuations of the harvest (e.g., Appendix E of Landolt et al. 1985). These factors should be determined on a case-specific basis.

Assumed Consumption Rate

In many cases, comprehensive data on fisheries catch and consumption patterns are not available. For some risk assessment problems (e.g., ranking of potential problem chemicals in aquatic organisms or development of consumption advisories) extensive catch/consumption data are not needed. Moreover, catch/consumption patterns undoubtedly vary over time. Extensive long-term monitoring of catch/consumption for all areas of interest within a large water body may not be warranted. Despite its obvious limitations, extrapolating consumption data from one area (or time) to another may be a suitable approach when:

- Site-specific data are unavailable
- Differences among areas (or times) are expected to be small
- Precise estimation of average fish or shellfish consumption is unnecessary to meet the study objectives.

In the past, many risk analysts have simply assumed standard values for food consumption rates based on previous analyses of dietary patterns of the U.S. population (U.S. EPA 1980b; SRI 1980). Average values for fish and shellfish consumption for the U.S. population generally range from 6.5 to 20.4 g/day (Nash 1971; National Marine Fisheries Service 1976, 1984; SRI 1980; U.S. Department of Agriculture 1984; also see Appendix F). Most estimates include fish and shellfish (molluscs, crustaceans) in marine, estuarine, and fresh waters, but saltwater species form the bulk of consumed items. Most estimates also include commercially harvested fisheries products. Also, estimates of average U.S. consumption do not account for subpopulations in areas such as the Great Lakes that consume large quantities ($\geq$20 g/day) of locally caught sport fish.

An estimate of 6.5 g/day for consumption of commercially and recreationally harvested fish and shellfish from estuarine and fresh waters was used by U.S. EPA (1980b) to develop water quality criteria based on human health guidelines. The value of 6.5 g/day is an average per-capita consumption rate for the U.S. population, including nonconsumers, based on data in SRI (1980). Consumption rates for portions of the U.S. population (e.g., by region, age, race, and sex) show that average consumption of fisheries organisms may vary from about 6 to 100 g/day (e.g., Suta 1978; SRI 1980; Puffer et al. 1982). Finch (1973) determined that approximately 0.1 percent (i.e., the 99.9th percentile) of the U.S. population consumes 165 g/day of commercially harvested fish and shellfish. Pao et al. (1982) provided estimates of 48 g/day for the average and 128 g/day for the 95th percentile consumption rates by U.S. consumers of fish and shellfish. Rupp (1980) presented estimates of average daily consumption of freshwater fish, saltwater fish, and all shellfish according to age group within the U.S. population. SRI (1980) presents average and 95th percentile rates of consumption of all fish and shellfish according to age group, race, region and other demographic variables. Estimates of food consumption rates for specific subpopulations in the U.S. are also available from a database maintained by the EPA Office of Pesticide Programs (see Appendix F). Limitations of fisheries consumption data are discussed by SRI (1980) and Landolt et al. (1985).

One or more of the following values of average consumption rate may be assumed when site-specific data are unavailable:

- 6.5 g/day to represent an estimate of average consumption of fish and shellfish from estuarine and fresh waters by the U.S. population (U.S. EPA 1980b)
- 20 g/day to represent an estimate of the average consumption of fish and shellfish from marine, estuarine, and fresh waters by the U.S. population [U.S. Department of Agriculture (USDA) 1984]
- 165 g/day to represent average consumption of fish and shellfish from marine, estuarine, and fresh waters by the 99.9th percentile of the U.S. population (Finch 1973)

- 180 g/day to represent a "reasonable worst case" based on the assumption that some individuals would consume fish at a rate equal to the combined consumption of red meat, poultry, fish, and shellfish in the U. S. (EPA Risk Assessment Council assumption based on data from the USDA Nationwide Food Consumption Survey of 1977-1978; see Appendix F).

Extrapolation of these values to local populations and recreational fisheries should generally be avoided. Limited estimates of average consumption rates for recreational fisheries are given in SRI (1980). Whenever possible, data on local consumption patterns should be collected or obtained from a current database. Alternatively, risk estimates may be expressed on a unit consumption basis (i.e., per unit weight of fish/shellfish consumed). This latter approach is used by some states in issuing sportfishing advisories. If average consumption values listed above are assumed for local risk assessment, it is recommended that a range of values be used. The references cited earlier should be consulted for consumption rate data for fish and shellfish separately, or for individual species (also see references cited in Appendix F).

EXPOSURE DOSE DETERMINATION

In the next step of the exposure analysis, information on estimated contaminant concentrations and rate of consumption of fish and shellfish are combined to estimate chemical intake by exposed humans. Analyses of single-species diets and mixed-species diets are discussed separately in the following sections.

Single-species Diets

The general model to calculate chemical intake for a single-species diet is:

$$E_{ijkm} = \frac{C_{ikm}\, I_{ijk}\, X_m}{W} \qquad (6)$$

where:

E_{ijkm} = Effective ingested dose of chemical m from fishery species i for human subpopulation j in area k (mg kg^{-1} day^{-1} averaged over a 70-yr lifetime)
C_{ikm} = Concentration of chemical m in edible portion of species i in area k (mg/kg)
I_{ijk} = Mean daily consumption rate of species i by subpopulation j in area k (kg/day averaged over 70-yr lifetime)
X_m = Relative absorption coefficient, or the ratio of human absorption efficiency to test-animal absorption efficiency for chemical m (dimensionless).
W = Average human weight (kg).

Values of subscripted terms above may be estimated means or uncertainty interval bounds (e.g., 95 percent confidence intervals) depending on the exposure scenario being modeled (e.g., worst case vs. average case vs. lower-limit case). Note that E_{ijkm} is analogous to the dose "d" in Equations 1 and 2. The term "effective" ingested dose (E_{ijkm}) is introduced to emphasize that estimates of chemical intake (i.e., ingested dose) may be modified by the term X_m to account for differential absorption of contaminants by humans and bioassay animals.

Absorption coefficients (X_m) are assumed equal to 1.0 unless data for absorbed dose in animal bioassays used to determine toxicological indices (carcinogenic potency or RfD) are available and the human absorption coefficient differs from that of the animal used in the bioassay. Assuming that X_m is equal to 1.0 is equivalent to assuming that the human absorption efficiency is equal to that of the animal used in the bioassay. In the absence of data to the contrary, this is appropriate. Toxicological indices are determined from bioassays that usually measure administered (ingested) dose. Therefore, the estimated chemical intake by humans, E_{ijkm}, is usually the ingested dose, not the absorbed dose. If the toxicological index used to estimate risk is based on the absorbed dose, then an estimate of human absorption efficiency for the chemical of concern may take the place of the term X_m in Equation 6 above. In most cases, however, information or assumptions about absorption efficiencies has been incorporated into EPA's estimates of RfDs and Carcinogenic Potency Factors. Therefore, X_m is usually dropped from Equation 6 and E_{ijkm} becomes simply the ingested dose.

W is usually assumed to be 70 kg for the "reference man" (U.S. EPA 1980b). Assuming other average values to account for growth from a child's body weight to adult weight over a lifetime would not change the results of carcinogen risk assessment substantially. Concerns about exposures over a time period of less than about 15 yr may require modeling of early childhood exposures. Standard values for age-specific body weight and other factors used in exposure assessment are provided by Anderson et al. (1985).

Mixed-species Diets

Estimation of chemical exposure due to a mixed-species diet is complicated by variation in the dietary habits of individuals. The various diets of individual humans may differ from one another in the kinds and relative proportions of fishery species consumed. The sum of species-specific exposures (E_{ijkm}) is not equivalent to total exposure for a mixed-species diet. In a diverse fishery, each individual consumer is likely to consume only a subset of the total available species. Thus, the sum of species-specific exposures might overestimate the average consumption rate for mixed-species diets.

To estimate average chemical exposure resulting from a mixed-species diet, an exposure dose should first be estimated for each individual in a subpopulation as follows:

$$E_{hjkm} = \sum_i \frac{C_{ikm}\, I_{hijk}\, X_m}{W} \qquad (7)$$

where:

E_{hjkm} = Effective exposure dose of chemical m from a mixed-species diet eaten by individual human h in subpopulation j in area k (mg kg^{-1} day^{-1} averaged over a 70-yr lifetime)

I_{hijk} = Average consumption rate of species i by individual h in subpopulation j in area k (kg/day averaged over a 70-yr lifetime)

and other terms are defined as above. The average exposure dose for mixed species diets is:

$$E_{jkm} = \frac{\sum_{h} E_{hjkm}}{H_{jk}} \quad (8)$$

where:

E_{jkm} = Average effective exposure dose of chemical m from mixed-species diet for subpopulation j in area k (mg kg^{-1} day^{-1})
H_{jk} = Number of persons in subpopulation j in area k.

Uncertainty estimates can be obtained by calculating 95 percent confidence limits for E_{jkm}.

SOURCES OF INFORMATION

References to protocols for sampling and analysis of toxic chemical residues in fish and shellfish are provided above (see Tissue Concentrations of Contaminants). For the updated status of protocols and new developments, contact a representative of the EPA Office of Water (Appendix A) or one of the EPA Office of Research and Development Laboratories (Appendix G). Information on sampling and analysis of commercial fisheries products collected from the marketplace is available in FDA Compliance Program Guidance Manuals (available from FDA, Freedom of Information (HFI-35), 5600 Fishers Lane, Rockville, MD 20857).

Compilations of data on concentrations of chemical contaminants in fish and shellfish are available in the EPA Ocean Data Evaluation System (ODES), reports of the NOAA Status and Trends Program (e.g., Matta et al. 1986), Tetra Tech (1985b), and Capuzzo et al. (1987). For current local information, contact a member of the EPA Regional Network for Risk Assessment/Risk Management Issues (Appendix H). Many state health and environmental agencies maintain regional databases on chemical residues in fish and shellfish. For example, the New York State Department of Environmental Conservation and the New Jersey Department of Environmental Protection publish periodic reports on contaminants levels in fish (e.g., Armstrong and Sloan 1980; Belton et al. 1983; Sloan and Horn 1986). The Wisconsin Department of Natural Resources (Bureau of Water Quality) maintains computerized records of long-term data on PCB concentrations in fish of the Great Lakes.

Summaries of data on contaminant concentrations in a variety of foods are available in Grasso and O'Hare (1976), Lo and Sandi (1978), Stich (1982), U.S. FDA (1982), and Vaessen et al. (1984). FDA is developing a data system called FOODCONTAM for pesticide and industrial contaminant residues in foods.

References containing estimates of the rates of consumption of fish and shellfish by the U.S. population were presented above (see Assumed Consumption Rate). The EPA Office of Pesticide Programs maintains the Tolerance Assessment System (Saunders and Petersen 1987). The Tolerance Assessment System uses a U.S. Department of Agriculture database (based on a 1977-1978 survey) to generate estimates of consumption of various foods stratified by specific subpopulations (e.g., infants, children, and adults in the northeastern U.S.). The Office of Pesticide Programs is also developing information on the effects of food preparation methods on chemical residues in food.

RISK CHARACTERIZATION

In the risk characterization stage, results of the hazard, exposure and the dose-response assessments are combined to estimate the probability and extent of adverse effects associated with consumption of contaminated fish or shellfish. An overview of the risk characterization process is shown in Figure 6. In human health risk assessment, carcinogens and noncarcinogens are treated separately. Indices of risk for these different categories of toxicants are based on different dose-response models (see above, Dose-Response Assessment).

The procedures for generating quantitative estimates of risk are emphasized in the following sections. However, it is critical that numerical estimates of risk not be presented in isolation from the assumptions and uncertainties inherent in the process of risk assessment. The risk characterization should include a discussion of assumptions and uncertainties and their potential impact on numerical estimates of risk; i.e., the degree to which the numerical estimates are likely to reflect the actual magnitude of risk to humans. For example, if upper confidence limits for mean chemical concentrations are used to develop risk estimates, the effects of compounding assumptions of upper-bound estimates of carcinogenic potency and conservatively high estimates of consumption rate should be evaluated. A risk characterization should include a summary of the preceding steps of the risk assessment: hazard assessment, dose-response assessment, and exposure assessment. The weight-of-evidence classification and other supporting information should be summarized concisely. Approaches to presentation of summary information to be included in risk characterization are presented in the next chapter (see below, Presentation and Interpretation of Results).

CARCINOGENIC RISK

Numerical estimates of carcinogenic risk can be presented in one or more of the following ways (U.S. EPA 1986a):

- Unit risk - the excess lifetime risk corresponding to a continuous constant lifetime exposure to a unit carcinogen concentration (e.g., 1 mg/kg carcinogen in edible tissue of fish or shellfish)

- Dose or concentration corresponding to a specified level of risk - for example, a guideline for maximum allowable contamination of a specified medium may be derived from a maximum allowable risk value established by risk managers

- Individual and population risks - upper-limit estimates of excess lifetime cancer risk may be expressed for individuals (as a probability estimate) or for the exposed population (as an estimate of the number of cancers produced within a population of specified size per generation).

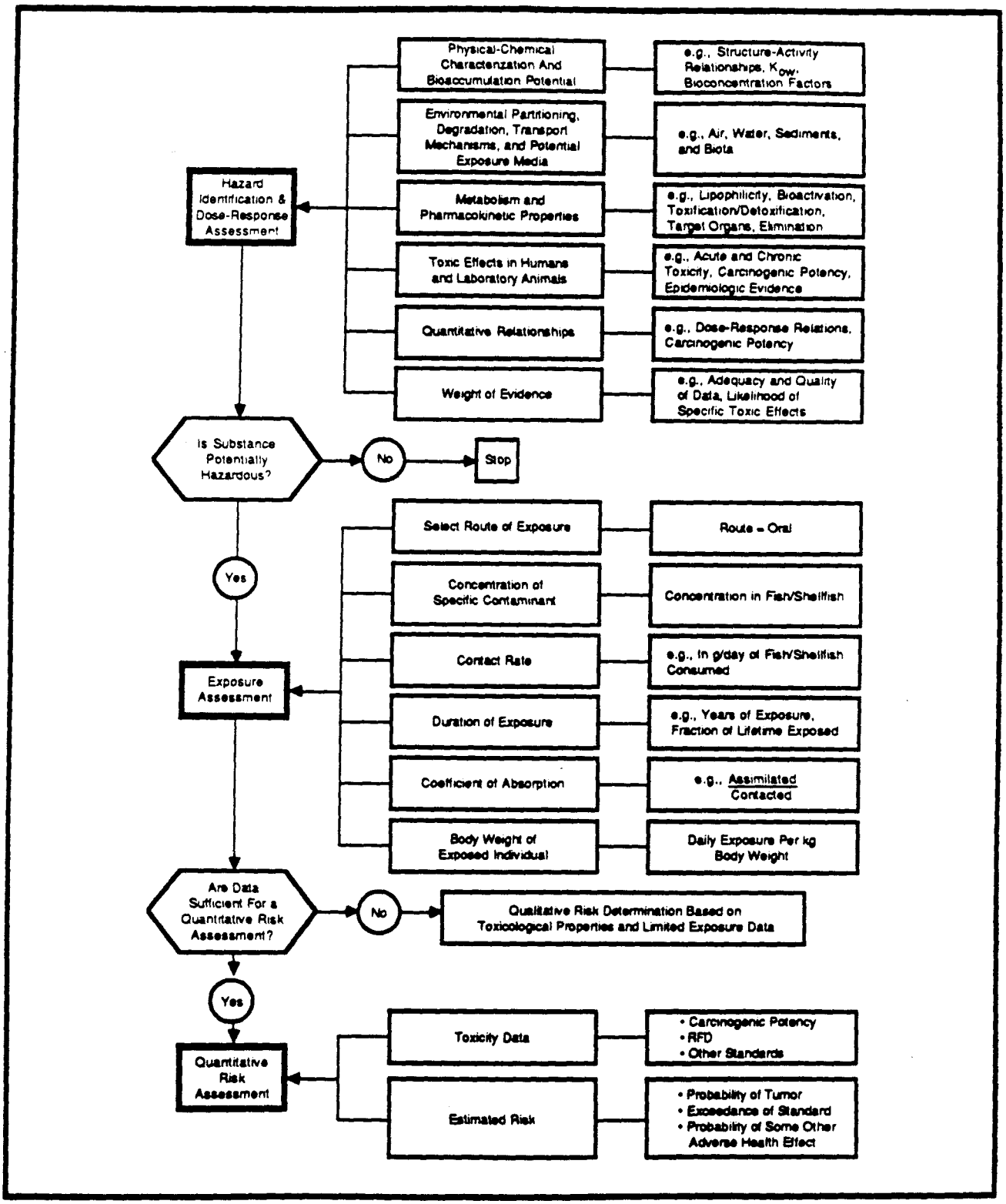


Figure 6 Conceptual structure of quantitative health risk assessment model.

Regardless of the option chosen for expressing risk, final numerical estimates should be presented as one significant digit only, followed by the EPA classification of the weight of evidence for carcinogenicity in brackets (U.S. EPA 1986a).

The general model for estimating a plausible upper limit to excess lifetime risk of cancer at low doses for a single-species diet is:

$$R^*_{ijkm} = q_1^*_m \quad E_{ijkm} \tag{9}$$

where:

R^*_{ijkm} = Plausible-upper-limit risk of cancer associated with chemical m in fishery species i for human subpopulation j in area k (dimensionless)

$q_1^*_m$ = Carcinogenic Potency Factor for chemical m [(mg kg^{-1} $day^{-1})^{-1}$] estimated as the upper 95 percent confidence limit of the slope of a linear dose-response curve

E_{ijkm} = Exposure dose of chemical m from species i for subpopulation j in area k (mg kg^{-1} day^{-1})

The actual risk is likely to be below the estimated upper-limit value calculated from Equation 9, and may be zero in some instances. Equation 9 corresponds to Equation 2 above, except that an estimate of human exposure (E_{ijkm}) has replaced the dose (d), which is usually a known quantity administered to a bioassay animal. All E_{ijkm} are calculated as discussed above (see Exposure Dose Determination in Exposure Assessment). When local consumption rate data are unavailable, a range of E_{ijkm} and corresponding risk estimates may be calculated based on a range of assumed consumption values. Estimates of $q_1^*_m$ are available in IRIS. Note that Equation 9 is only valid for estimated risks below 10^{-2}.

Estimation of upper-limit risk associated with the average mixed-species diet follows a similar approach, except that the average effective dose (E_{jkm}) of chemical m from a mixed-species diet, calculated from Equation 8 above, replaces the species-specific exposure (E_{ijkm}) in Equation 9. Calculation of the average effective dose was discussed earlier (see Exposure Assessment, Exposure Dose Determination).

NONCARCINOGENIC EFFECTS

Noncarcinogenic risk may be evaluated by calculating the ratio of the estimated chemical intake to the RfD as follows:

$$H_{ijkm} = \frac{E_{ijkm}}{RfD_m} \tag{10}$$

where:

H_{ijkm} = Hazard Index of a health effect from intake of chemical m associated with fishery species i for human subpopulation j in area k (dimensionless)

RfD_m = Reference Dose for chemical m (mg kg^{-1} day^{-1})

and E_{ijkm} is defined as above. RfD_m values are given in IRIS (U.S. EPA 1987a).

When all significant exposure routes and sources are taken into account, the estimated total exposure for all routes replaces E_{ijkm} in the numerator of Equation 10 and the resulting hazard index is compared to a value of 1.0 to evaluate the chemical hazard (Stara et al. 1983; U.S. EPA 1985b). Values of the hazard index for total exposure or of H_{ijkm} that are above 1.0 indicate that the estimated exposure is potentially of concern. Above 1.0, increasing values of either hazard index indicate increasing hazard. However, the hazard index does not define a dose response relationship, and its numerical value should not be regarded as a direct estimate of risk.

Because H_{ijkm} as calculated by Equation 10 do not account for exposures other than that from consumption of single fisheries species, values of H_{ijkm} substantially below 1.0 do not necessarily indicate a lack of significant risk overall. Although species-specific hazard indices are useful for evaluating whether contamination of any single species is of concern, two problems remain:

- How can hazards from mixed-species diets of fish and shellfish be evaluated?
- How should exposures from sources other than consumption of contaminated fish and shellfish (either single-species or mixed-species diets) be taken into account?

To address the first question above, one approach would be to sum H_{ijkm} values across all species to obtain a hazard index, H_{jkm}, associated with the entire fishery. However, H_{jkm} could not be interpreted as representative of actual hazard to individuals, since the sum of estimated exposures across species will not be the same as exposures associated with the mixed-species diets of individuals (see above, Exposure Assessment, Exposure Dose Determination, Mixed-species Diet). An alternative approach recommended here is to use the average effective dose (E_{jkm}) for mixed-species diets to calculate a hazard index. This hazard index for mixed-species diets still does not account for exposures due to other sources.

To address the second question above, the sum of exposures from all sources should be compared to the RfD to evaluate total hazard. Guidance on estimation of exposures due to other sources is available in U.S. EPA (1986b,f). If exposure estimates for sources other than the fishery are not available, then some relatively small fraction of the RfD (e.g., 0.1) could be assigned to intake from consumption of fish and shellfish. This fractional RfD would then replace the RfD in the denominator of the hazard index. The index would be compared to a value of 1.0 to evaluate the potential for concern. However, the uncertainties associated with such an approach should be clearly stated. Further research on this problem is clearly needed.

The margin of exposure (MOE) is an alternative indicator of noncarcinogenic risk. The MOE is the ratio of the No-Observed-Adverse-Effect-Level to an estimated exposure dose. When the MOE is equal to or greater than the product of the uncertainty factor and the modifying factor used to derive the RfD, the level of regulatory concern is usually low (see U.S. EPA 1987a for details of the derivation of RfDs). Concerns about mixed-species diets and exposures from non-fishery sources, as discussed above for hazard indices, also apply to MOE for exposure to contaminated fisheries.

CHEMICAL MIXTURES

U.S. EPA (1986d) discussed various models for assessment of the upper limit to risk from chemical mixtures. Because of present data limitations and the complexity of possible contaminant interactions, it is virtually impossible at present to predict synergistic or antagonistic effects of most chemical mixtures. Moreover, such effects may be unlikely at low environmental concentrations of contaminants. The approach used most frequently for multiple-chemical assessment is the additive-risk (or response-additive) model. Thus, total upper-limit risk for a chemical mixture is usually estimated as the sum of upper-limit risks for carcinogens or of hazard indices for noncarcinogens. A sum of noncarcinogenic hazard indices should be calculated only for a group of chemicals acting on the same target organ (Stara et al. 1983). The numerical estimates obtained using the response-additive model are useful in terms of relative comparisons (e.g., among fishing areas or among fishery species). However, risk estimates for chemical mixtures should be regarded only as very rough measures of absolute risk (U.S. EPA 1986d). Because technological limitations preclude analyzing fishery samples for all potentially toxic chemicals, risk estimates for chemical mixtures should not be interpreted as estimates of total chemical risk associated with ingestion.

PRESENTATION AND INTERPRETATION OF RESULTS

Examples of formats for presenting the results of risk assessments are provided below. These formats are adaptable to any level of summary analysis (e.g., subpopulation vs. total exposed population, individual fishery species vs. average across species). Approaches to presentation of supporting documentation on assumptions and uncertainties are also described. Interpretation of the results is largely a function of risk management. As such, guidance on interpretation of risk estimates to support decision-making is beyond the scope of this manual. Nevertheless, a brief discussion of risk comparisons (e.g., estimated risks for various fish species; estimated risk vs. acceptable risk defined by policy) is provided to alert the reader to the interface between risk assessment and risk management. Supplementary information, such as comparisons of contaminant concentrations with FDA action levels, is addressed in the final section below.

PRESENTATION FORMAT

The results of risk assessment may be summarized in both tabular and graphic format. All final estimates of risk should be rounded to one significant digit (or an order of magnitude if appropriate). The EPA classification of the qualitative weight of evidence for carcinogenicity should be shown in brackets adjacent to final risk estimates for carcinogens (U.S. EPA 1986a). To guide the reader's interpretation of the information presented, supporting text should describe assumptions, uncertainties, and any caveats about the results All risk estimates should be interpreted as plausible-upper-limit values for the stated assumptions and exposure conditions.

Summary Tables

An example format for summarizing an exposure analysis is shown in Table 6. The table format allows storage of quantitative information in a computer spreadsheet. Columns of notes containing references to sources of information can easily be added to the spreadsheet to further document the exposure analysis.

It should be emphasized that some of exposure variables are capable of being measured relatively precisely (e.g., contaminant concentrations in fish tissue), whereas others may only be estimated on an order-of-magnitude basis (e.g., consumption rate). The precision and accuracy of the final risk estimates are directly related to the precision and accuracy of the variables incorporated into the equations used to calculate exposure and risk.

Quantitative uncertainty analyses such as sensitivity analysis are easily performed with a spreadsheet by calculating exposure estimates for low, mid, and high values of key variables within their respective plausible ranges. Specification of probability distributions for key variables is an alternative method of uncertainty analysis requiring graphical models (see below, Uncertainty Analysis). In the example shown in Table 6, the average, minimum, and maximum concentrations of each contaminant [PCBs and mercury (Hg)] are used to estimate potential health risk, thereby accounting for uncertainty

TABLE 6. EXAMPLE TABULAR FORMAT FOR DISPLAY OF QUANTITATIVE RISK ASSESSMENT FOR CONSUMPTION OF FISH AND SHELLFISH

	Exposure Determination							Risk Determination				
								Carcinogens			Noncarcinogens	
Substance	Concentration in Medium (mg/kg)[a]	Contact Rate (g/day)[b]	Total Daily Contact (mg/day)	Exposure Duration (years)	Absorption Coefficient (0-1.0)[c]	Body Weight (kg)	Exposure Value (mg/kg/d)	Potency Factor l/(mg/kg/d)	Upper Limit Risk	Weight of Evidence	RfD (mg/kg/d)	Hazard Index
PCBs	0.007	6.5	4.6E-05	70.0	1.0	70	6.5E-07	4.34	3E-06	B2	N/A[d]	N/A
	0.004	6.5	2.6E-05	70.0	1.0	70	3.7E-07	4.34	2E-06	B2	N/A	N/A
	0.010	6.5	6.5E-05	70.0	1.0	70	9.3E-07	4.34	4E-06	B2	N/A	N/A
PCBs	0.007	20.0	1.4E-04	70.0	1.0	70	2.0E-06	4.34	9E-06	B2	N/A	N/A
	0.004	20.0	8.0E-05	70.0	1.0	70	1.1E-06	4.34	5E-06	B2	N/A	N/A
	0.010	20.0	2.0E-04	70.0	1.0	70	2.9E-06	4.34	1E-05	B2	N/A	N/A
Hg	0.157	6.5	1.0E-03	70.0	1.0	70	1.5E-05	N/A	N/A	e	2.9E-04	5E-02
	0.008	6.5	5.2E-05	70.0	1.0	70	7.4E-07	N/A	N/A	e	2.9E-04	3E-03
	0.478	6.5	3.1E-03	70.0	1.0	70	4.4E-05	N/A	N/A	e	2.9E-04	2E-01
Hg	0.157	20.0	3.1E-03	70.0	1.0	70	4.5E-05	N/A	N/A	e	2.9E-04	2E-01
	0.008	20.0	1.6E-04	70.0	1.0	70	2.3E-06	N/A	N/A	e	2.9E-04	8E-03
	0.478	20.0	9.6E-03	70.0	1.0	70	1.4E-04	N/A	N/A	e	2.9E-04	5E-01

[a] Concentration of contaminant in fisheries species of concern (mg/kg = ppm by mass, wet weight).

[b] Amount of fish/shellfish ingested per day, prior to accounting for absorption efficiency, etc.

[c] Ratio of g of contaminant absorbed per g of contaminant ingested, or correction factor to account for differential absorption by humans and bioassay animals (see text, Exposure Assessment, Exposure Dose Determination).

[d] N/A = not applicable.

[e] Carcinogenicity of methyl Hg has not been evaluated by EPA Carcinogen Assessment Group. Hg is typically treated as a noncarcinogen in risk assessment.

in chemical analyses. Also, risks are estimated for two consumption rate estimates (6.5 g/day and 20 g/day). Note that spreadsheet summaries of quantitative information should be supported by a text discussion of qualitative uncertainties such as the weight of evidence for the health effect of concern.

Summary Graphics

Presentation of risk assessment results in graphic form may include:

- Plots of estimated risk vs. consumption rate
- Plots of estimated risk vs. contaminant concentration in edible tissue of fish or shellfish
- Summary maps of risk estimates for different geographic locations or individual sampling stations
- Histograms of estimated risk by fishery species, human subpopulation, or geographic location.

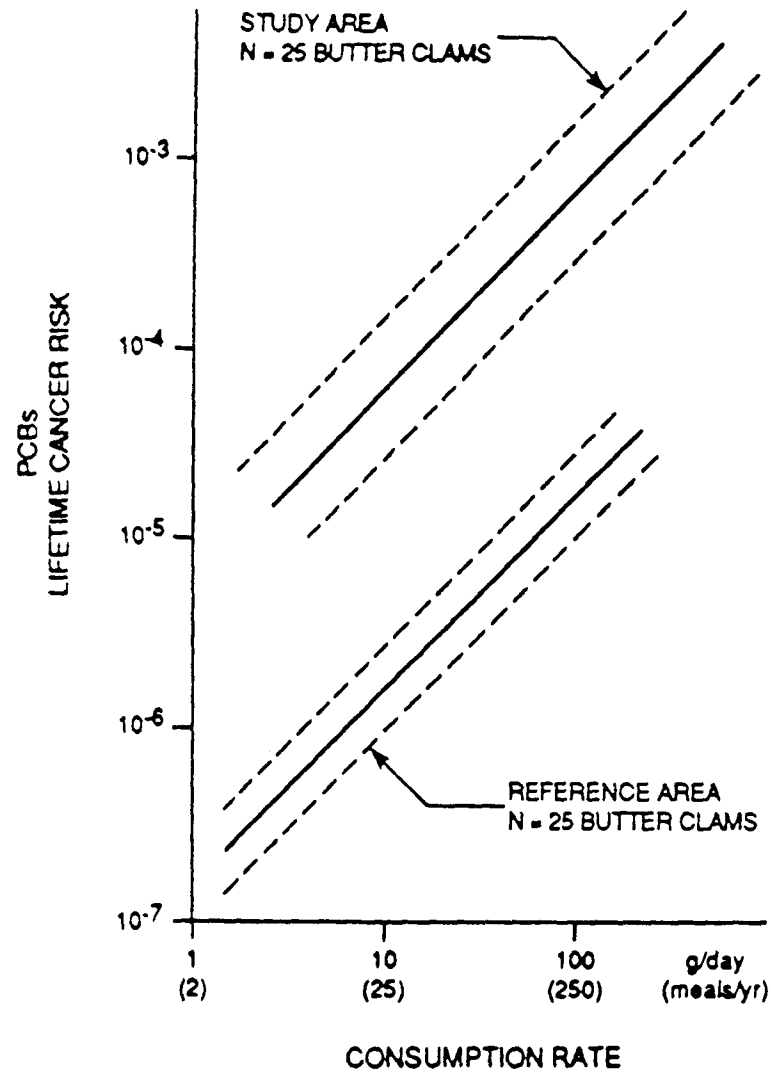
Because estimated risk for a given area and fishery species varies with consumption rate and because consumption rates vary greatly among individual humans, the first approach above is recommended as a primary means of presenting risk assessment results. Actual consumption patterns of the exposed population may or may not be estimated (see above, Exposure Assessment). If they are, estimates of average consumption rate (and 95 percent confidence limits) can be identified in a footnote (e.g., Figure 7). Uncertainty in chemical measurements can be illustrated by plotting lines corresponding to the minimum and maximum (or 95 percent confidence limit) values of contaminant concentrations in fishery species, as well as the mean concentration (e.g., each solid line in Figure 7). As an interpretive aid, risk assessment results for a reference area can be presented along with those for the study area. Coupled with information on comparative risks (see below, Risk Comparisons), Figure 7 is an appropriate format for graphic display of results to lay public.

Other approaches noted above can be used to supplement plots of risk vs. consumption. Summary maps and histograms may be especially useful for presentation of detailed results of spatial analyses by human subpopulation or by fishery species. Plots of risk vs. contaminant concentration for selected consumption rates and species (e.g., Figure 8) aid in rapid interpretation of tissue contamination data.

RISK COMPARISONS

Interpretation of carcinogenic risk assessment results may be based on comparison of estimated health risks for the study area with:

- Estimated health risks for consumption of fishery species from a reference area
- Estimated health risks for consumption of alternative foods (e.g., charcoal-broiled steak, marketplace foods).



PCBs Weight-of-evidence classification:
PROBABLE HUMAN CARCINOGEN [B2]

All cancer risks are plausible-upper-limit estimates of excess risk based on linearized multistage procedure and assumptions summarized in the text. Solid lines are risks associated with average PCB concentrations in butter clams. Dashed lines are for uncertainty range (e.g., 95 percent confidence limits) for average concentrations of PCBs, not the total uncertainty. Actual risks are likely to be lower than those shown above and may be zero.

Figure 7 Example graphic format for display of quantitative risk assessment results for hypothetical study area and reference area.

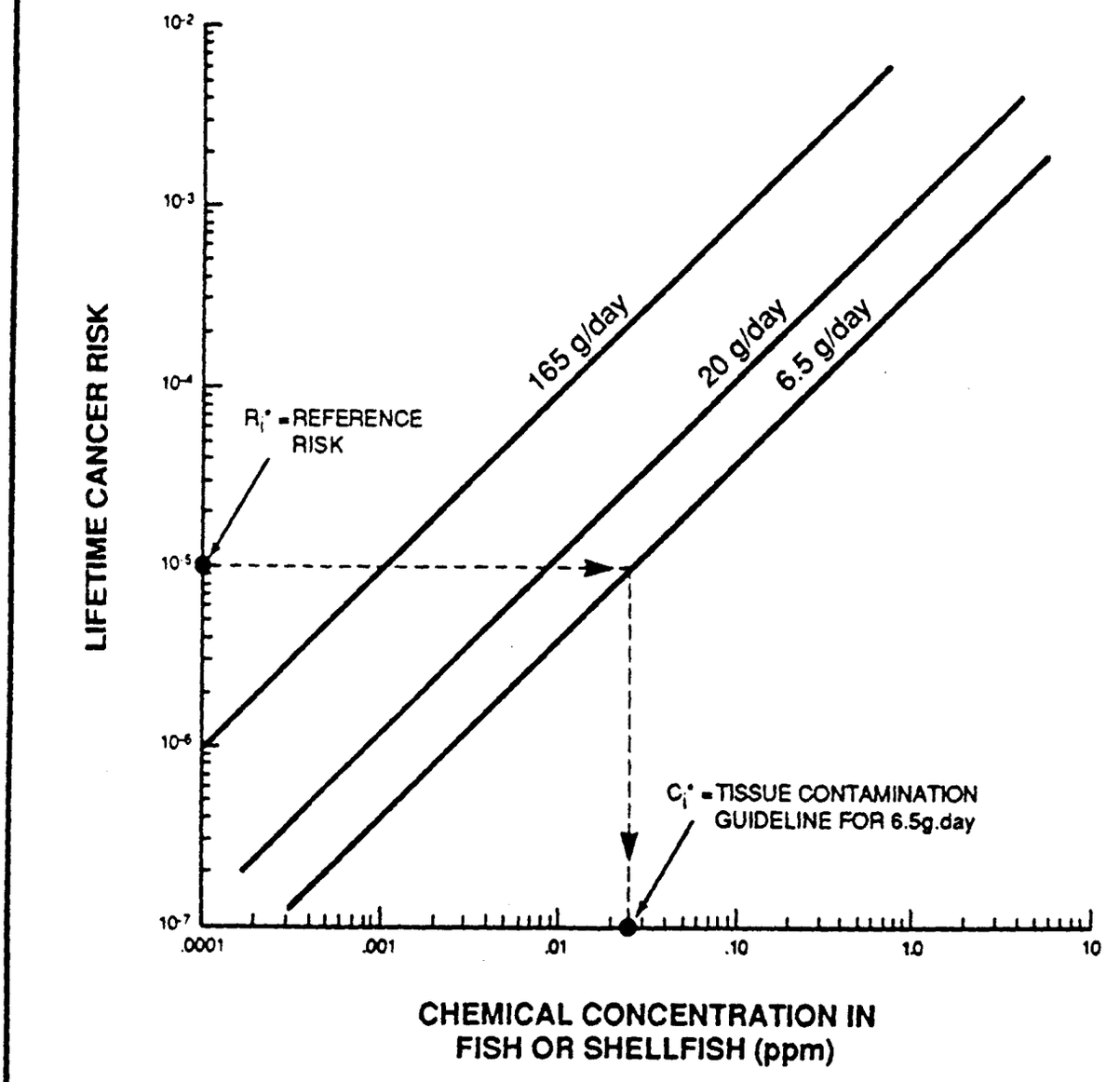


Figure 8 Plausible-upper-limit estimate of lifetime excess cancer risk vs. concentration of a chemical contaminant in fish or shellfish (ppm wet wt.) at selected ingestion rates.

An example of comparison with reference-area risk estimates is shown in Figure 7 above. Comparative risks for alternative foods can be summarized in a table or histogram. Wilson and Crouch (1987) point out the importance of comparing the results of risk assessments with similar assessments of common activities to provide perspective for interpretation of the results by risk managers and the general public.

Risk comparisons should be based on consistent exposure analysis and risk extrapolation models. Analogous exposure scenarios should be used for each risk estimate being compared (i.e., either worst case, plausible-upper limit, average, or lower limit). A single model should be applied consistently to calculate exposure and risk. A linear extrapolation model, such as Equations 2 and 6 above, is justified in general if the excess risk attributed to the contaminant of concern is regarded as a marginal risk, added to a background of relatively high cancer incidence from all other causes not being modeled (Crump et al. 1976; Omenn 1985).

When interpreting the results of risk assessments, risk managers may define an acceptable level of risk to provide a criterion for judging the significance of potential health effects. The term "acceptable risk" is used to denote the maximum risk considered tolerable by an individual or a regulatory agency. An acceptable risk level has not been strictly determined by EPA. Although acceptable risk levels must be defined on a case-specific basis, past regulatory decisions that apply to the U.S. population have generally set allowable levels for environmental risks on the order of 10^{-5} to 10^{-6} (Travis et al. 1987).

SUMMARY OF ASSUMPTIONS

Assumptions underlying the risk assessment model and estimates of model variables should be summarized in a concise format (see Table 7 for summary of some assumptions and numerical estimates used in the approach presented in this manual). Specific assumptions adopted on a case-by-case basis should be summarized in a similar fashion.

Other assumptions, such as general approaches or assumptions underlying models that are commonly used to estimate risk, can be summarized in the text of a risk assessment document. Some additional assumptions involved in applying the risk assessment approach described in this manual include the following:

- Adverse effects in experimental animals are indicative of adverse effects in humans (e.g., lifetime incidence of cancer in humans is the same as that in animals receiving an equivalent dose in units of mg per surface area)
- Dose-response models can be extrapolated beyond the range of experimental observations to yield plausible-upper-bound estimates of risk at low doses
- A threshold dose does not exist for carcinogenesis
- A threshold dose (e.g., No-Observed-Adverse-Effect-Level) exists for noncarcinogenic effects

TABLE 7. SUMMARY OF ASSUMPTIONS AND NUMERICAL ESTIMATES USED IN RISK ASSESSMENT APPROACH

Parameter	Assumptions/Estimates	Reference
Exposure Assessment:		
Contaminant concentrations in tissues of indicator species	No effect of cooking	Worst case for parent compounds. Net effect on risk is uncertain.
Average consumption rate[a]	6.5 g/day 20 g/day 165 g/day	Low, moderate, and high values for U.S. population (see text).
Gastrointestinal absorption coefficient	1.0 Assumes efficiency of absorption of contaminants is same for humans and bioassay animals	U.S. EPA 1980b; 1986a,b
Exposure duration	70 yr	U.S. EPA 1980b; 1986a,b
Human body weight	70 kg (= avg. adult male)	U.S. EPA 1986a,b
Risk Characterization:		
Carcinogenic risk model	Linearized Multistage At risks less than 10^{-2}: Risk = Exposure x Potency	U.S. EPA 1980b, 1986a, 1987a
Carcinogenic potency	Potency factors are based on low-dose extrapolation from animal bioassay data Upper bound of 95 percent confidence interval on potency is used	U.S. EPA 1987a
Noncarcinogenic risk	RfDs for noncarcinogens compared with estimated exposure	U.S. EPA 1987a

[a] Estimates of consumption for local population should be used in place of values shown for U.S. population whenever possible.

- The most sensitive animal species is appropriate to represent the response of humans
- Cumulative incidence of cancer increases in proportion to the third power of age (this assumption is used to estimate lifetime incidence when data are available only from less-than-lifetime experiments)
- For carcinogens, average doses are an appropriate measure of exposure dose, even if dose rates vary over time
- In the absence of pharmacokinetic data, the effective (or target organ) dose is assumed to be proportional to the administered dose
- Risks from multiple exposures in time are additive
- For each chemical, the absorption efficiency of humans is equal to that of the experimental animal
- If available, human data are preferable to animal data for risk estimation
- For chemical mixtures, risks for individual chemicals are additive. However, the total sum of individual chemical risks is not necessarily the total risk associated with ingestion of contaminated fish or shellfish because some important toxic compounds may not have been identified and quantified.

UNCERTAINTY ANALYSIS

Uncertainty analysis is an integral part of risk assessment. A general discussion of uncertainties present in the risk assessment approach described in this manual is presented in the next section. The EPA guidelines on exposure assessment describe general approaches for characterizing uncertainty (U.S. EPA 1986b). Methods for uncertainty analysis are discussed by Cox and Baybutt (1981), Morgan (1984), and Whitmore (1985). A detailed discussion of procedures is beyond the scope of the present effort. General approaches to uncertainty analysis will be described briefly after a discussion of sources of uncertainty.

Sources of Uncertainty

Uncertainties in the risk assessment approach presented in this manual arise from the following factors:

1. Uncertainties in the determination of the weight-of-evidence classification for potential carcinogens.
2. Uncertainties in estimating Carcinogenic Potency Factors or RfDs, resulting from:

- Uncertainties in extrapolating toxicologic data obtained from laboratory animals to humans

- Limitations in quality of animal study

- Uncertainties in high- to low-dose extrapolation of bioassay test results, which arise from practical limitations of laboratory experiments and variations in extrapolation models

3. Variance of site-specific consumption rates and contaminant concentrations

4. Uncertainties in the selection of 6.5 g/day, 20 g/day, and 165 g/day as assumed consumption rates when site-specific data are not available

5. Uncertainties in the efficiency of assimilation (or absorption) of contaminants by the human gastrointestinal system (assumed to be the same as assimilation efficiency of the experimental animal in the bioassay used to determine a Carcinogenic Potency Factor or RfD)

6. Variation of exposure factors among individuals, such as:

   - Variation in fishery species composition of the diet among individuals

   - Variation in food preparation methods and associated changes in chemical composition and concentrations due to cooking.

Variance in estimates of carcinogenic potency or RfDs (#1 above) account for one major uncertainty component in most risk assessments. Chemical potencies are estimated only on an order-of-magnitude basis, whereas analytical chemistry of tissues is relatively precise (on the order of ±20 percent). The choice of a low-dose extrapolation model greatly influences estimates of the Carcinogenic Potency Factor and calculated risks. This uncertainty contributed by the model is substantial when predicting risks below 10^{-2}. For example, the plausible-upper limit to lifetime cancer risk associated with 50 ug/L tetrachloroethene in drinking water ranges from about 10^{-6} for the probit model to 10^{-2} for the Weibull model (Cothern et al. 1986). Model uncertainty is important when considering absolute risk estimates (e.g., Cothern et al. 1986), but less important for relative risk comparisons.

Uncertainty analysis conducted by previous researchers illustrates the variability of risk estimates and potency factors for a given extrapolation model. For example, the coefficient of variation for the mean value of potency generally ranged from 2 to 105 percent for each drinking water contaminant studied by Crouch et al. (1983). This uncertainty arose mainly from error associated with experimental bioassay data for a single animal species. Among bioassay species, the potency of a given chemical may vary only slightly or up to approximately 1,000-fold, depending on the chemical in question (Clayson et al. 1983). Thus, the uncertainty associated with extrapolating potency factors from laboratory animals to humans may be much greater than the uncertainty associated with animal bioassay techniques. By comparison, the range of potencies among carcinogens covers 7-9 orders of magnitude (Clayson et al. 1983; U.S. EPA 1985a). Relative risk comparisons among chemicals can be made more confidently when the range of potency factors is broad. Note that such comparisons should also include consideration of the qualitative uncertainty (e.g., weight of evidence) in assessing the

specific health effects of chemicals, including mode of action, latency period, and target organs.

In conclusion, uncertainty ranges (e.g., 95 percent confidence intervals) around estimates of mean risk may typically span at least several orders of magnitude. The approach taken by U.S. EPA (1980b, 1985a, 1986a) and followed herein is to estimate a plausible-upper limit to risk. In this way, it is unlikely that risk will be underestimated substantially. Moreover, the plausible-upper-limit estimate serves as a consistent basis for relative risk comparisons. However, the effects of compounding conservative assumptions should be evaluated to provide perspective on risk assessment results.

Approaches to Uncertainty Analysis

Analysis of uncertainty in a risk assessment should address both quantitative and qualitative uncertainty. Quantitative uncertainty analysis deals primarily with variation in numerical estimates of exposure and risk that results from changing the values of variables in mathematical models used to calculate the estimates (e.g., low-dose extrapolation models). Characterization of variability in chemical measurements, food consumption rates, and Carcinogenic Potency Factors (or RfDs) and its effect on estimates of exposure and risk is an example of quantitative uncertainty analysis. A qualitative uncertainty analysis includes primarily a summary of limitations of the data and the weight of evidence for toxic effects of concern. A discussion of qualitative uncertainties should present information from IRIS on the level of confidence that EPA places in each Carcinogenic Potency Factor and RfD.

General approaches to treatment of uncertainty in variables used in risk analysis models include the following (Morgan 1984):

- Perform analysis using **single-value-best-estimates** for model variables **without uncertainty analysis**
- Perform **single-value-best-estimate** analysis, **with sensitivity calculations** and appropriate discussion of uncertainty
- Estimate some **measure of uncertainty** (e.g., standard deviation) for each model variable and use **error propagation** methods to estimate uncertainty of final exposure or risk value
- Characterize subjectively the **probability distribution** of each model variable and **propagate error** through stochastic simulation
- Characterize important model variables using a **parametric model** and perform risk analysis using various **plausible values** of each of the variables
- Determine upper and lower **bounds** on model variables to yield **order-of-magnitude estimates** and range of possible answers.

Morgan (1984) refers to the first two approaches as "single-value-best-estimate analysis," to the second two as "probabilistic analysis," and to the final two as "parametric/bounding analysis." The analytical strategies listed above are in roughly descending order, based on the amount of uncertainty in the model variables. Single-value-best-estimate analysis

is appropriate when model variables are precisely known. Bounding analysis is most appropriate when values of model variables are not well-known. The techniques listed above do not address model uncertainty, which must be handled by exploratory examination of outcomes based on alternative model equations.

The choice of a method for uncertainty analysis will depend on the amount and quality of exposure data and on the study objectives. Quantitative uncertainty analysis is applied mainly to exposure variables, such as contaminant concentration in fishery species and consumption rate. Following U.S. EPA (1980b, 1984a, 1985a), an upper-bound estimate of the Carcinogenic Potency Factor is used in carcinogenic risk calculations. Substitution of the mean estimate or the lower bound of the 95 percent confidence interval for the potency factor in the risk calculations is generally not done because of the instability of these estimates (U.S. EPA 1980b, 1986a).

The U.S. EPA (1986b) guidelines on exposure assessment and Whitmore (1985) summarize the primary methods for characterizing uncertainty in exposure estimates in relation to attributes of the exposed population and the exposure data. In many cases, data will be sufficient only to use parametric/bounding analysis, as described above. In any case, a discussion of qualitative uncertainties in the analysis should always accompany presentation of risk assessment results. For example, limitations of data related to inadequate survey design or insensitive analytical chemistry methods should be described. The extent of chemical data for geographic locations of interest should be summarized. Insufficient information on characteristics of the exposed population should be noted. The level of confidence in data used to develop RfDs, Carcinogenic Potency Factors, and weight-of-evidence classifications based on IRIS Chemical Files should be indicated.

SUPPLEMENTARY INFORMATION

Additional information to support risk assessment of contaminated fish and shellfish consumption may include:

- Comparisons of tissue concentrations of contaminants with FDA action (or tolerance) levels
- Statistical comparisons of mean contaminant concentrations among fishery species and among locations
- Statistical comparisons of mean contaminant concentrations in fishery species with those in other foods.

FDA limits on contaminants in fishery products are shown in Appendix I. Limitations to use of these values for assessing health risk were discussed earlier (see above, Overview of Risk Assessment). For comparison, legal limits on fishery contaminants established by other countries are also provided in Appendix I.

Some resource management agencies have developed advisories based simply on comparisons between contaminant concentrations in fishery species and those in corresponding species from reference or control areas. For example, the Northeast Shellfish Sanitation Commission has established "alert levels" for metals in shellfish as the concentration equal to one standard deviation above the mean background (reference)

concentration. These alert levels are not based on health effects, but assume that the level of concern is related to an elevation above average background conditions.

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APPENDIX A

EPA OFFICE OF WATER CONTACTS ON RISK ASSESSMENT FOR FISH CONSUMPTION

APPENDIX A

EPA OFFICE OF WATER CONTACTS ON RISK ASSESSMENT FOR FISH CONSUMPTION

Name	Organization	Phone	Subject Area
Kim Devonald	Office of Marine and Estuarine Protection	(202) 475-7114	EPA Coordination on Fish Health Risk Assessment
Frank Gostomski	Office of Water Regulations and Standards	(202) 475-7321	Derivation of Reference Doses for Toxic Chemicals

APPENDIX B

INTEGRATED RISK INFORMATION SYSTEM (IRIS)

(excerpt from U.S. EPA 1987a)

INTRODUCTION TO IRIS

OVERVIEW

IRIS is a computer-housed, electronically communicated catalogue of Agency risk assessment and risk management information for chemical substances. This system is designed especially for federal, state, and local environmental health agencies as a source of the latest information about Agency health assessments and regulatory decisions for specific chemicals.

The development of IRIS is a response to repeated requests for Agency risk assessment information to deal with various environmental issues and a response to the need for consistency and quality in EPA risk assessment and risk management decisions. IRIS is intended to introduce the user to Agency information which may be useful for building the database necessary to make a risk assessment.

IRIS is not a primary toxicologic data base or a conclusive risk resource; rather, it is an introduction to EPA's risk information, and should be used with an understanding of its capabilities as well as its limitations and constraints (see background documents in Service Code 4). Supportive documentation included in the system provides instruction and explanation for the risk information presented. The information contained in IRIS is intended for users without extensive training in toxicology, but with some knowledge of health science.

The risk assessment information contained in IRIS, except as specifically noted, has been reviewed and agreed upon by intra-agency review groups, representing an Agency consensus. An intra-agency work group has been responsible for the development of IRIS.

As intra-agency review groups continue to review and verify risk assessment values, additional chemicals and data components will be added to IRIS. Although IRIS is available in hardcopy, it is also available through Dialcom, Inc.'s Electronic Mail, the computer-based electronic communications system to which the EPA subscribes. Designed as an electronic loose-leaf notebook, IRIS provides users with the ability to access, copy, and print information from the data base. IRIS hardcopy, which will be available in the future through the National Technical Information Service (NTIS), is provided initially to help users get started. This material can then be expanded and updated by users through electronic retrieval of new and revised data.

SYSTEM STRUCTURE

The information contained within IRIS is divided into two major components: the chemical files, which form the heart of the system, and the supportive documentation, which provides instruction and explanation in support of the system and the chemical files. This information is distributed among six Service Codes, with the chemical files (the functional files in IRIS) contained in one Service Code and the supporting documentation contained in the remaining five. The Service Codes and their functions are as follows:

Service Code 1 — *Chemical Files*: This is the heart of the system. It is within this file that the actual chemical-specific data have been compiled. A detailed presentation of the content and format of this Service Code will be provided later in this Introduction and in the Chemical File Structure description in Service Code 4.

Service Code 2 — *List of Chemicals on IRIS*: A simple alphabetical and Chemical Abstract System (CAS) number listing of all the chemicals contained in IRIS.

Chemical File Update Information: The chemical files which have been recently updated are listed here. Chemical name, CAS No. and date of revision are given.

Service Code 3 — *Chemical File Revision History*: This Service Code contains a running record of specific revisions to each chemical file. The information is more specific than that found in Service Code 2, which is just a list of updated files. The specific file sections that have been changed or modified are given and the type of change is indicated (e.g., "Oral RfD: UF text modified", "Risk Estimates for Carcinogens: slope factor corrected", "Risk Management Section added", etc.). The date of the change is also given.

Service Code 4

Introduction to IRIS (this document): a brief overview of IRIS.

Chemical File Structure: General background information is provided on each of the data elements contained in the chemical files. This section is intended to help the user understand the information contained in the chemical files. In addition, there is some discussion of the general limitations, restrictions, and qualifications placed on the EPA data so as to minimize misinterpretation of the data presented.

Background Documents (Appendices): Concept papers are provided for the categories of information contained in the chemical files (oral RfD, carcinogenicity assessment, risk management actions, and supplementary data). As background documents are prepared for other information categories, such as inhalation RfDs or Drinking Water Health Advisories, they will be added to the system.

EPA Chemical Profile Database References: List of references cited in the Supplementary Data section of the chemical files is provided at the end of the background document for that section.

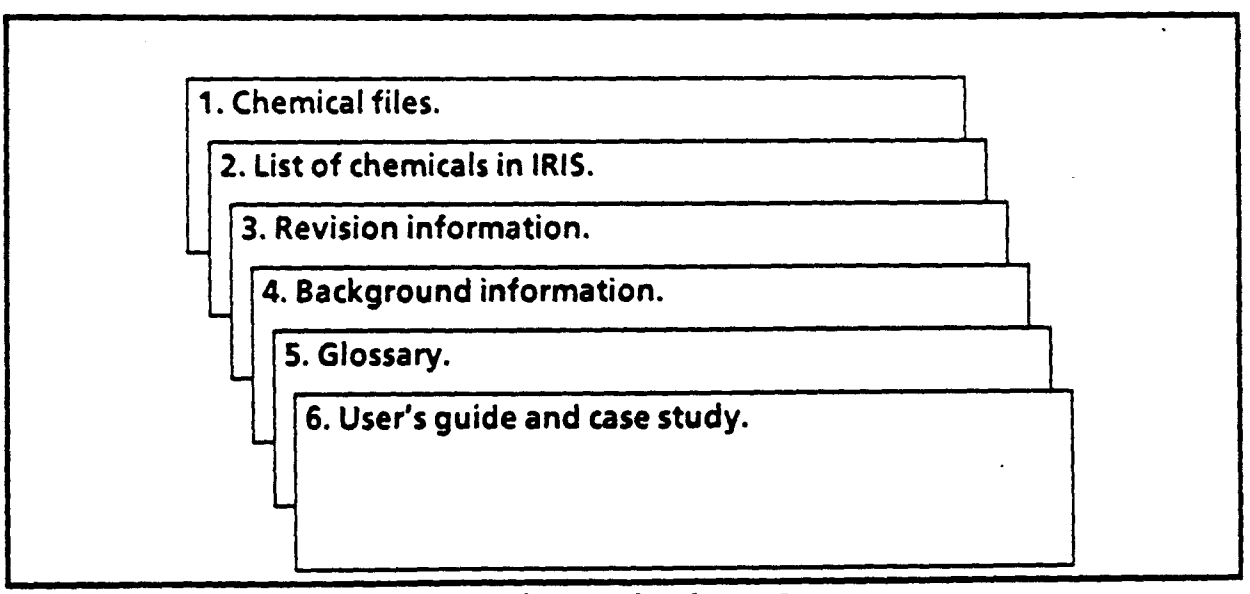
Service Code 5

Glossary: A glossary of terms and abbreviations used in the chemical files and supportive documentation is provided for user reference.

Service Code 6

User's Guide: An operations manual is provided which describes how to use the system and lists commands, procedures, helpful hints, and a series of examples for illustration.

Case Study: A case study is included to provide an example of a situation to which IRIS can be applied and how the information it contains might be used.



Service Codes in IRIS

CHEMICAL FILE FORMAT

The chemical files are intended to assist the user in developing risk assessments which can be used in making management decisions for specific situations. For reference, agency risk management information is also included. One is cautioned, however, that the EPA risk management data have been developed for conditions and with constraints which may have little applicability to a given user's specific situation.

Each chemical file begins with a short introductory paragraph followed by a status table indicating the availability of various components of the chemical file. The information contained within the chemical file includes risk assessment and risk management information. The specific chemical file content is outlined below:

IRIS CHEMICAL FILE STRUCTURE

INTRODUCTION AND STATUS

I. CHRONIC SYSTEMIC TOXICITY (NON-CARCINOGENIC HEALTH EFFECTS)

A. REFERENCE DOSE (RfD) FOR ORAL EXPOSURE

1. REFERENCE DOSE SUMMARY TABLE
2. PRINCIPAL AND SUPPORTING STUDIES
3. UNCERTAINTY AND MODIFYING FACTORS
4. ADDITIONAL COMMENTS
5. CONFIDENCE IN THE RfD
6. DOCUMENTATION AND REVIEW
7. U.S. EPA CONTACTS

B. REFERENCE DOSE (RfD) FOR INHALATION EXPOSURE

(same format as for oral exposure)

II. RISK ESTIMATES FOR CARCINOGENS

A. U.S. EPA CLASSIFICATION AND BASIS

1. HUMAN DATA
2. ANIMAL DATA
3. SUPPORTING DATA

B. ORAL QUANTITATIVE ESTIMATE

1. UNIT RISK SUMMARY TABLE
2. DOSE RESPONSE DATA
3. ADDITIONAL COMMENTS
4. STATEMENT OF CONFIDENCE

C. INHALATION QUANTITATIVE ESTIMATE

1. UNIT RISK SUMMARY TABLE
2. DOSE RESPONSE DATA
3. ADDITIONAL COMMENTS
4. STATEMENT OF CONFIDENCE

D. DOCUMENTATION AND REVIEW

1. REFERENCES
2. REVIEW
3. U.S. EPA CONTACTS

III. DRINKING WATER HEALTH ADVISORIES

(format in preparation)

IV. RISK MANAGEMENT SUMMARIES

A. RISK MANAGEMENT ACTIONS

B. RISK MANAGEMENT RATIONALE

V. SUPPLEMENTARY DATA

A. ACUTE HEALTH HAZARD INFORMATION

B. PHYSICAL-CHEMICAL PROPERTIES

SYNONYMS

Each section consists of a data and rationale summary of two or three pages in length. In addition, EPA contacts who are familiar with the chemical are provided in each section (except for the Supplementary Information section).

Unavailability of data for a section will be indicated, and, if known, other information pertaining to the status of the data will be provided. A more detailed description of each of these sections is provided in the Chemical File Structure document following this Introduction.

ELECTRONIC REPRESENTATION OF SPECIAL CHARACTERS

The use of a computerized telecommunication system for IRIS imposes limits on the number and types of nonalphanumeric characters that can be represented. Special characters such as degree symbols or Greek letters, and print codes such as superscripts and subscripts cannot be reproduced on most display terminals. Therefore, very small numbers are given in scientific notation using the "E" format. That is, a number such as 0.0006 is expressed as 6E-4, which is equivalent to saying "6 times 10 to the power of -4." Large numbers are given in "E" format in some instances, for consistency (for example, 2E2 for the number, 200). Some other substitutions for notations generally represented by superscripts or subscripts are: "cu. m" for cubic meter, "**" for exponentiation in formulas (for example, "Y = X**2" represents "Y equals X squared"), and Ca(CN)2 for the chemical formula of calcium cyanide (chemical formula subscripts are subscripted one full line in other instances). Upper case "L" is occasionally used as the abbreviation for liter in those cases where the lower case "l" may be misinterpreted as the number, one.

IRIS CHEMICAL FILE STRUCTURE

PREFACE

The user is directed to Service Code 6 for instructions on how to call up information on specific chemicals. The discussion below supplements the introduction under Service Code 4 by describing in detail the information displayed in each of the chemical-specific files. The Appendices are background documents which provide more detailed information on risk assessments and risk management concepts and terms.

When one calls up a chemical, sections of information are displayed in the following order: INTRODUCTION & STATUS, CHRONIC SYSTEMIC TOXICITY: NONCARCINOGENIC HEALTH EFFECTS, RISK ESTIMATES FOR CARCINOGENS, DRINKING WATER HEALTH ADVISORIES, RISK MANAGEMENT SUMMARIES, SUPPLEMENTARY DATA, and SYNONYMS. Each numbered section (all sections except the Introduction and Synonyms) begin with a heading with the following information:

Chemical: The chemical name of the agent is given, with the common name in parentheses where appropriate.

CAS No.: The Chemical Abstract Service number unique to the compound.

Preparation date: The date of the most recent revision of the summary sheet.

The subsections and data entries found in each of the sections are discussed below.

INTRODUCTION AND STATUS

The chemical name and Chemical Abstracts Service (CAS) number which uniquely identifies this substance is given, along with the latest revision date for the chemical file. An introductory statement is included in each file, followed by a status table indicating the availability of each section. A status of "review pending" means that a chemical is currently under review, or is scheduled for review by an EPA work group.

I. CHRONIC SYSTEMIC TOXICITY: NON-CARCINOGENIC HEALTH EFFECTS

Risk assessors are often faced with the task of interpreting the significance of long-term exposure to chemicals which might produce toxic effects other than cancer. These effects are sometimes referred to as the "systemic toxicity" of the compound. Traditionally, these effects have been assessed by identifying the lowest No Observed Effect Level (NOEL) and reducing this amount by some factor (Safety Factor or Uncertainty Factor) to estimate a level which is judged to be without significant toxicologic concern to humans.

The CHRONIC SYSTEMIC TOXICITY section contains chemical-specific information couched in terms of a Reference Dose (RfD), a concept which is discussed in greater detail in Appendix A. The RfD is related to a formerly used notion of "acceptable daily intake (ADI)" but has been tailored to the risk assessment/risk management approach used at EPA.

A. REFERENCE DOSE (RfD) FOR ORAL EXPOSURE

Chemical name, CAS No., and preparation date are given.

1. REFERENCE DOSE SUMMARY TABLE

This table summarizes the data used in the derivation of the reference dose.

Critical Effect

This first column lists the critical effect, the species and type of study, and the reference.

Experimental Doses

The second column is a summary of the information on the highest level at which no adverse effects were found (i.e., the No Observed Adverse Effect Level [NOAEL]) and/or

the lowest level tested at which adverse effects were found (i.e., the Lowest Observed Adverse Effect Level [LOAEL]). The dose levels are usually given in the units presented in the original study and in units of milligrams per kilogram body weight per day (mg/kg/day or mg/kg-day).

UF

The Uncertainty Factor which contributes as a divisor to the NOAEL (or LOAEL) in calculating the Reference Dose is given. In most instances, these uncertainty factors are standardized, based on the particular data set available. See the paper on the Reference Dose in Appendix A for a more complete description.

MF

The Modifying Factor which also contributes as a divisor to the NOAEL in calculating the Reference Dose is given. In most cases, this factor is 1; however, in certain instances, the review group uses its collective professional judgment to adjust the RfD through the use of a Modifying Factor. In such cases, explanations are provided in the text following the table.

RfD

The RfD is an estimate (uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a liftime. The RfD is expressed in units of milligrams per kilogram body weight per day (mg/kg/day or mg/kg-day). See Appendix A for a full discussion of the concept and its use in risk assessment and risk management.

Dose Conversion Factors And Assumptions

The factors used to convert the dose to mg/kg-day are listed, as well as any assumptions made. These factors include food and water consumption, and, in some cases, inhalation-to-oral conversion factors.

2. PRINCIPAL AND SUPPORTING STUDIES

An elaboration of the material in the summary table immediately above is presented, providing descriptions of the critical study and other germane studies.

3. UNCERTAINTY AND MODIFYING FACTORS

An explicit presentation of the individual Uncertainty Factors contributing to the overall Uncertainty Factor is given. The UFs are:

10-fold factor for extrapolation from animal to human (10a)
10-fold factor for variability in the human population (10h)
10-fold factor for use of a less-than-chronic study (10s)
1 to 10-fold factor for extrapolation from a LOAEL (1 --> 10e)

See Appendix A for a more complete discussion.

An explicit explanation of the selection of any Modifying Factor is also presented.

4. ADDITIONAL COMMENTS

Ancillary information is given which may be of use or interest, e.g., other approaches taken to establishing an RfD and why EPA prefers its approach.

5. CONFIDENCE IN THE RfD

This entry provides a qualitative estimate, expressed in both summary and narrative form, of the confidence that the EPA review group had in the quality of the critical study, the supporting data base, and the RfD. A "Low" designation for the RfD suggests that the value is likely to change as new data are generated.

6. DOCUMENTATION AND REVIEW

The EPA document(s) in which the RfD (ADI) was originally derived, and the level of review of that document, are given. The dates of the RfD work group meetings at which the chemical was discussed are also given.

7. U.S. EPA CONTACTS

Persons to contact for additional details on the technical issues associated with the RfD of this chemical are listed.

B. REFERENCE DOSE (RfD) FOR INHALATION EXPOSURE

Inhalation RfD methods are under development.

II. RISK ESTIMATES FOR CARCINOGENS

A. U.S. EPA CLASSIFICATION AND BASIS

Classification

The EPA weight-of-evidence classification of the agent, as described in the Hazard Identification section (IIA) of appendix B.

1. HUMAN DATA

A description of the human evidence leading to the classification. Difficulties in determining the final classification are also given where necessary.

2. ANIMAL DATA

A description of the experimental animal evidence leading to the classification. Difficulties in determining the final classification are given where necessary.

3. SUPPORTING DATA

A description of data lending support to the classification, such as genotoxicity.

B. ORAL QUANTITATIVE ESTIMATE

Slope Factor

The upper-bound incremental lifetime cancer risk estimated to result from a continuous orally absorbed dose of 1 mg per kg body weight per day. Since the oral absorption fraction is usually assumed to be 100%, the same oral slope factor is used for continuous oral intake.

1. UNIT RISK SUMMARY TABLE

Water concentration producing risk levels of E-4, E-5, E-6

The concentration of the agent (micrograms per liter) in drinking water estimated to result in upper-bound incremental lifetime cancer risk of E-4, E-5, E-6, if 2 liters of water which is contaminated with the agent were ingested per day continuously for a lifetime.

Unit Risk

The upper-bound incremental lifetime cancer risk estimated to result from ingestion of 2 liters of water per day of drinking water contaminated with the agent at a concentration of one microgram per liter.

Model

The abbreviation for the dose extrapolation model used to estimate cancer risk at low doses from experimental observations at higher doses. M is the multistage procedure, W is Weibull, P is probit, LO is logit, OH is one-hit, GM is gamma multi-hit.

2. DOSE-RESPONSE DATA

This table shows the animal data set from which the risk parameters were estimated. The table shows the species and strain of the animals used, the tumor type or types used for the estimate, the dose administered in the experiment, the lifetime tumor incidence observed, a code for the literature citation of the report where the data was published, and the route of administration used in the experiment. The table is modified when human data are used for the estimation of risk parameters.

3. ADDITIONAL COMMENTS

An explanation of the assumptions used in deriving the risk estimate. For each agent the following information is presented:

method of selecting the data set,

animal-to-human equivalent dose assumption,

statement of whether the administered animal dose or a pharmaco-kinetically-derived effective metabolized dose was used, and

relevant non-cancer toxicity.

Other comments describing the estimation procedure for the agent are included. A statement is also made that the risk estimate should not be used if the water concentration is larger than x µg/l and the air concentration is larger than y µg/cu.m. In this statement the values of x and y are the concentrations above which the risk exceeds 1.0%.

4. STATEMENT OF CONFIDENCE

A high, medium, or low rating based on the factors enumerated in section II of appendix B. A description of the main factors leading to this rating is included.

C. INHALATION QUANTITATIVE ESTIMATE

The entries in this subsection are analogous to those in the Oral Quantitative Estimate subsection above.

D. DOCUMENTATION REVIEW

1. REFERENCES

Literature citations for the major papers used in the classification of the agent and in quantitative estimates.

2. REVIEW

Description of the review procedure received by the EPA evaluation document which is summarized by these sheets:

Agency CRAVE Work Group Review

Dates on which the Agency review committee met to review data on the agent.

Verification Date

Date on which the Agency review committee agreed that the information is accurate.

3. U.S. EPA CONTACTS

The person or persons at EPA who can explain the origin of the items on the summary sheet.

III. DRINKING WATER HEALTH ADVISORIES

Health advisories are still under development.

IV. RISK MANAGEMENT SUMMARIES

INTERPRETATION OF RISK MANAGEMENT DATA

A cautionary statement is presented concerning the interpretation of the data.

A. RISK MANAGEMENT ACTIONS

A table summarizing the risk management actions taken by the U.S. EPA is given. This table includes the following categories:

Risk Management Action

The type of action (i.e., official name)

Status

Current status of this action

Date

Date of the action

Risk Management Value

The numeric risk management value. Some values are specific for duration of exposure, and are so indicated. Values that vary according to a given set of conditions (e.g., site-specific values) will not be listed here. Call the EPA Contact for specific information.

Considers Econ/Tech Feasibility

Indicates whether or not the economical or technical feasibility of the risk management action has been considered prior to setting the value.

Reference

The document in which the value was published.

B. RISK MANAGEMENT RATIONALE

The chemical-specific information underlying each of the risk management actions is described. U.S. EPA contacts are also given.

V. SUPPLEMENTARY DATA

A. ACUTE HEALTH HAZARD INFORMATION

In response to concerns raised following the tragic release of toxic substances from a chemical plant in Bhopal, India in 1985, EPA has generated a list of chemicals which could conceivably pose acute hazards to people living in the neighborhood of production or storage facilities. The list includes a range of chemical-specific information which would be useful in assessing the significance of levels determined in the environment.

B. PHYSICAL-CHEMICAL PROPERTIES

The chemical and physical properties of the compound are listed and other properties of the substance are presented.

SYNONYMS

A listing of synonyms for the chemical as extracted from a number of sources is given.

100-42-5	Styrene
62476-59-9	Tackle
5902-51-2	Terbacil
95-94-3	1,2,4,5-Tetrachlorobenzene
79-34-5	1,1,2,2-Tetrachloroethane
127-18-4	Tetrachloroethylene
58-90-2	2,3,4,6-Tetrachlorophenol
961-11-5	Tetrachlorovinphos
78-00-2	Tetraethyl Lead
1314-32-5	Thallic Oxide
563-68-8	Thallium Acetate
6533-73-9	Thallium Carbonate
7791-12-0	Thallium Chloride
10102-45-1	Thallium Nitrate
12039-52-0	Thallium Selenite
7446-18-6	Thallium(I) Sulfate
23564-05-8	Thiophanate-methyl
108-88-3	Toluene
2303-17-5	Triallate
615-54-3	1,2,4-Tribromobenzene
120-82-1	1,2,4-Trichlorobenzene
71-55-6	1,1,1-Trichloroethane
79-00-5	1,1,2-Trichloroethane
79-01-6	Trichloroethylene
75-69-4	Trichloromonofluoromethane
95-95-4	2,4,5-Trichlorophenol
88-06-2	2,4,6-Trichlorophenol
96-18-4	1,2,3-Trichloropropane
76-13-1	1,1,2-Trichloro-1,2,2-trifluoroethane (R-113)
no CAS No.	Tridiphane
1314-62-1	Vanadium Pentoxide
1929-77-7	Vernam
50471-44-8	Vinclozolin
81-81-2	Warfarin
557-21-1	Zinc Cyanide
1314-84-7	Zinc Phosphide
12122-67-7	Zineb

I. CHRONIC SYSTEMIC TOXICITY: NONCARCINOGENIC HEALTH EFFECTS

INTERPRETATION OF CHRONIC SYSTEMIC TOXICITY DATA

The Reference Dose (RfD) is based on the assumption that thresholds may exist for certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. The RfD is considered to be the level unlikely to cause significant adverse health effects associated with a threshold mechanism of action in humans exposed for a lifetime. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to section II, and other sources as well, for risk assessment information pertaining to the carcinogenicity of this compound. Please refer to the Background Document on the RfD (Appendix A) in Service Code 4 for an elaboration of these concepts.

A. REFERENCE DOSE (RfD) FOR ORAL EXPOSURE

Chemical: Lindane
CAS No.: 58-89-9 Preparation Date: 04/28/86

1. REFERENCE DOSE SUMMARY TABLE

Critical Effect	Experimental Doses *	UF	MF	RfD
Liver and kidney toxicity Rat, subchronic oral bioassay RCC (1983)	4 ppm diet 0.3 mg/kg bw/day (females) (NOAEL) 20 ppm diet 1.55 mg/kg bw/day (males) (LOAEL)	1000	1	3E-4 mg/kg/day

* Dose Conversion Factors & Assumptions: none

2. PRINCIPAL AND SUPPORTING STUDIES

Research and Consulting Co., Ltd. 1983. Acc. Nos. 250340-250342. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Twenty male and 20 female Wistar KFM-Han (outbred) SPF rats/treatment group were administered 0, 0.2, 0.8, 4, 20 or 100 ppm lindane (99.85%) in the diet. After 12 weeks, 15 animals/sex/group were sacrificed. The remaining rats were fed the control diet for an additional 6 weeks before sacrifice. No treatment-related effects were noted on mortality, hematology, clinical chemistry or urinalysis. Rats receiving 20 and 100 ppm lindane were observed to have greater-than-control incidence of the following: liver hypertrophy, kidney tubular degeneration, hyaline droplets, tubular distension, interstitial nephritis and basophilic tubules. Since these effects were mild or rare in animals receiving 4 ppm, this represents a NOAEL. The reviewers of the study calculated the dose to be 0.29 mg/kg/day for males and 0.33 mg/kg/day for females, based on measured food intake.

In a 2-year feeding study (Fitzhugh, 1950), 10 Wistar rats/sex/group were exposed to 5, 10, 50, 100, 400, 800 or 1600 ppm lindane. Slight liver and kidney damage and increased liver weights were noted at the 100 ppm level. If a food intake equal to 5% body weight is assumed, a NOAEL of 2.5 mg/kg bw/day (50 ppm) can be determined from this assay. In a 2-year bioassay (Rivett et al., 1978), four beagle dogs/sex/group were administered 0, 25, 50 or 100 ppm lindane in the diet. Treatment-related effects noted in the animals of the 100 ppm group were increased serum alkaline phosphatase and enlarged dark friable livers. A NOAEL was determined to be 50 ppm (1.6 mg/kg bw/day).

Use of the NOAEL derived from the RCC (1983) study is most appropriate, in keeping with the practice of utilizing data from the most sensitive species (or strain) as a surrogate for humans when human data are lacking.

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3. UNCERTAINTY AND MODIFYING FACTORS

UF = 1000. A factor of 10 each was employed for use of a subchronic vs. a lifetime assay, to account for interspecies variation and to protect sensitive human subpopulations.

MF = 1

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4. ADDITIONAL COMMENTS

Data on reproductive effects of lindane are inconclusive. Most reports indicate that hexachlorocyclohexane isomers are nonteratogenic.

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5. CONFIDENCE IN THE RfD

Study: Medium Data Base: Medium RfD: Medium

The RCC (1983) study used an adequate number of animals and measured multiple end points. Since there are other reported chronic and subchronic studies, confidence in the study, data base and RfD is considered medium.

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6. DOCUMENTATION AND REVIEW

U.S. EPA. 1985. Drinking Water Criteria Document for Lindane. Office of Drinking Water, Washington, DC.

The RfD in the Drinking Water Criteria Document has been extensively reviewed by U.S. EPA scientists and selected outside experts.

Agency RfD Work Group Review: 01/22/86

Verification Date: 01/22/86

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7. U.S. EPA CONTACTS

Primary: M.L. Dourson FTS/684-7544 or 513/569-7544
Office of Research and Development

Secondary: C.T. DeRosa FTS/684-7534 or 513/569-7534
Office of Research and Development

B. REFERENCE DOSE (RfD) FOR INHALATION EXPOSURE

Chemical: Lindane
CAS No.: 58-89-9

Information is not available at this time.

II. RISK ESTIMATES FOR CARCINOGENS

Chemical: Lindane
CAS No.: 58-89-9

This chemical is among those substances evaluated by the U.S. EPA for evidence of human carcinogenic potential. This does not imply that this chemical is necessarily a carcinogen. The evaluation for this chemical is under review by an inter-office Agency work group. A risk assessment summary will be included on IRIS when the review has been completed.

III. DRINKING WATER HEALTH ADVISORIES

Chemical: Lindane
CAS No.: 58-89-9

Information is not available at this time.

IV. RISK MANAGEMENT SUMMARIES

Chemical: Lindane
CAS No.: 58-89-9 **Preparation Date:** 09/30/86

INTERPRETATION OF RISK MANAGEMENT DATA

EPA risk assessments may be continuously updated as new data are published and as assessment methodologies evolve. Risk management (RM) decisions are frequently not updated at the same time. Carefully read the dates for the risk management actions (in this section) and the verification dates for the risk assessments (in sections I & II), as this may explain apparent inconsistencies. Also note that some risk management decisions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated in the table below (Considers Econ/Tech Feasibility). Please direct any questions you may have concerning the use of risk assessment information in making a risk management decision to the contact listed in Part B of this section (Risk Management Rationale). Users are strongly urged to read the background information on each RM action in Appendix E in Service Code 4.

INTEGRATED RISK INFORMATION SYSTEM: Chemical Files

Lindane; CAS No. 58-89-9 (Revised 11/16/1986)

USE AND INTERPRETATION OF THE DATA IN IRIS

Health risk assessment information on chemicals is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Agency Program Offices. The summaries presented in Sections I and II represent a consensus reached in those reviews. The conceptual bases of these risk assessments are described in Appendices A & B in Service Code 4. The other sections are supplementary information which may be useful in particular risk management situations, but have not yet undergone comprehensive U.S. EPA review. The risk management numbers (Section V) may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of risk management numbers for a particular situation, note the date of their development, the date of the most recent risk assessment, and whether technological factors were considered. For a more detailed description of procedures used in these assessments and the development of risk management numbers, see Appendix E in Service Code 4.

STATUS OF DATA FOR Lindane

I.	Chronic Systemic Toxicity: Noncarcinogenic Health Effects	
A.	Oral RfD:	available
B.	Inhalation RfD:	none
II.	Risk Estimates for Carcinogens:	review pending
III.	Drinking Water Health Advisories:	none
IV.	Risk Management Summaries:	available
V.	Supplementary Data:	available

A. RISK MANAGEMENT ACTIONS

Risk Management Action	Status Date	Risk Management Value	Considers Econ/Tech Feasibility	Reference
Reportable Quantity (RQ)	Statutory 1980	1 lb	no	50 FR 13456 04/04/85
Water Quality Criteria (WQC):				
a. Human Health		18.6 ng/l	no	45 FR 79318 11/28/80
b. Aquatic Toxicity				
1) Freshwater	Final 1980	Acute 2.0 ug/l Chronic 0.080 ug/l	no	45 FR 79318 11/28/80
2) Marine	Final 1980	Acute 0.16 ug/l Chronic none	no	ibid.
Pesticide Active Ingredient:				
a. Registration Standard	Current 1985	various	no	Reg. Std. Sept. 1985
b. Special Review	Termination of RPAR 1983	P.D. 1	no	42 FR 9816 02/18/77
		P.D. 2/3	yes	45 FR 45362 07/03/80
		P.D. 4	yes	48 FR 48512 09/30/83

B. RISK MANAGEMENT RATIONALE

RQ

The statutory RQ of 1 pound established pursuant to CERCLA Section 102(b) is retained until the assessment of potential carcinogenicity is complete.

Contact: Office of Emergency and Remedial Response
202\382-2180 or FTS\382-2180

WQC

Contact: Office of Water Regulations and Standards
202-382-5400 or FTS-382-5400

a. Human health: The WQC of 18.6 ng/l represents a cancer risk level of 1E-6 based on consumption of contaminated organisms and water. A WQC of 62.5 ng/l has been established based on consumtion of contaminated aquatic organisms alone.

b. Aquatic toxicity: Water quality criteria for the protection of aquatic life are derived from a minimum data base of acute and chronic tests on a

variety of aquatic organisms. The data are assumed to be statistically representative and are used to calculate concentrations which will not have significant short or long term effects on 95% of the organisms exposed. Recent criteria (1985 and later) contain duration and frequency stipulations: the acute criteria maximum concentration is a 1-hour average and the chronic criteria continuous concentration is a 4-day average which are not to be exceeded more than once every three years, on the average (see Stephen et al. 1985). Earlier criteria (1980-1984) contained instantaneous acute and 24-hour average chronic concentrations which were not to be exceeded. (FR 45: 79318: November 28, 1980). The freshwater chronic WQC is a 24-hour average.

Pesticide Active Ingredient
a. Regulation Standard: Lindane Pesticide Registration Standard. September 1985. Registration Support and Emergency Response Branch, Office of Pesticide Programs.
Contact: Office of Pesticides Programs
202/557-7760 or FTS/557-7760

b. Special Review: Negotiated settlements have been made for Lindane in dog dips [49 FR 26282 (06/27/84)] and in smoke bombs [50 FR 5424 (02/08/85)].
Contact: Office of Pesticides Programs, Special Review Branch
202/557-7420 or FTS/557-7420

V. SUPPLEMENTARY DATA

Chemical: Lindane
CAS No.: 58-89-9 Preparation Date: 11/07/86

USE AND INTERPRETATION OF SUPPLEMENTARY DATA

The information contained in this section (subsections A and B) has been extracted from the EPA Chemical Profiles Database, which has been compiled from a number of secondary sources and has not undergone formal Agency review. The complete reference listings for the citations below are provided in Service Code 4. The user is urged to read the background document for this section (Appendix E in Service Code 4) for further information on the sources and limitations of the data presented here.

A. ACUTE HEALTH HAZARD INFORMATION

Lindane is a stimulant of the nervous system, causing violent convulsions that are rapid in onset and generally followed by death or recovery with 24 hours (Hayes, 1982, p. 218). The probable human oral lethal dose is 50-500 mg/kg, or between 1 teaspoon and 1 ounce for a 150-lb (70-kg) person (Gosselin, 1984, p. II-286).

Medical Conditions Generally Aggravated by Exposure: Not Found

Signs and Symptoms of Exposure: Lindane in contact with the eyes or skin may produce irritation (DASE, 1980, p. 529). Vomiting, faintness, tremor, restlessness, muscle spasms, unsteady gait, and convulsions may occur as a result of exposure. Elevated body temperature and pulmonary edema have been

reported in children. Coma, respiratory failure and death can result. Exposure to vapors of this compound, or its thermal decomposition products, may lead to headache, nausea, vomiting, and irritation of the eyes, nose, and throat (Gosselin, 1984, pp. III-240, 241).

B. PHYSICAL-CHEMICAL PROPERTIES

Chemical Formula: $C_6H_6Cl_6$
Molecular Weight: 290.83
Boiling Point: 614F, 323.4C; Decomposes
Specific Gravity (H2O=1): 1.9
Vapor Pressure (mmHg): 9.4 x 10-6 at 20C
Melting Point: 234.5F, 112.5C
Vapor Density (AIR=1): Not Found
Evaporation Rate (Butyl acetate=1): Not Found
Solubility in Water: Insoluble
Flash Point [Method Used]: Not Found
Flammable Limits: Not Found

Appearance and Odor: Colorless solid with a musty odor; pure material is odorless (NIOSH/OSHA, 1978, p. 120).

Conditions or Materials to Avoid: Not Found

Hazardous Decomposition or Byproducts: Thermal decomposition products may include chlorine, hydrochloric acid, and phosgene (Sax, 1984, p. 366).

Use: Lindane is used as a pesticide (Hawley, 1981, p. 617) and scabicide (Hayes, 1982, p. 221).

Synonyms: (NIOSH/RTECS 1983 Synonyms, Volume 1, p. 1,000): Cyclohexane, 1,2,3,4,5,6-Hexachloro-, Gamma-Isomer; Aalindan; Aficide; Agrisol G-20; Agrocide; Agrocide 2; Agrocide 7; Agrocide 6G; Agrocide III; Agrocide WP; Agronexit; Ameisenatod; Ameisenmittel Merck; Aparasin; Aphtiria; Aplidal; Arbitex; BBH; Ben-Hex; Bentox 10; Benzene Hexachloride-gamma-isomer; gamma-Benzene Hexachloride; Bexol; BHC; gamma-BHC; Celanex; Chloresene; Codechine; DBH; Detmol-Extrakt; Detox 25; Devoran; Dol Granule; Drill Tox-Spezial Aglukon; Ent 7,796; Entomoxan; Exagama; Forlin; Gallogama; Gamacid Gamaphex; Gamene; Gammahexa; Gammahexane; Gammalin; Gammalin 20; Gammaterr; Gammex; Gammexane; Gammopaz; Gexane; HCCH; HCH; gamma-HCH; Heclotox; Hexa; Hexachloran; gamma-Hexachloran; Hexachlorane; gamma- Hexachlorane; gamma-Hexachlorobenzene; 1-alpha,2-alpha,3-beta,4-alpha, 5-alpha,6-beta-Hexachlorocyclohexane; gamma-Hexachlorocyclohexane; gamma-1,2,3,4,5,6-Hexachlorocyclohexane; Hexachlorocyclohexane, gamma-Isomer; 1,2,3,4,5,6-Hexachlorocyclohexane, gamma-Isomer; Hexatox; Hexaverm; Hexicide; Hexyclan; HGI; Hortex; Inexit; Isotox; Jacutin; Kokotine; Kwell; Lendine; Lentox; Lidenal; Lindafor; Lindagam; Lindagrain; Lindagranox; gamma-Lindane; Lindane (DOT); Lindapoudre; Lindatox; Lindosep; Lintox; Lorexane; Milbol 49; Mszychol; NCI-C00204; NEO-Scabicidol; Nexen FB; Nexit; Nexit-Stark; Nexol-E; Nicochloran; Novigam; Omnitox; Ovadziak; Owadzlak; Pedraczak; Pflanzol; Quellada; Sang gamma; Silvanol; Spritz-Rapidin; Spruehpflanzol; Streunex; Tap 85; TRI-6; Viton

APPENDIX C

SOURCES OF INFORMATION FOR TOXICITY PROFILES

TABLE C-1. TOXICITY PROFILES AVAILABLE FROM U.S. EPA OFFICE OF WASTE PROGRAMS ENFORCEMENT (OWPE) AND OFFICE OF EMERGENCY AND REMEDIAL RESPONSE (OERR)

Chemical	OWPE Chemical Profile	OERR Health Effects Assessment
Acenaphthene	X	
Acenaphthylene	X	
Acetic acid	X	
Acetone	X	X
Acrolein	X	
Acrylonitrile	X	
Aldrin	X	
Anthracene	X	
Antimony	X	
Arsenic	X	X
Asbestos	X	X
Barium	X	X
Benzene	X	X
Benzidine	X	
Benzo(a)anthracene	X	
Benzo(a)pyrene		X
Benzothiazole	X	
Beryllium	X	
alpha-BHC	X	
beta-BHC	X	
gamma-BHC (lindane)	X	X
delta-BHC	X	
Butanol	X	
Butyl acetate	X	
Cadmium	X	X
Carbon tetrachloride	X	X
cis-Chlordane	X	X
trans-Chlordane	X	X
Chlorine	X	
Chlorobenzene	X	X
Chlorobenzilate	X	
Chloroethane	X	
Chloroform	X	X
p-Chloro-m-cresol	X	
1-Chloro-3-nitrobenzene	X	
bis(2-Chloroethoxy)ethane	X	
Chromium (total)	X	
Chromium (hexavalent)		X
Chromium (trivalent)		X
Chrysene	X	
Coal tars		X
Cobalt	X	
Copper	X	X
Cresol	X	X
Cyanides	X	X
Cyanuric acid	X	
p,p'-DDD	X	
o,p'-DDD	X	
p,p'-DDE	X	
p,p'-DDT	X	X
o,p'-DDT	X	X
Dibromochloropropane	X	
1,2-Dichlorobenzene	X	
1,3-Dichlorobenzene	X	
1,4-Dichlorobenzene	X	
1,1-Dichloroethane	X	X
1,2-Dichloroethane	X	X
1,1-Dichloroethylene	X	X
1,2-cis-Dichloroethylene		X
1,2-trans-Dichloroethylene	X	X
2,4-Dichlorophenol	X	
2,4-Dichlorophenoxyacetic acid	X	
1,2-Dichloropropane	X	

TABLE C-1. (Continued)

Chemical	OWPE Chemical Profile	OERR Health Effects Assessment
1,3-Dichloropropane	X	
1,3-Dichloropropene	X	
Dicofol	X	
Dieldrin	X	
Diethyl benzene	X	
Diethylene glycol	X	
Diethyl phthalate	X	
Diisobutyl ketone	X	
Dimethylaminoethyl methacrylate	X	
Dimethyl aniline	X	
Dimethylnitrosamine	X	
2,4-Dimethyl pentane	X	
2,4-Dimethylphenol	X	
n-Dioctyl phthalate	X	
1,4-Dioxane	X	
Diphenyl ethane	X	
Endrin	X	
Ethanol	X	
bis(2-Chloroethyl) ether	X	
Ether	X	
Ethyl acetate	X	
Ethylbenzene	X	X
Ethylene glycol	X	
Ethyl hexanediol	X	
bis-2-Ethylhexyl phthalate	X	
Ethyl toluene	X	
Fluoranthene	X	
Formaldehyde	X	
Glycol ethers		X
Heptachlor	X	
Heptane	X	
Hexachlorobenzene	X	X
Hexachlorobutadiene	X	X
Hexachlorocyclohexane	X	
Hexachlorocyclopentadiene		X
Hexachloroethane	X	
Hexachlorophene	X	
Hexane	X	
Iron	X	X
Isobutyl alcohol	X	
Isopropyl benzene	X	
Isopropyl ether	X	
Lead	X	X
Lithium	X	
Magnesium	X	
Manganese	X	X
Mercury	X	X
Methacrylic acid	X	
Methanol	X	
Methyl chloride	X	
2-Methyl dodecane	X	
Methylene chloride	X	X
Methyl ethyl benzene	X	
Methyl ethyl ketone	X	X
3-Methyl hexane	X	
Methyl isobutyl ketone	X	
Methyl methacrylate	X	
Methyl parathion	X	
2-Methyl pentane	X	
3-Methyl pentane	X	
2-Methyl-1-pentene	X	
2-Methyl tetradecane	X	
2-Methyl tridecane	X	

TABLE C-1. (Continued)

Chemical	OWPE Chemical Profile	OERR Health Effects Assessment
Monethanolamine	X	
Naphthalene	X	X
Nickel	X	X
Nitrocellulose	X	
2-Nitrophenol	X	
Pentachlorophenol	X	X
Pentadecane	X	
Phenanthrene	X	X
Phenol	X	X
Phenyl ether	X	
Phosphoric acid	X	
Phosphorus	X	
Picric acid	X	
Polychlorinated biphenyls (PCBs)	X	X
Polychlorinated dibenzo-p-dioxin	X	
Polycyclic aromatic hydrocarbons (PAHs)		X
Pyrene		X
Selenium	X	X
Silver	X	
Sodium chlorate	X	
Sodium cyanide		X
Sodium	X	
Stoddard solvent	X	
Sulfuric acid		X
1,2,4,5-Tetrachlorobenzene	X	
2,3,7,8-Tetrachloro-dibenzo-p-dioxin (TCDD)	X	X
1,1,2,2-Tetrachloroethane	X	X
Tetrachloroethylene	X	X
Tetraethyl lead	X	
Tetrahydrofuran	X	
Tetramethyl benzene	X	
Thallium	X	
Titanium	X	
Toluene	X	X
Toxaphene	X	
1,2,3-Trichlorobenzene	X	
1,2,4-Trichlorobenzene	X	
1,3,5-Trichlorobenzene	X	
2,3,6-Trichlorobenzoic acid	X	
1,1,1-Trichloroethane	X	X
1,1,2-Trichloroethane	X	X
Trichloroethylene	X	X
Trichlorofluoromethane	X	
2,4,5-Trichlorophenol	X	X
2,4,6-Trichlorophenol		X
2,4,5-Trichlorophenoxyacetic acid	X	
2,4,5-Trichlorophenoxy propionic acid	X	
Trimethylbenzene	X	
1,3,5-Trimethylbenzene	X	
1,2,4-Trimethylbenzene	X	
tris(2,3-Dibromopropyl)phosphate	X	
Undecane	X	
Vanadium	X	
Vinyl chloride	X	X
Xylene	X	X
m-Xylene	X	
o-Xylene	X	
p-Xylene	X	
Zinc	X	X

Reference: Life Systems (1985).

TABLE C-2. U.S. EPA SOURCES OF TOXICITY PROFILES

Document	Availability	Description
Criteria Document - Air	Office of Air Quality Planning and Standards (OAQPS)	Summary of the latest scientific knowledge on the effects of varying quantities of a substance in the air. Usually prepared for OAQPS by the Office of Health and Environmental Assessment (OHEA).
Criteria Document - Drinking Water	Office of Drinking Water (ODW)	Summary of important experimental results from the literature relevant to the chemistry and health effects of a specific drinking water contaminant. Serves as a foundation to support regulatory standards or guidelines for the acceptable concentration of the contaminant in the drinking water.
Criteria Document - Ambient Water Quality	Office of Water Regulations and Standards (OWRS)	Information on the type and extent of identifiable toxic effects on health and welfare expected from the presence of pollutants in any body of water. Objective of document is to protect most species in a balanced and healthy aquatic community and/or to protect human health.
Chemical Hazard Information Profile (CHIP)	Office of Toxic Substances (OTS)	Summary of readily available information concerning the health and environmental effects and potential exposure to a chemical.
Chemical Profile	Office of Waste Programs Enforcement (OWPE)	Brief summary of the chemical/physical properties, fate and transport, health effects and environmental toxicity levels for 202 chemicals identified at hazardous waste sites. Currently 183 of the planned Chemical Profiles are available in draft form.
Health Advisory	ODW	Develops toxicological analyses to establish an acceptable level in drinking water for unregulated contaminants for various exposure durations.
Health Assessment Document	Office of Health and Environmental Assessment (OHEA)	Inventories the scientific literature and evaluates key studies. Discusses dose-response relationships so that the nature of the adverse health response is evaluated in perspective with observed environmental levels. Usually prepared by OHEA for another office.
Health and Environmental Effects Profile	Office of Solid Waste (OSW)	Profiles are "mini-" criteria documents prepared usually as summaries of existing water quality criteria documents. They serve as a support for the listing of hazardous wastes in the RCRA program.
Health Effects Assessments	Office of Emergency and Remedial Response (OERR)	Summary of the pertinent health effects information on 58 chemicals found most often at hazardous waste sites. Developed by the Environmental Criteria and Assessment Office (ECAO) for OERR.

Address for all offices listed above: U.S. Environmental Protection Agency, 401 M Street S.W., Washington, DC 20460 (202) 382-2090

Reference: Life Systems (1985).

TABLE C-3. SELECTED CHEMICAL AND TOXICOLOGICAL DATABASES

Database vendor	Database Name	Database Contents	Access Procedures
MEDLARS (National Library of Medicine)	Toxline	1.5 million references on environmental and toxicological effects of chemicals.	Contact: MEDLARS Management Section National Library of Medicine 8600 Rockville Pike Bethesda, MD 20209 (301) 496-6193
	Chemline	An online chemical dictionary of 500,000 records.	
	RTECS (Registry of Toxic Effects of Chemical Substances)	Basic acute and chronic toxicity for more than 57,000 toxic chemicals.	
	AQUIRE (Aquatic Information Retrieval System	Toxicity data for 2,000 chemicals, each cross referenced by CAS number. Lists any studies on bioaccumulation, sublethal effects, and environmental fate of the chemical.	
CIS (Chemical Information System)	CESARS (Chemical Evaluation Search and Retrieval System)	Detailed toxicity and environmental fate information and evaluation on 150 chemicals of importance to Great Lakes.	Contact: CIS, Inc. Fein-Marquart Associates 7215 York Road Baltimore, MD 21212 (800) 247-8737
	CTCP (Clinical Toxicology of Commercial Products)	Ingredient and product information for most commercially available nonfood items.	
	Envirofate	Information on the environmental fate of approximately 500 chemicals.	
	ISHOR (Information System for Hazardous Organics in Water)	Physical and chemical properties of 14,000 organic compounds and associated aquatic toxicity data.	
	OHMTADS (Oil and Hazardous Materials Technical Assistance Data System)	Created by U.S. EPA Superfund. Includes information on environmental effects of 11,000+ hazardous substances.	

TABLE C-3. (Continued)

CAS Online (Chemical Abstracts)	Chemical Abstracts	Physical and chemical properties on 6 million chemical substances.	Contact: Chemical Abstracts Office Customer Service P.O. Box 3012 Columbus, OH 43210 (800) 848-6533
DOE/RECON	35 energy-related and environmental databases including Energy Database, Water Resources Abstracts, Environmental Mutagens, and Environmental Teratology.		Contact: Technical Information Center U.S. Department of Energy P.O. Box 62 Oak Ridge, TN 37380 (615) 575-1272

Reference: U.S. Fish and Wildlife Service (1986).

APPENDIX D

EVALUATION OF THE EFFECTS OF COMPOSITE SAMPLING ON STATISTICAL POWER OF A SAMPLING DESIGN

APPENDIX D: EVALUATION OF THE EFFECTS OF COMPOSITE SAMPLING ON STATISTICAL POWER OF A SAMPLING DESIGN

Tetra Tech (1986b) used simulation methods to make a direct comparison of grab and composite-sampling strategies. Simulation refers to the use of numerical techniques to generate random variables with specified statistical properties. For the analyses described below, Tetra Tech (1986b) developed computer programs to 1) produce individual random samples from populations with normally distributed concentrations of contaminants, and other statistical properties similar to those of historical bioaccumulation data sets described in Tetra Tech (1986b), 2) construct composite samples, and 3) calculate statistical power of sampling designs using individual or composite samples.

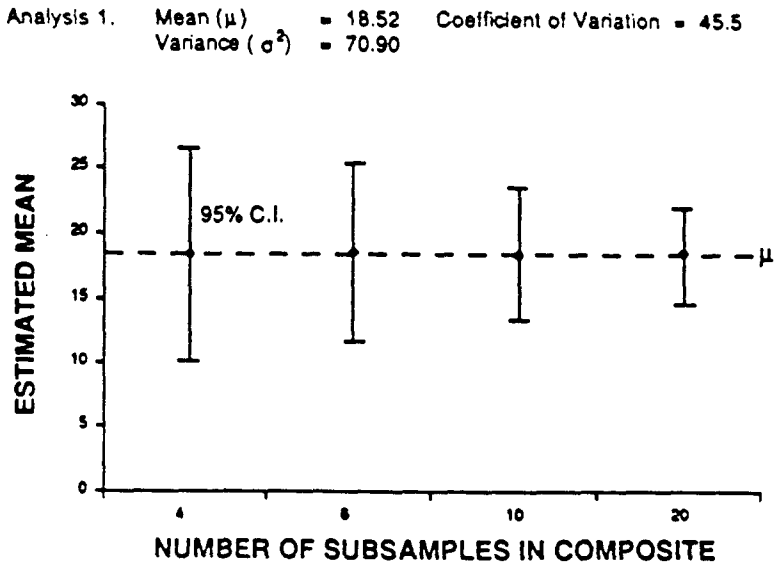
Two sets of analyses were performed by Tetra Tech (1986b). In the first set, simulation methods were used to show the effect of sample compositing on the estimate of the population mean. Power analyses were used in the second set of analyses to demonstrate the effect of increasing the number of subsamples in a composite sample on the probability of detecting specified levels of differences among stations.

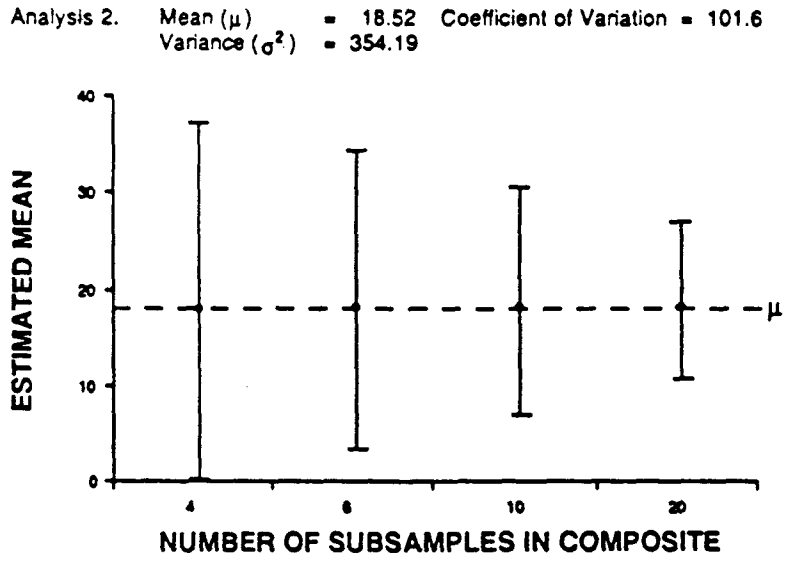
The first set of analyses demonstrated that the confidence in the estimate of the mean increases as the number of subsamples in the composite increases (Figure D-1). The simulated sampling consisted of randomly selecting 10,000 composite samples from two populations exhibiting two different levels of variability in the sampling environment. The mean value in both populations was fixed at 18.52, but the population variances were set at 70.90 or 354.19, corresponding to coefficients of variation of 45.5 and 101.6, respectively. These population characteristics were selected as representative of the range of values for the coefficient of variation observed in the historical data sets for selected metals and organic compounds in marine organisms (Tetra Tech 1986b). For a series of individual fish samples taken from the corresponding populations used in Analysis 1, the 95 percent confidence intervals would range from 1.7 to 35.4 concentration units (e.g., ppm).

To demonstrate the effect of sample compositing on the power of the statistical test of significance, Tetra Tech (1986b) performed statistical power analyses using a one-way Analysis of Variance (ANOVA) model. In these analyses (Figure D-2), the number of stations (5), number of replicate composite samples at each station (5), significance level of the test (0.05), residual error variance level, and level of minimum detectable difference (100 percent of overall mean) were fixed. The power of the test (i.e., the probability of detecting the specified minimum difference) was then calculated as a function of the number of subsamples constituting each replicate composite sample.

Power analyses were conducted for three levels of sample variability. All design parameters except the residual error variance were identical in each set of analyses. Values of the residual error variance were selected to represent the range of values found in the historical data sets described by Tetra Tech (1986b). The coefficients of variation selected for these three sets of analyses were 45.5, 101.6, and 203.5.

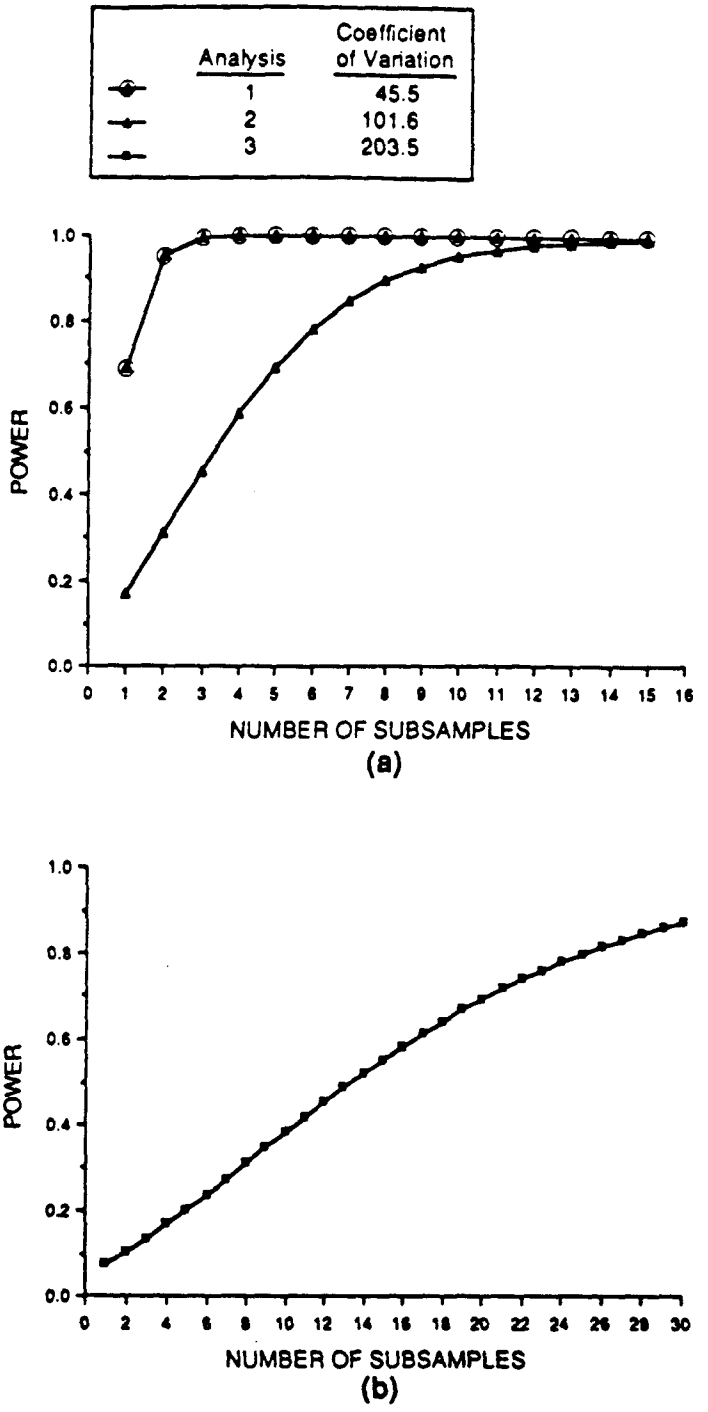
As shown in Figure D-2, the probability of statistically detecting a difference equal to the overall sample mean among stations increases with the collection of replicate composite samples at each station and as the number of subsamples constituting the composite increases. The results of both sets of analyses shown in Figure D-2 also demonstrate the phenomenon of diminishing returns for continued increases in the number of subsamples per composite. In Analysis Set 1, for example, virtually no





Reference: Tetra Tech (1986b)

Figure D-1 Effects of increasing composite sample size on confidence in the estimate of the mean.



Reference: Tetra Tech (1986b)

Figure D-2 Power of statistical tests vs. number of subsamples in composite replicate samples. Fixed design parameters: number of stations = 5, number of replicates = 5, significance level = 0.05, minimum detectable difference = 100 percent of overall mean value.

increase in the power of the statistical test was achieved with increasing the subsample size above three. In the second analysis set, substantial increases in statistical power were achieved by increasing the number of subsamples in each composite from 2 to 10. However, with each successive increase in subsample size, the relative benefit was reduced until very little was gained by increasing the subsample size above 10. For moderate levels of variability, 6-10 subsamples within each of 5 replicate composite samples may be adequate to detect a treatment difference equal to 100 percent of the mean among treatments. At the highest level of variability analyzed, the collection of replicate composite samples composed of 25 subsamples each is required to obtain a testing power of 0.80 (Figure D-2).

APPENDIX E

EVALUATION OF THE EFFECTS OF SAMPLE REPLICATION ON STATISTICAL POWER OF A SAMPLING DESIGN

APPENDIX E: EVALUATION OF THE EFFECTS OF SAMPLE REPLICATION ON STATISTICAL POWER OF A SAMPLING DESIGN

Statistical power analysis can be used to evaluate alternative sampling designs with varying levels of replication (Cohen 1977; Gordon et al. 1980; Tetra Tech 1986b). In statistical power analysis, relationships among the following study design parameters are evaluated:

- **Power** - Probability of detecting a real difference among treatments (e.g., species, stations, times)
- **Type I error (α)** - Probability of wrongly concluding that there are differences among treatments
- **Minimum detectable difference** - Magnitude of the smallest difference that can be detected for given power and Type I error
- **Residual error** - Natural variability
- **Number of stations**
- **Number of replicate samples.**

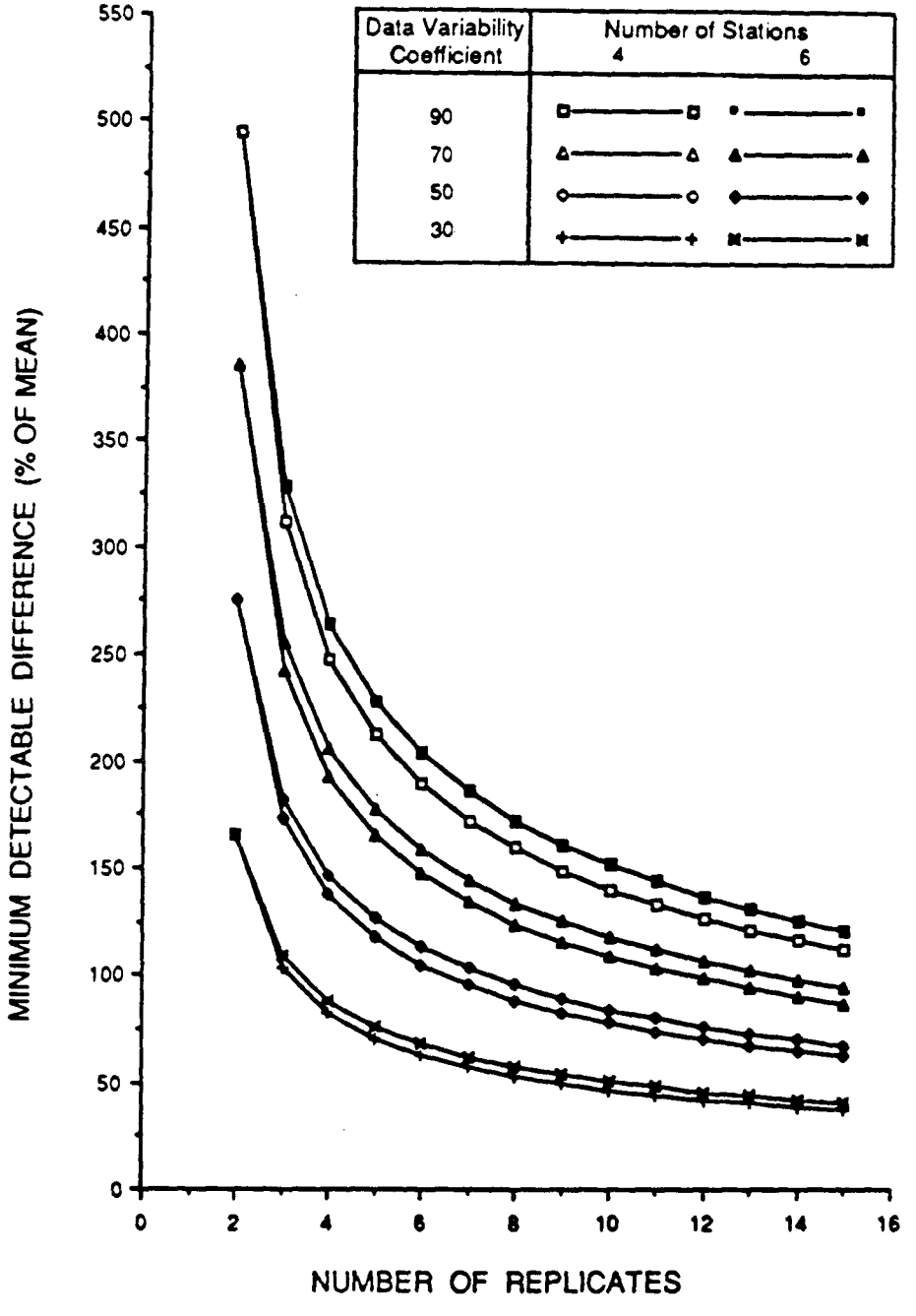
The analyses presented below were conducted with the objective of providing guidance in selecting levels of sampling replication. This objective was addressed by determining the magnitudes of difference among variables that can be reliably detected with varying levels of sampling effort.

A one-way ANOVA model was used to evaluate statistical sensitivity relative to level of sample replication. Tetra Tech (1986b,d) provides details of the ANOVA model and results of the analyses. All power analyses were conducted using the Ocean Discharge Evaluation System (ODES) maintained by EPA's Office of Marine and Estuarine Protection (Tetra Tech 1986d). The measure used to evaluate the statistical sensitivity of the monitoring design was the minimum detectable difference between two mean values. To generalize the results of the power analysis, the minimum detectable difference was expressed as a percentage of the grand mean among treatments. The power of the test was fixed at 0.80.

Predicted values of minimum detectable difference are shown for various levels of sample replication in Figures E-1 and E-2. For these analyses, the Type I error was fixed at 0.05. Minimum detectable difference was plotted vs. number of replicate samples for the following cases:

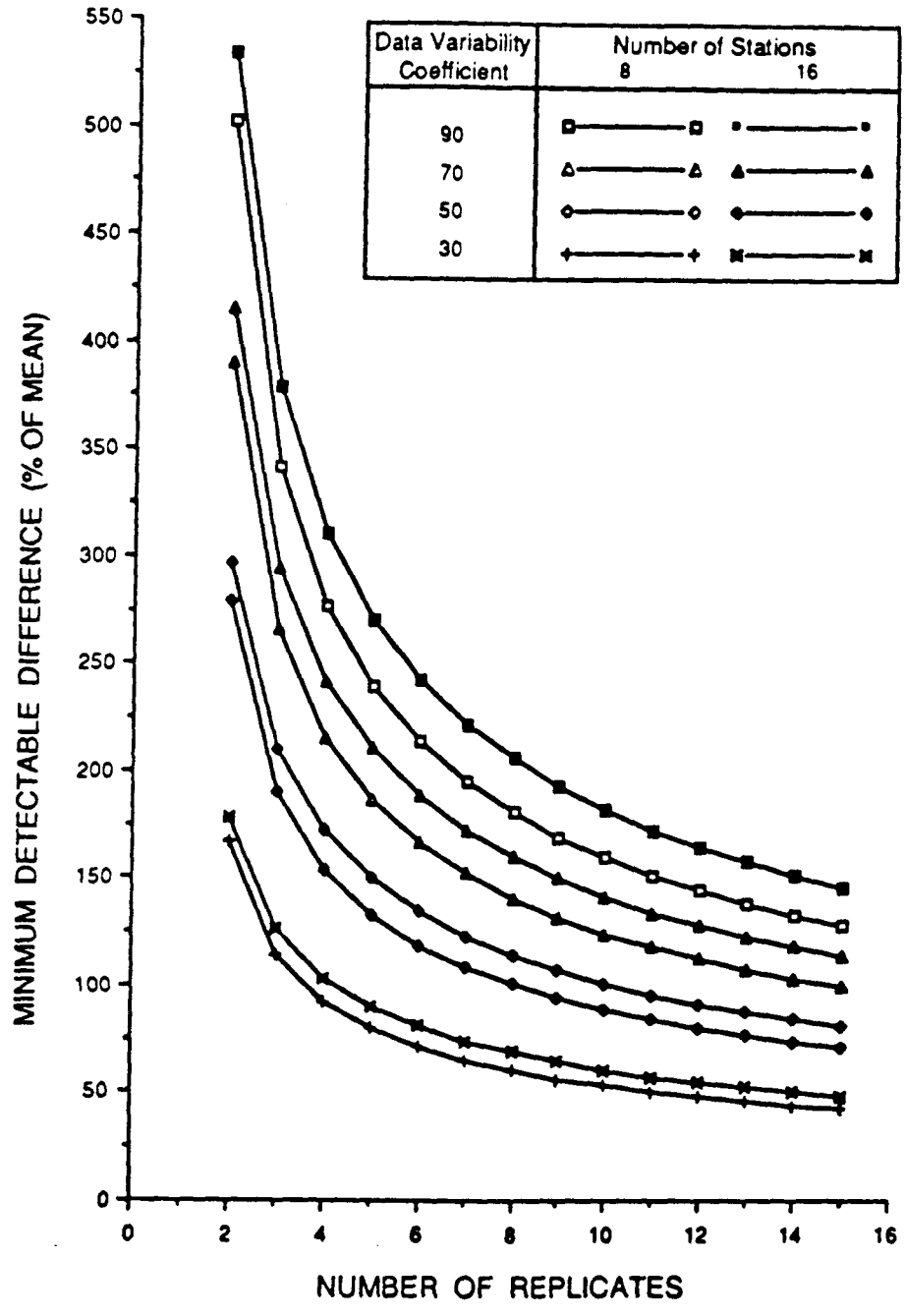
- Number of stations (or sampling times) equal to 4, 6, 8, and 16 stations (or times)
- Data Variability Coefficient (across treatments) equal to 30, 50, 70, and 90 percent.

The Data Variability Coefficient is equal to the within-groups mean square divided by the grand mean among groups (and multiplied by 100 to convert to a percentage). In designing a bioaccumulation study, the Data Variability Coefficient can be estimated by



Reference: Tetra Tech (1986b)

Figure E-1 Minimum detectable difference versus number of replicates at selected levels of unexplained variance for 4 and 6 stations. Power of test = 0.80, significance level = 0.05.



Reference: Tetra Tech (1986b)

Figure E-2 Minimum detectable difference versus number of replicates at selected levels of unexplained variance for 8 and 16 stations. Power of test = 0.80, significance level = 0.05.

performing an ANOVA on available data from the literature or on a preliminary data set. If such data cannot be obtained, the average Coefficient of Variation (within groups) can be used as a rough estimate of the Data Variability Coefficient.

The effect of setting a different value for Type I error is shown in Figure E-3. The effect of changes in Type I error is greater for higher levels of data variability. Note that substantial increases in sensitivity (i.e., decreases in minimum detectable difference) are achieved only for the case of three replicate samples in Figure E-3.

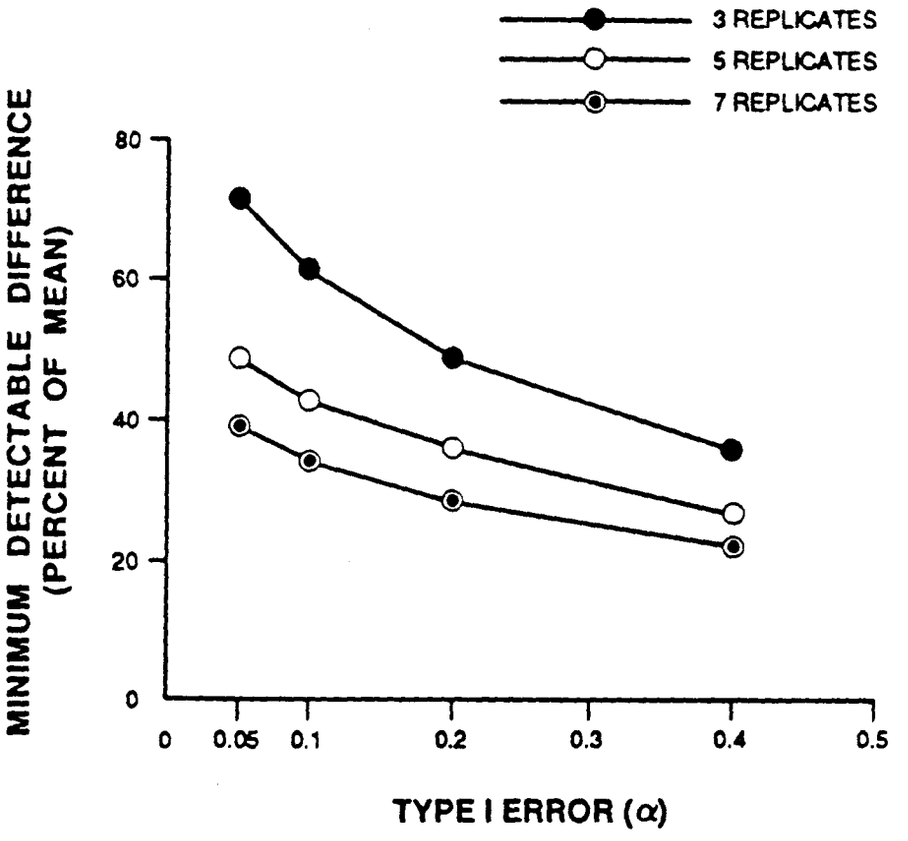


Figure E-3 Minimum detectable difference versus Type I Error for one-way ANOVA design with 3, 5, and 7 replicate samples.

APPENDIX F

ESTIMATION OF FISH/SHELLFISH CONSUMPTION FROM A NATIONAL DATABASE

(by U.S. EPA Office of Pesticide Programs)

APPENDIX F: ESTIMATION OF FISH/SHELLFISH CONSUMPTION FROM A NATIONAL DATABASE

The EPA Office of Pesticide Programs (OPP) has evaluated comprehensive data on dietary consumption of fish and shellfish within the conterminous United States. Selected consumption rate data for the U.S. population were used to provide an overview of potential exposure of humans to toxic chemicals associated with the consumption of contaminated fish and shellfish. Many surveys and reports were examined to determine probable sources for data on patterns of fish and shellfish consumption. Some economic reports are useful only for estimating average fish and seafood consumption. In contrast, polls have the potential to provide estimates of individual consumption trends by consumer, ethnic, or geographical subgroup (Table 1).

DEVELOPMENT OF A NATIONAL DATABASE

Based on sample size and relevance to recent trends in fish consumption, OPP concluded that the most reliable database for average daily consumption of fish and shellfish was the U.S. Department of Agriculture (USDA) Nationwide Food Consumption Survey of 1977-1978. In addition to being relatively recent, the USDA survey had a weighted sample size of 36,000 individuals. The consumption values listed in this survey are based on 3 days of individual consumption (from a 1-day recall and a 2-day diary) gathered by interviewers over the course of 1 year. Although the USDA 1977-1978 National Food Consumption Survey is an excellent source of fish consumption data, this survey was conducted 9-10 years ago. Fish consumption in the United States has been rising slowly for several years. Based upon the USDA 1977-1978 survey and their National Food Consumption Survey CSFII Report No. 85-3, the U.S. National Marine Fisheries Services estimated that average per capita consumption of fish and shellfish increased from 13 g/day in 1960 to 21 g/day in 1986. Because of the nature of these surveys and limitations of polls in terms of duration of individual records and numbers of people surveyed, precise statistical distributions for life-time fish consumption cannot be obtained with existing data.

Consumption values derived from the 1977-1978 USDA study were used to develop EPA's Tolerance Assessment System (TAS). Mean and percentiles of fish and shellfish consumption rates are provided in TAS for the U.S. population in the 48 conterminous states and various population subgroups (Tables 2-7). These estimates are for "acute" consumption (i.e., the amount of fish eaten in a single day). The average per capita fish/shellfish consumption rate of 15 g/day in TAS (No. 4 of Table 1) is generally consistent with the per capita consumption values listed for other surveys and reports.

The distribution of consumption provided in Tables 2-7 is the distribution among fish or shellfish eaters only, and is not a distribution for the entire population. The column titled "% Population as Consumers" provides the percentage of each population subgroup that is estimated to be a consumer of each category of fish/shellfish on any given day. The mean consumption estimates shown in Tables 2-7 are also for eaters only, and should not be confused with the mean per capita consumption estimates that are more commonly used in TAS analyses. These numbers provide valid estimates of the amounts of fish eaten in a single day. However, because of the way the data were derived, the frequency of fish consumption and, hence, annual consumption applies only

Table 1 : Fish Consumption Data Summary

Survey Data

Source	Survey Date[1]	Average Consumption g/day	Extreme Consumption g/day	Caveats
1. USDA Nationwide Food Consumption Survey (for individuals) note: Figure obtained from Environ 1985.	1977-1978	12.0		Sample size > 36,000 (weighted). Fish and shellfish in the conterminous 48 states. Based on a three day survey that included a 1 day recall and a 2 day diary.
2. USDA Nationwide Food Consumption Survey Continuing Survey of Food Intakes by Individuals Report # 85-3	1985	21 14 (from 1977-1978 survey above)		Sample size = 658 for men 19-50 only. 1 day recall. Fish and shellfish.
3. USDA NFCS, CSFII Report # 86-1	1986	11 13 (from a CSFII concucted in 1985) 11 (from 1977-1978 survey above)		Sample size = 1501 women and 509 children. This survey included women 19-50 and their children 1-5. 1 day recall. Fish and shellfish.
4. USDA NFCS, CSFII Report # 85-2	1985	11 (women) 5 (children)		Sample size = 2,210 women, 1,314 children. This survey included low income women 19-50 and their children 1-5. Fish and shellfish. 1 day recall

[1]Those dates which reflect publication or communication rather than the date of the survey are enclosed in parenthesis.

Table 1 cont.

Source	Survey Date	Average Consumption g/day	Extreme Consumption g/day	Caveats
5. EPA Tolerance Assessment System (computed for a 60kg individual)	1977-1978			Based on USDA 1977-1978 NFCS survey. The discrepency between TAS's 15.2 g/day and the USDA's 12 g/day is due to conversion of the TAS fig from g/kg body weight/day to g/day by multiplying by 60 kg.
a. Total			15.2	
b. Freshwater finfish			1.8	
note: Although the USDA survey figure listed is for fish and shellfish, the TAS data summary includes roe and caviar as well. It is unclear whether the USDA figure of 12 g/day obtained from Environ 1985 includes roe and caviar.				
6. USDA's Foods Commonly Eaten by Individuals: Amounts Per Day and Per Eating Session	(1982)	54		Consumers of finfish other than canned, dried or raw. Mean does not equal the median. Sample size ?
a. 50th percentile			38	
b. 90th percentile			96	
c. 95th percentile			132	
d. 99th percentile			221	
note: Obtained from Environ 1985.				
7. National Purchase Diary (analyzed by SRI International)	1973-1974	14.3		Sample size = greater than 25,000. 1/12 of the sample was surveyed each month. It appears that this survey was for the conterminous 48 states. The SRI
a. 95th percentile			41.7	
note: Obtained from SRI International. It is unclear whether the sample size of 25,000 included nonconsumers as well as consumers of fish.				

Table 1 cont.

Source	Survey Date	Average q/day	Extreme q/day	Caveats
8. National Marine Fisheries Service Market Facts Survey	1969-1970	16.8		Sample size = 4,864. Survey yielded a per canita fish consumption figure. It is not clear whether recreationally caught fish are included. Representative households completed diaries twice a month for 1 year regarding fish consumption patterns at home and outside the home.
a. 99th percentile			77	
b. 99.9th percentile			165	
note: The average value of 16.8 q/day was derived from Environ, and the extreme figures came from Roland Finch's article listed in the reference section. There is a discrepency between the 16.8 figure and the average figure of 14q/day based on the same survey cited by Finch.				
9. Guide to Eating Ontario Sport Fish	1983	13.8		Sample size unknown. Self selection biases possible. This survey is for Ontario fishermen consumption of freshwater finfish.

Table 1 cont.

Source	Survey Date	Average g/day	Extreme g/day	Caveats
10. Environ 1985 Estimate of Humphrey's Lake Michigan Data	(1976)	45		Estimate is extremely rough, and is for Lake Michigan sports fishermen consumption of Lake Michigan fish. Subjects were selected because of how much fish they caught.
11. Personal Communication with R. Sonstegard concerning intensive Lake Ontario sports fishermen.	1987		373	Intensive Lake Ontario sports fishermen.

TAS MEAT CONSUMPTION VALUES (g/day)

a. Red meat ---------- 134
b. Poultry ---------- 30.4
c. Fish ---------- 15.2

Table 1 cont.

Market Data

Source	Date	Average g/day	Extreme g/day	Caveats
12. USDA Agricultural Statistics note: Unclear what fish connotes.	1983	18.4		Per capita market data. Retail weight. Fish.
13. USDA, ERS, Statistical "Food Consumption, Prices, and Expenditures." note: Unclear whether seafood other than fish and shellfish included.	1985	18.0		Per capita market data. Edible weight. Fish and shellfish.
14. National Marine Fisheries Service Current Fisheries Report	1986 1985 1984 1960	18.3 17.9 17.0 10.3		Commercial fish and shellfish per capita. The military population is excluded and no information on fish caught through non-commercial activities.
a. Recreationally caught fish consumption cited in 1986 Current Fisheries Report table footnote and not included in that table.	1970	3.7-5.3		
15. New York State Department of Environmental Conservation Average Fish Consumption for Recreational Fishermen. note: From Environ 1985.	?	32.4		Based on 90th percentile of nationwide fish consumption figures. The source of the fi[illegible]s [illegible] not

TABLE 2 CONSUMPTION OF FRESHWATER FINFISH

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	1.10	2.7038	100	100	98	97	93	87	79	72	64	58	51	30	17	10	2	0	0
INFANTS(<1 YEAR)	0.11	2.6724	100	100	100	100	100	100	100	100	100	44	44	44	44	0	0	0	0
CHILDREN(1-6 YRS)	0.62	4.8498	100	100	100	99	98	96	93	93	92	89	84	68	50	32	8	3	0
FEMALES(13+ YRS)	1.14	2.4986	100	100	98	97	93	87	78	69	62	55	48	27	14	7	2	0	0
MALES(13+ YRS)	1.37	2.5524	100	100	98	95	91	84	77	70	61	54	47	27	15	8	1	0	0

TABLE 3 CONSUMPTION OF SALTWATER FINFISH

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	10.73	1.7510	100	97	91	84	75	65	56	47	40	35	30	14	7	4	0	0	0
INFANTS(<1 YEAR)	0.93	4.5676	100	100	95	89	83	77	77	66	65	58	58	58	51	45	6	0	0
CHILDREN(1-6 YRS)	9.36	3.4117	100	99	96	93	90	86	82	78	74	71	67	46	30	20	3	1	0
FEMALES(13+ YRS)	11.69	1.4970	100	97	90	82	72	61	51	41	34	28	23	9	4	1	0	0	0
MALES(13+ YRS)	10.32	1.5181	100	97	90	81	71	61	51	41	34	29	25	10	4	2	0	0	0

TABLE 4 CONSUMPTION OF SALTWATER FINFISH--DRIED

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	0.02	0.4758	100	26	26	26	26	26	26	26	6	0	0	0	0	0	0	0	0
INFANTS(<1 YEAR)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FEMALES(13+ YRS)	0.02	0.4511	100	25	25	25	25	25	25	25	13	0	0	0	0	0	0	0	0
MALES(13+ YRS)	0.03	0.5016	100	27	27	27	27	27	27	27	0	0	0	0	0	0	0	0	0

TABLE 5 CONSUMPTION OF FISH-ROE,CAVIAR

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	0.01	2.3449	100	100	100	100	85	85	85	69	69	69	69	38	15	0	0	0	0
INFANTS(<1 YEAR)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FEMALES(13+ YRS)	0.01	2.5632	100	100	100	100	100	100	100	100	100	100	100	42	0	0	0	0	0
MALES(13+ YRS)	0.00	0.7346	100	100	100	100	0	0	0	0	0	0	0	0	0	0	0	0	0

TABLE 6 CONSUMPTION OF SHELLFISH

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	2.61	1.3313	100	88	76	64	55	47	41	34	28	24	21	9	4	2	0	0	0
INFANTS(<1 YEAR)	0.11	0.8432	100	100	100	49	49	49	49	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.98	2.1878	100	90	80	71	64	61	59	55	52	49	43	22	13	11	1	0	0
FEMALES(13+ YRS)	2.98	1.3156	100	87	75	64	56	46	39	34	28	24	21	9	4	2	0	0	0
MALES(13+ YRS)	3.10	1.2159	100	88	76	64	53	44	39	30	25	21	17	7	4	2	0	0	0

TABLE 7 CONSUMPTION OF FISH-UNSPECIFIED

POPULATION SUBGROUP:	% POPULATION AS CONSUMERS	MEAN CONSUMPTION G/KG	ESTIMATED % OF POPULATION OF CONSUMERS WITH CONSUMPTION EXCEEDING X, FOR X= 0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20 G/KG
U.S. POP.--48 STATES	0.02	1.6519	100	100	96	96	69	60	60	56	46	40	28	12	5	0	0	0	0
INFANTS(<1 YEAR)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHILDREN(1-6 YRS)	0.00	0.0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FEMALES(13+ YRS)	0.02	1.9775	100	100	100	100	79	79	79	79	79	64	43	18	0	0	0	0	0
MALES(13+ YRS)	0.03	0.9956	100	100	92	92	54	35	35	26	7	7	0	0	0	0	0	0	0

to the "average" person. It is not possible to predict from that survey the population distribution for frequency of consumption and range in annual consumption.

ESTIMATION OF LOCAL CONSUMPTION

Since the estimates of fish consumption just discussed are national averages, they are not predictive of all subgroups and regions on a scale fine enough to address local situations of potential concern. If local fish consumption information is not available, the Fish Contamination Subcommittee of the Risk Assessment Council suggests that other estimates of extreme consumption can be made by assuming that fish consumption by some subgroups would be equal to the average consumption of red meat (130 g/day) and, as a "reasonable" worst case, that some people would consume fish at levels equal to the combined TAS average consumption of red meat, poultry, and fish/shellfish (180 g/day) (Table 8). Conceivably, these values could be exceeded locally, especially when economically disadvantaged people rely on fishing to survive. Adding on an additional equivalent for egg consumption would bring the average estimate up to 215 g/day, and this might not be unreasonable for special situations. The above values are based on consumption by an average 60-kg individual.

Based on 114 g (0.25 pound) for a single serving of fish/shellfish, an average annual consumption of 18 g/day (e.g., see Data Source Nos. 12 and 13 of Table 1) corresponds to approximately 1 meal per week of fish or shellfish. Using the TAS estimate of 180 g/day for total meat protein consumption (consisting of red meat, poultry, and fish/shellfish), and an estimate of 114 g for an average single serving, the total average meat consumption corresponds to about 11 meals per week.

Table 8

Fish Consumption - TAS

	g/day/kg body weight	g/day[1]	meals/year[1]	(assuming a meal size of approximately 4 ounces or 114 grams)
1. EPA TAS Average Per capita Fish/shellfish	0.25	15	48	
2. EPA TAS Average Per capita Red meat	2.2	130	420	
3. EPA TAS Average Per capita Red Meat + Poultry + Fish	3.0	180	580	

1 Based on TAS values for average consumption presented in g/day/kg body weight and adjusted to g/day for a 60 kg individual.

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APPENDIX G

EPA OFFICE OF RESEARCH AND DEVELOPMENT, ENVIRONMENTAL RESEARCH LABORATORIES

EPA OFFICE OF RESEARCH AND DEVELOPMENT, ENVIRONMENTAL RESEARCH LABORATORIES

Region 1	Environmental Research Laboratory/ORD South Ferry Road Narragansett, RI 02882 FTS: 8-838-5087 DDD:(401) 789-1071	
Region 4	Environmental Research Lab/ORD Laboratory/ORD Sabine Island Gulf Breeze, FL 32561 FTS: 8-686-9011 DDD:(904) 932-5311	Environmental Research Laboratory/ORD College Station Road Athens, GA 30613 FTS: 8-250-3134 DDD:(404) 546-3134
Region 5	Environmental Research Lab/ORD Laboratory/ORD 6201 Congdon Boulevard Duluth, MN 55804 FTS: 8-780-5550 DDD:(218) 720-5550	Center for Environmental Research Information/ORD 26 West St. Clair Street Cincinnati, OH 45268 FTS: 8-684-7391 DDD:(513) 569-7391
	Environmental Ecological and Support Laboratory/ORD 26 W. St. Clair Street Cincinnati, OH 45268 FTS: 8-684-7301 DDD:(513) 569-7301	
Region 6	Robert S. Kerr Environmental Research Laboratory/ORD P.O. Box 1198 Ada, OK 74820 FTS: 8-743-2011 DDD:(405) 332-8800	
Region 10	Environmental Research Laboratory--Corvallis/ORD 200 S.W. 35th Street Corvallis, OR 97333 FTS: 8-420-4601 DDD:(503) 757-4601	Pacific Division - Environmental Research Lab/ORD Hatfield Marine Science Marine Science Drive FTS: 8-867-4040 DDD:(503) 867-4040

APPENDIX H

EPA REGIONAL NETWORK FOR RISK ASSESSMENT AND RISK MANAGEMENT ISSUES

EPA REGIONAL NETWORK FOR
RISK ASSESSMENT/RISK MANAGEMENT ISSUES

Region	Senior Contact	Staff	Other Memberships
I	Paul Keough Deputy Regional Admin. J.F. Kennedy Federal Bldg. Room 2203 Boston, MA 02203 (FTS) 835-3402 E-Mail EPA9102	Tom D'Avanzo, Chair Toxics Coord. Comm. (FTS) 835-3222 E-Mail EPA9136	Barbara Beck[1] Toxicologist Air Management Div. Harley Laing[5] Director Planning & Mgmt. Div.
II	Alice Jenik, Acting Chief Policy & Program Integration Branch 26 Federal Plaza New York, NY 10278 (FTS) 264-4296 E-Mail EPA9243	Maria Pavlova Office of Emergency & Remedial Response (FTS) 264-1918 E-Mail EPA9231	Bill Muzynski[2] Deputy Regional Administrator
III	Greene Jones, Director Environmental Services Div. 841 Chestnut Bldg. Philadelphia, PA 19107 (FTS) 597-4532 E-Mail EPA9380	Roy Smith Environmental Scientist Environmental Serv. Div. (FTS) 597-9857 E-Mail EPA9381	Stan Laskowski[3] Deputy Regional Administrator Steve Wassersug[2] Director, Hazardous Waste Management
IV	Lee DeHihns[3,4] Deputy Reg. Admin. 345 Courtland St., N.E. Atlanta, GA 30365 (FTS) 257-4727 E-Mail EPA9400	Susan Deihl Risk Assessment Coord. Office of the Regional Administrator (FTS) 256-3776 E-Mail EPA9400	
V	Bill Sanders, Director Environmental Services Div. 230 South Dearborn St. Chicago, IL 60604 (FTS) 353-3808 E-Mail EPA9580	David Dolan (5S-PTSB-7) Environmental Scientist Pesticides & Toxic Substances Branch (FTS) 886-5518 E-Mail EPA9575 Milt Clark (5HT) Chairman, Health Effects Forum Pesticides & Toxic Substances Branch (FTS) 886-3388 E-Mail EPA9575	

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VII	William W. Rice Deputy Region. Admin. 726 Minnesota Avenue Kansas City, KS 66101 (FTS) 757-2800 E-Mail EPA9703	Bob Fenemore Air & Toxics Div. (FTS) 757-2835 E-Mail EPA9761	Art Spratlin[5] Director Air & Toxics Div.
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[1]Risk Assessment Forum
[2]Risk Assessment Council
[3]Risk Management Council
[4]Agency for Toxic Substances Disease Registry
[5]Comparative Risk Task Force

Reference: U.S. EPA 1987b.

APPENDIX I

COMPILATION OF LEGAL LIMITS FOR CHEMICAL CONTAMINANTS IN FISH AND FISHERY PRODUCTS

TABLE I-1. COMPILATION OF LEGAL LIMITS FOR HAZARDOUS METALS IN FISH AND FISHERY PRODUCTS

Country	Metals (ppm)								
	As	Cd	Cr	Cu	Hg	Pb	Sb	Se	Zn
Australia[a]	1.0,1.5[b]	0.2-5.5		10-70	0.5,1.0	1.5-5.5	1.5	1.0,2.0	40-1,000
Brazil					0.5[c]				
Canada	3.5				0.5	0.5			
Chile	0.12,1.0	0.5		10		2.0		0.05,0.3	100
Denmark					0.5				
Ecuador	1.0			10	1.0	5.0			
Finland	5.0				1.0	2.0			
France					0.5,0.7				
Germany		0.5			1.0	0.5			
Greece					0.7				
Hong Kong	1.4-10	2.0	1.0		0.5	6.0	1.0		
India	1.0			10	0.5[c]	5.0			50
Israel					0.5				
Italy					0.7[c]	2.0			
Japan					0.3,0.4[c]				
Korea					0.5				
Netherlands		0.05-1.0			1.0[c]	0.5,2.0			
New Zealand	1.0	1.0		30	0.5[c]	2.0	1.0	2.0	40
Philippines	3.0				0.5	0.5			
Poland	4.0			10-30		1.0-2.0			30-50
Spain					0.5				
Sweden					1.0[c]	1.0-2.0			
Switzerland		0.1			0.5	1.0			
Thailand	2.0			20	0.5	1.0			
United Kingdom	1.0			20		2.0-10			50
United States					1.0[c]				
U.S.S.R.					0.2-1.0				
Venezuela	0.1	0,0.1		10	0.1-0.5	2.0			
Zambia	3.5-5.0			100	0.2-0.3	0.5-10			100
Range									
Minimum	0.1	0	1.0	10	0.1	0.5	1.0	0.05	30
Maximum	10	5.5	1.0	100	1.0	10	1.5	2.0	1,000

[a] Limit varies among states.

[b] Inorganic.

[c] Total.

References: Nauen (1983); U.S. Food and Drug Administration (1982, 1984).

TABLE I-2. COMPILATION OF LEGAL LIMITS FOR ORGANIC PRIORITY POLLUTANTS AND PESTICIDES IN FISH AND FISHERY PRODUCTS (ppm)

	Hexachloro-benzene	PCBs	TCDD	Aldrin/ Dieldrin	Chlordane	DDT	DDE	DDD	DDTs	Endrin	Heptachlor/ Heptachlor-epoxide	Kepone	HCH (Lindane)	Malathion	Mirex	Parathion	Toxaphene	Vinyl Chloride
Canada		2.0	20[a]	0.1[b]	0.1[b]	5.0	5.0	5.0	5.0	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	0.1[b]	
Denmark						2.0-5.0												
Germany[c]	0.5			0.5-1.0	0.01				2.0-5.0	0.01	0.01		2.0		0.01			
Iceland													0.5					
Netherlands		5.0																
Sweden	0.2	2.0-5.0		0.1					5.0				0.2					0.01
Switzerland		1.0																
Thailand				0.1,0.3		5.0				0.3	0.3		0.5	0.6		0.2		
United States		2.0		0.3	0.3	5.0	5.0	5.0	5.0	0.3	0.3	0.3-0.4			0.1		5.0	
Range																		
Minimum	0.2	1.0	20[a]	0.1	0.01	2.0	5.0	5.0	2.0	0.01	0.01	0.1	0.1	0.1	0.01	0.1	0.1	0.01
Maximum	0.5	5.0	20[a]	1.0	0.3	5.0	5.0	5.0	5.0	0.3	0.3	0.4	2.0	0.6	0.1	0.2	5.0	0.01

[a] ppt (parts per trillion).

[b] Legal limit exists for agricultural chemicals in general.

[c] Legal limits exist for other organic chemicals that are not priority pollutants (see references).

Reference: Hawon (1983); U.S. Food and Drug Administration (1982, 1984).