M E M O R A N D U M

TO: Participants in the EPA Case Study on Risk and Decision Making

RE: Purpose of the Case Study and Your Role

An analysis of risk is becoming an increasingly important component of regulatory decision making within EPA. Even so, the specific ways in which the concept of risk can be used in a particular situation are not well defined. The result can be confusion and ultimately frustration among those who must carry out or are affected by the regulations.

The concept of risk, however, need not be overwhelming and can provide guidance in thinking about an environmental problem. The purpose of this workshop is to help individuals in the EPA Regions understand the basis of risk assessment, develop a common base of knowledge and terminology, use the concept in formulating a site-specific decision, and help refine skills in communicating those decisions. The workshop is not intended, however, as a step-by-step "how to" on risk assessment. Rather, we are trying to explain the concepts of risk assessment, risk management, and risk communication in the context of a case study. There are many uncertainties and issues, and often no clear "right" answers. As you proceed through the case, you will be asked to consider those issues. Some of the issues you normally would not confront in your day-to-day activities, and some of the terms may be new. But, regardless of your background, we hope you will address those issues and develop your own conclusions. By helping you understand the issues, we hope to make you more informed consumers of information on risks and increase your understanding of both the potential and the limitations of the concepts. In addition, we hope to encourage discussion of the unique circumstances involved in developing risk assessments for the site-specific, localized problems that confront individuals in the EPA regional offices.

The workshop case study will focus on a hypothetical site-specific problem that EPA regional staff might encounter in their day-to-day work. You will have to decide what actions should be taken at the site.

BACKGROUND ON THE CASE

The Company

Electrobotics was formed 15 years ago as a privately held company. Its two owners have lived in the community for many years. Electrobotics manufactures electronic components for the computer industry. In the past few years, the bulk of the company's sales has been in parts for personal computers, particularly the popular Bananachrome® personal computer.

Electrobotics has had a rocky history and has been close to bankruptcy several times. However, with the recent growth in demand for personal computers, its performance has improved. Last year Electrobotics had revenues of $7.5 million, compared with $1.5 million five years ago. Even so, the company was only marginally profitable, with after-tax profits of less than $50,000.

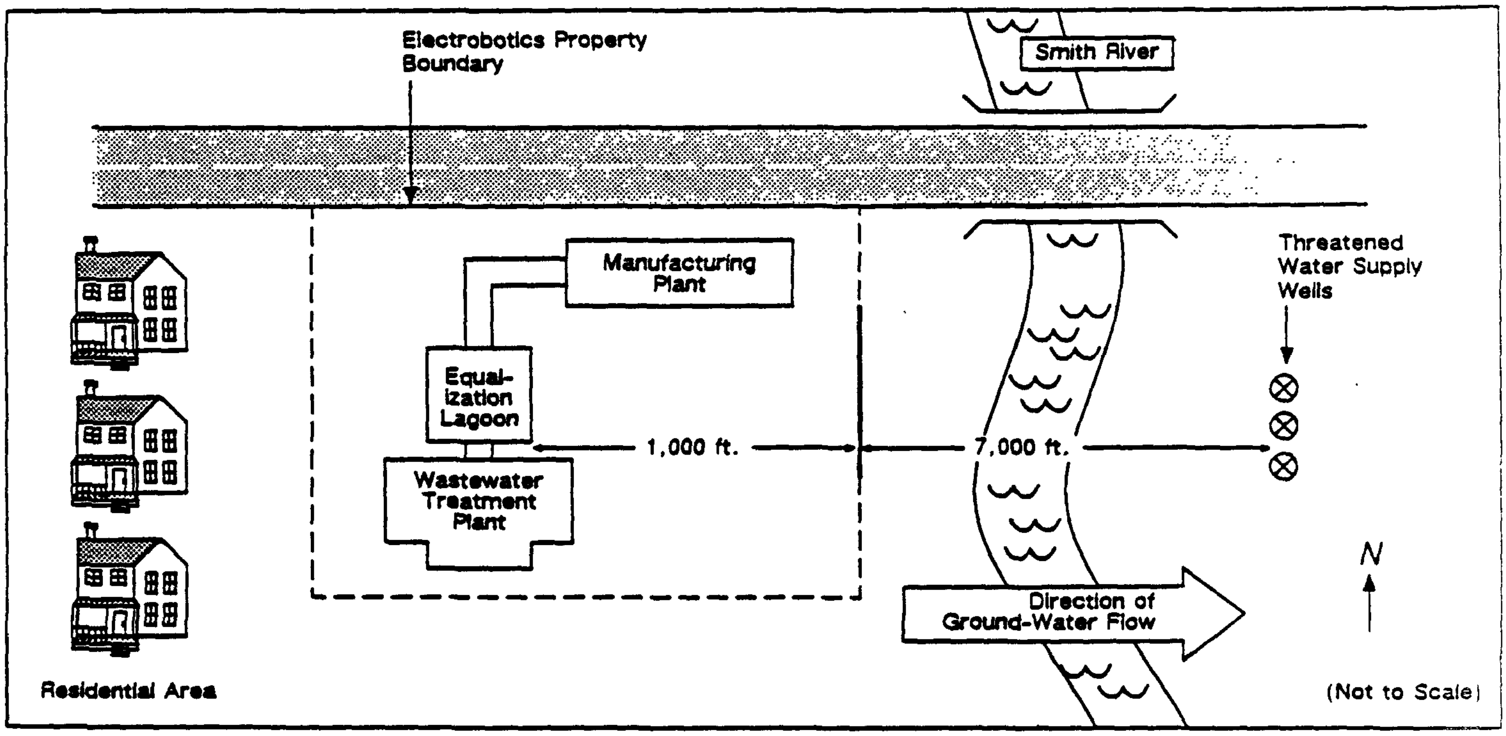
Electrobotics employs about 150 people and has a reputation for treating its employees well. It has never laid off an employee, even during difficult periods.

Location

Electrobotics is situated in a sparsely populated region. A residential development was recently built near the facility's western boundary, and approximately 80 people live in 20 homes there. In addition, the town of Utopia lies a little more than 1 mile east of the facility. The area between the facility and the town has few homes, none closer than three quarters of a mile to the plant's eastern boundary. There has been some discussion about building housing on the property, but no definite plans exist at this time. Utopia relies on ground water for its public water system and has 40 wells in a nearby well field. The well field supplies approximately 50,000 residents, including those in the development west of Electrobotics. The ground water from the Electrobotics site flows toward the public well field. Initial indications are that any ground-water contamination from the Electrobotics site would affect only three of the public wells. (Figure 1 provides a schematic of the Electrobotics site and the surrounding area.)

Figure 1

Site Plan



Nature of the Problem

About five years ago, Electrobotics changed its production process as it introduced a new product. The process required the use of an industrial solvent--dinitrochickenwire (DNC). Wastewater containing the spent solvent is stored in a flow equalization lagoon that is part of the Electrobotics wastewater treatment plant (see Figure 1). After treatment, the wastewater is discharged to the Smith River. Electrobotics' treatment plant uses an activated sludge process.

EPA has classified the solvent as a hazardous waste. Studies on the carcinogenic risks from DNC were only recently presented and will be discussed in more detail as you assess the risks at the site.

STATUTORY AND REGULATORY ISSUES

The hazardous waste regulations developed under RCRA require that owners and operators of hazardous waste facilities, like Electrobotics' storage lagoon, utilize design features and control measures to prevent the leaking of hazardous waste into ground water. Furthermore, all regulated units (a regulated unit, such as the storage lagoon, is a facility that received hazardous waste after July 26, 1982) are subject to monitoring and corrective action requirements if a ground-water problem is identified. The ground-water protection standards require the Regional Administrator to establish in the facility permit, for each hazardous constituent entering the ground water from a regulated unit, a concentration limit beyond which degradation of ground-water quality is not allowed. The concentration limits determine when corrective action is required.

Three possible concentration limits can be used to establish the ground-water protection standards:

- Background levels of the hazardous constituents
- Maximum concentration limits (MCLs) established by regulation
- Alternate concentration limits (ACLs)

Background levels and MCLs are established in the facility permit unless the facility owner or operator applies for an ACL. The background level of DNC is zero, and no MCL exists for the solvent.

In October 1985, the owners of Electrobotics submitted to EPA, as required under the RCRA regulations, a Part B application for an RCRA permit. This application provides the Regional Administrator with information necessary to evaluate the safety of the site. It generally includes:

- A description of the facility
- Chemical and physical analyses of the hazardous waste to be handled
- Information from a hydrogeological investigation of the site
- The potential for the public to be exposed to hazardous wastes or hazardous constituents through releases related to the unit, including identification of the

potential pathways of human exposure and the magnitude and nature of the human exposure resulting from such releases

In addition, Electrobotics' owners have been conducting ground-water monitoring as required under the regulations.

The wastewater treatment system has been permitted under EPA's National Pollution Discharge Elimination System (NPDES). The discharge permit issued by EPA sets forth effluent quality standards, which Electrobotics must meet if it is to discharge the plant's wastewater to the Smith River. Under the requirements of the NPDES permit, conventional pollutants and indicator parameters are monitored at the plant's outfall on a daily, weekly, or monthly basis. These parameters include the following:

- Biochemical oxygen demand
- Chemical oxygen demand
- Total organic carbon
- Total suspended solids
- Ammonia
- Temperature
- pH

These monitoring requirements serve to ensure the proper functioning of the wastewater treatment system.

DNC is not included among the pollutants monitored in accordance with Electrobotics' NPDES permit. However, included in Electrobotics' Part B application is information on samples taken from the plant's outfall to the Smith River and tested for DNC.

The results presented in the Part B application and from other sources indicate that DNC was found in the ground water below the lagoon. The initial monitoring wells were located at the immediate edge of the lagoon, referred to as the "point of compliance." Additional monitoring wells have been installed to characterize the plume, and results indicate that it has moved to the eastern edge of the facility boundary. In addition, DNC was found in the air around the plant. No DNC was found in the wastewater treatment plant effluent.

YOUR ROLE

You, as the EPA representative responsible for the Electrobotics site, will evaluate the available information on the risks posed by DNC and decide whether to issue a permit and what, if any, corrective actions should be taken at the facility.

Part I

During Part I, you wish to determine whether and to what extent the DNC found at the Electrobotics plant endangers the public health. Thus, you have decided to conduct a risk assessment. Your staff has prepared a document summarizing much of the information you will need for assessing the risks. This document, attached as Part I, reviews the potential risks from DNC.

The first section, which contains toxicological data on the solvent, constitutes the hazard evaluation.

The second section of Part I contains a summary of data on the exposure of various population groups to DNC. Several issues arise concerning the interpretation and use of this information, and it will be necessary for you to formulate appropriate conclusions.

The relationship between exposure to DNC and the risk of adverse health effects is determined by a dose-response evaluation. In the third section of Part I, you must review possible approaches to defining this relationship for the solvent. There may be several plausible options for describing this relationship in the region of human exposure. Normally, you would not examine the hazard evaluation data and the dose-response information; these results would be provided by EPA headquarters. However, in this instance you have asked your staff to provide the material for your review because you feel it is important to your understanding of the problem.

In the final section of Part I, you must present your conclusions regarding the human health risks posed by DNC from the Electrobotics facility, and the uncertainties in your knowledge. You must characterize the risks.

Part I will be completed during the first day of the workshop.

Part II

Once you have assessed the risks from DNC, you must decide what actions should be required by Electrobotics' owners. You must manage the risks. Part II of the case is currently being prepared by your staff. It will be given to you at the end of the first day of the workshop, when you have completed your assessment of the risks, and will be discussed the next morning. The new document will contain information on the options for cleaning up the storage lagoon and ground water at the Electrobotics site. In particular, you will have an approach proposed by the owners of Electrobotics and alternatives identified by your staff.

For each of the options, you will be presented with information describing the approach, predicting the effect of the option on the risks identified in Part I, and estimating the costs.

At each of the steps in Part I and Part II, issues and data will be presented and alternative conclusions listed. After discussion, you may select the conclusion that seems most appropriate; if none seems appropriate you should offer your own.

Your review and evaluation will take place within a working group of 10 to 12 people. After you discuss the issues with the other members, your group should attempt to reach a consensus on what action should be taken about Electrobotics' permit application. If you cannot reach a consensus, present the alternative views. You should note, however, that you must ultimately decide what cleanup actions will be required of Electrobotics' owners.

Part I

ASSESSING THE RISKS FROM DNC

CONTENTS

I. BACKGROUND ON THE CHEMICAL DETECTED AT THE ELECTROBOTICS SITE

<u>Dinitrochickenwire (DNC)</u>

- Solvent used to degrease fabricated metal parts
- Impurities: commercial product contains trace amounts of trinitrochickenwire
- Physical state: liquid, moderate volatility
- Stability: degrades slowly in aqueous environments
- Solubility: moderately soluble in water

II. HAZARD EVALUATION

Normally, you would not review information on the hazards of specific chemicals; the results would probably be provided to you by EPA toxicologists. But by working through the material in this section, you will develop an understanding of the nature and quality of information used by the toxicologists. You will not become toxicologists, but we hope you will become more informed users of the information they provide.

SOME PRINCIPLES FOR HAZARD EVALUATION

1. The purpose of hazard evaluation is to identify the types of adverse health effects that may be associated with exposure to DNC, and to characterize the quality and strength of evidence supporting this identification.

2. The specific hazard of concern in this review is cancer, although systemic toxic effects will also be discussed.

3. Epidemiological studies in exposed human populations are generally considered the best source of information for hazard identification. Unfortunately, they are not available for most substances. Moreover, establishing firm causal links between exposure and chronic human disease (such as cancer) is very difficult.

4. Studies with experimental animals also provide useful information for hazard identification. Such studies can be controlled, and thus can more easily establish causality. Results from such studies suffer from the obvious limitation that experimental animals are not the species of ultimate interest.

5. With one possible exception (arsenic), all known human carcinogens are also carcinogenic in one or more species of experimental animals. Most animal carcinogens have not been established as human carcinogens.

6. Biological data support the proposition that responses in experimental animals should be mimicked in humans. For some agents, however, species differences in response can be substantial.

7. The specific sites of tumor formation in humans may differ from those observed in experimental animals.

8. Data obtained by administering a substance by the same route of exposure experienced by humans are considered more predictive than data obtained by a different route. If tumors form at internal body sites, however, the route of exposure may not be important.

9. In general, a varied response in experimental animals--tumor formation or systemic effects in several species and both sexes, at different exposure levels with increasing response at increasing exposure, and at multiple body sites--provides more convincing evidence of potential human carcinogenicity or systemic damage than does a response limited to a single species or sex, or to body sites at which tumors or systemic effects commonly occur in untreated animals (e.g., liver tumors in untreated male mice).

BACKGROUND ON DNC TOXICITY

The toxic properties of DNC were first investigated in the 1940s and 1950s. In most of these tests, small groups of experimental animals were exposed to very high amounts of DNC to identify the exposure conditions that would cause death. Animals received either a single exposure, or exposures covering only a fraction of their lifetime.

During the 1950s and 1960s, more extensive animal toxicity tests were conducted, although none involved DNC exposures lasting more than about one-sixth of a lifetime. These tests revealed the range of doses that produced toxicity (the principal site of toxic action was the liver) and the exposure level below which no form of toxicity was identified.

Information available in 1970 showed that the most highly exposed humans received a daily DNC intake several hundred times lower than the "no-observed toxic effect" intake identified in the animal tests. Because the liver toxicity produced by DNC was of a type likely to occur only after a minimum threshold exposure was exceeded, it was concluded that the most highly exposed humans were protected from DNC toxicity by a wide safety margin. This is discussed in more detail later.

At least until 1980, no data had been published on the effects of DNC on exposed humans.

The Frankenstein Study

In late 1985, an article titled "Chronic Toxicity of Dinitrochickenwire in Rats and Mice" appeared in a respected scientific journal (Frankenstein, V., J. Environ. Tox.). The Frankenstein paper presented data on the effects of lifetime exposure to DNC in two species of rodents. These data revealed a form of toxicity--carcinogenicity--that had not been seen before. The design of the Frankenstein experiment and the major findings are presented in Tables 1 and 2.

Remarks on the Frankenstein Study

1. As far as can be determined from the published article, the Frankenstein study was carefully conducted, and there is no reason to doubt the accuracy of the reported data.

2. DNC increased the incidence of tumors (percentage or proportion of animals with tumors) in certain groups of animals. Not all animals in a group receiving DNC developed tumors. Tumor incidence is a measure of the risk (probability) of tumor development. Data in Table 2 can be interpreted as in the following example: the lifetime risk of stomach cancer in male rats exposed by gavage to the high dose of DNC daily, for their full lifetimes, is 0.40.

3. Rats developed spleen and liver tumors after both inhalation and gavage exposures. Lung tumors were produced only by inhalation, and stomach tumors only by gavage. Females of both species showed fewer tumors than males, and mice showed fewer tumors than rats.

4. The stomach tumors appeared at the point where DNC contacted the stomach when introduced by stomach tube. This point is in the rodent forestomach, an anatomical feature not present in humans.

5. Severe irritation was observed in the areas of the rodents' stomachs that were exposed to high doses of DNC delivered by stomach tube. No signs of irritation were observed in low-dose control animals. Dr. Frankenstein believes that the stomach tumors arose as a result of the severe toxic insult caused by the direct stomach exposure.

Table 1

DESIGN OF THE FRANKENSTEIN STUDY

Species and Route of Exposure	Groups Receiving DNC	Number of Animals: Male	Number of Animals: Female	Amount of DNC Received Each Day[1]	Duration of Exposure (weeks)[2]
Rat, inhalation	Control	60	60	0	104
	Low dose	60	60	30	104
	High dose	60	60	60	104
Rat, gavage[3]	Control	60	60	0	104
	Low dose	60	60	50	104
	High dose	60	60	100	104
Mouse, gavage[3]	Control	60	60	0	78
	Low dose	60	60	60	78
	High dose	60	60	120	78

[1]Milligrams of DNC per kilogram of the animal's body weight. The concentration of DNC in the air in the inhalation experiment has been converted to a unit of weight so it can be compared with the units in the gavage study.
[2]Approximate lifespans of the animals under laboratory conditions.
[3]Gavage is administration of a substance by means of a stomach tube.

Table 2

SIGNIFICANT FINDINGS FROM THE FRANKENSTEIN STUDY

Following are the only groups in which a statistically significant excess of tumors was found. Nearly 40 possible sites of tumor formation were examined in each sex of both species.

Study Group	Sex	Tumors Found	Percentage of Animals with Tumors (incidence rate): Control	Low Dose	High Dose
Rat, inhalation	Male	Lung	3	5	25[a]
Rat, inhalation	Male	Spleen	0	2	18[a]
Rat, inhalation	Male	Liver	3	7	12[a]
Rat, gavage	Male	Stomach	0	0	40[a]
Rat, gavage	Female	Stomach	0	0	30[a]
Rat, gavage	Male	Liver	3	7	15[a]
Rat, gavage	Male	Spleen	0	10[a]	33[a]
Mouse, gavage	Male	Liver	5	30[a]	50[a]
Mouse, gavage	Male	Stomach	0	0	10[a]

[a]A statistically significant excess of tumors relative to untreated control animals. This means it is unlikely that the difference in tumor incidence between the treated and control animals is due to chance. Because the only difference between the control and treated animals was the presence of DNC, it is likely that the excess tumor incidence is due to this compound. Tumors were found at other sites in both control and treated animals, but no other tumors occurred in statistically significant excess.

Issues to Be Considered on the Carcinogenicity of DNC

1. How do these data conform (or not conform) to the principles laid out on pages II-2 and II-3--particularly the last principle?

2. In view of these principles, is there any reason to conclude that DNC is not carcinogenic in rats of both sexes (by gavage exposures) and in male mice (by inhalation and gavage)?

3. Should the stomach tumors be considered relevant to low-exposure risks to humans?

4. Should the data obtained by gavage treatment be considered relevant to human exposure?

5. Is there any reason to believe that humans would not be at risk of developing the various tumors, assuming exposure to DNC?

6. Is there any way to determine, from the data given, whether responses in humans are likely to be similar to those of rats or mice? Males or females?

7. Do the data provide sufficient evidence to prove DNC is carcinogenic in animals? Are the data too limited or even inadequate?

Epidemiological Data

After the Frankenstein report was published, three DNC manufacturers decided to submit reports to EPA on their investigations into employee health. The information from these three reports is summarized below.

Manufacturer A

Manufacturer A had been producing DNC for 45 years, but none of the 161 employees in the mortality study had been exposed for more than 20 years; most were exposed for 10 to 15 years. Although employee exposure data were not extensive, they suggested that past exposures were relatively high, sometimes approaching the inhalation levels that produced an excess of tumors in animals. (Although the concentrations of air in the workplace approached those used in the animal experiment, the workers were exposed to these high levels for only a fraction of their lifetime.)

By January 1979, 35 of the 161 workers had died. No statistically significant increase in cancers (malignant neoplasms) of any type was noted among these workers (3 cases observed, 3.8 expected in a population of the same size, sex, and age). Cancers of the digestive system were elevated (2 cases observed, 0.7 expected), but this elevation was not statistically significant (i.e., it is not possible to say the observed difference was not due simply to chance). The workers were also exposed to several other chemicals, at least two of which are known animal carcinogens.

Manufacturers B and C

Reports from Manufacturers B and C are similar to the report of Manufacturer A. No cases of malignant neoplasms of the stomach were reported by either manufacturer. Both manufacturers reported slight elevations in lung cancer, but neither elevation was statistically significant. No data on worker smoking habits were available. Manufacturer C reported 33 deaths among 290 employees.

<u>Issue to Be Considered</u>

1. Should the information from the DNC manufacturers alter earlier conclusions about the inferences to be drawn from the animal data? If so, how? If not, why not?

2. Are the epidemiological data sufficient evidence to prove DNC is carcinogenic in humans? Are the data too limited or inadequate?

EPA's Risk Assessment Guidelines

The Office of Health and Environmental Assessment (OHEA) within EPA's Office of Research and Development has developed guidelines for carcinogen risk assessment. These guidelines discuss weighing the evidence that a substance is a carcinogen and classifying the chemical into one of five groups:

Group A--Human carcinogen
Group B--Probable human carcinogen
Group C--Possible human carcinogen
Group D--Not classified as to human carcinogenicity
Group E--Evidence of noncarcinogenicity for humans

OHEA developed an illustrative categorization of substances based on animal and human data, as shown in Table 3.

Table 3

ILLUSTRATIVE CATEGORIZATION OF EVIDENCE BASED ON ANIMAL AND HUMAN DATA

	Animal Evidence				
Human Evidence	Sufficient	Limited	Inadequate	No Data	No Evidence
Sufficient	A	A	A	A	A
Limited	B1	B1	B1	B1	B1
Inadequate	B2	C	D	D	D
No data	B2	C	D	D	E
No evidence	B2	C	D	D	E

You should note that the "No Data" category means no data are available indicating a substance is or is not carcinogenic. "No Evidence" means, for humans, no association was found between exposure and increased risk of cancer in well-conducted, well-designed analytical epidemiologic studies. When reviewing animal data "No Evidence" means no increased incidence of neoplasms was found in at least two well-designed and well-conducted animal studies of adequate power and dose in different species.

Some Possible Conclusions
About DNC Carcinogenicity

1. DNC is a human carcinogen (Group A). There is sufficient evidence from epidemiological studies to support a causal association between DNC exposure and cancer.

2. DNC is a probable human carcinogen (Group B2). There is sufficient animal evidence of carcinogenicity as demonstrated in the increased incidence of tumors at several sites in multiple species (rats and mice), in multiple experiments involving different routes of administration (inhalation, gavage), and at different dose levels. There is inadequate evidence of carcinogenicity from epidemiological studies.

3. DNC is a possible human carcinogen (Group C). There is limited animal evidence of carcinogenicity because the data obtained when DNC was administered by stomach tube may not be relevant to any route of human exposure. Thus, DNC resulted in increased tumors in only one species (rat) and in one experiment involving only the inhalation route of exposure. There is inadequate evidence of carcinogenicity from epidemiological studies.

4. DNC is not classifiable as to human carcinogenicity (Group D). Because of the extreme conditions under which tumors were produced in the animal experiments, there is no reason to believe that DNC is a possible human carcinogen. There is inadequate evidence of carcinogenicity from epidemiological studies.

5. Other (formulate your own conclusion).

SYSTEMIC TOXICITY OF DNC

Depending on the dose, exposure to a given chemical, such as DNC, may result in a variety of toxic effects of which cancer is only one. These may range from gross effects, such as death, to more subtle biochemical, physiological, or pathological changes. Chemicals that give rise to toxic endpoints other than cancer (and gene mutations) are often referred to as "systemic toxicants" because they affect the function of various organ systems. It should be noted that cancer-causing chemicals commonly also evoke other toxic effects (systemic toxicity).

So far, we have only discussed the carcinogenic properties of DNC. But as part of the hazard identification stage of a risk assessment, the risk assessor considers each of the toxic endpoints from all studies evaluated in assessing the risk posed by a chemical.

A chemical such as DNC may elicit more than one toxic effect, even in one test animal, in tests of the same or different duration (acute, subchronic, and chronic exposure studies). In general, the dose at which no adverse effect is demonstrated will differ from one effect to another. For example, the highest dose at which statistically significant increases in kidney damage are no longer observed may differ from the highest dose at which statistically significant increases in liver damage are no longer observed.

Primary attention usually is given to the effect exhibiting the lowest "no observed adverse effect level" (NOAEL), often referred to as the critical effect. In simplest terms, an experimental exposure level is selected from the critical study that represents the level at which "no adverse effect" was demonstrated. In our example above, if the highest NOAEL associated with kidney damage is greater than the highest NOAEL associated with liver damage, then liver damage is the critical endpoint for examining systemic toxic effects of DNC. This approach is based on the assumption that if the critical toxic effect is prevented, then all toxic effects are prevented.

The Shakespeare Study

Only one chronic study of oral exposure to DNC was located in the available literature. That study, conducted by Dr. Shakespeare et al. in 1978, presented data on the effects of exposure to DNC in rats. The design of the Shakespeare study and the major findings are presented in the following quote from the abstract:

"A total of 80 rats (40 males/40 females) were exposed to either 0 mg/kg/day, 2 mg/kg/day, 10 mg/kg/day, or 20 mg/kg/day of DNC for two years. The method of exposure was gavage (in water). At the 20 mg/kg/day level of exposure, a statistically significant reduction in the rate of body weight gain and weight changes in the kidney and liver were observed in both male and female rats. Pigmentation of the liver and a statistically significant reduction in the rate of body weight gain were observed in female rats exposed to at least 10 mg/kg/day of DNC. The 2 mg/kg/day level of exposure was reported as a chronic 'no observed adverse effect level.'"[1]

Remarks on the Shakespeare Study

1. As far as can be determined from the published article, the Shakespeare study was carefully conducted, and there is no reason to doubt the accuracy of the reported data.

2. The Shakespeare study has been identified by your lab as the critical study, with liver pathology as the critical effect or systemic toxic endpoint. That is, the primary target organ for the systemic effects of DNC is the liver.

3. DNC increased the incidence of liver and kidney changes in certain groups of animals. Not all animals in a group receiving DNC suffered from changes in liver or kidney weight.

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[1]Shakespeare, et al., "Chronic Systemic Toxicity of Dinitrochickenwire in Rats," Journal of Environmental Toxicology (1978).

Issues to Be Considered on the Systemic Toxicity of DNC

1. How do these data conform (or not conform) to the principles laid out on pages II-1 and II-2--particularly the last principle?

2. In view of these principles, is there any reason to conclude that DNC is not a systemic toxicant in rats of both sexes?

3. Should the data obtained by gavage treatment be considered relevant to human exposure?

4. Is there any reason to believe that humans would not be at risk of developing liver and kidney damage if exposed to DNC?

5. Is there any way to determine, from the data given, whether responses in humans are likely to be similar to those of rats?

Some Possible Conclusions About the Systemic Toxicity of DNC

1. DNC is a systemic toxicant to humans. There is clear evidence from animal studies to support a conclusion that DNC exposure will cause kidney and liver damage in humans.

2. It is highly likely DNC is a systemic toxicant to humans. There is sufficient evidence of toxicity as shown in the kidney and liver pathology found in rats exposed to DNC at relatively low doses.

3. DNC is a potential human systemic toxicant. We have reviewed a very limited amount of animal evidence showing that DNC is a systemic toxicant to rats resulting in liver and kidney damage.

4. DNC is not classifiable as to human systemic toxicity. The animal evidence is insufficient to make a decision at this time.

5. Other (formulate your own conclusion)

III. HUMAN EXPOSURE EVALUATION

SOME PRINCIPLES FOR EXPOSURE EVALUATION

1. The purpose of exposure evaluation is to identify the magnitude of human exposure to DNC, the frequency and duration of that exposure, and the routes by which humans are exposed. It may also be useful to identify the number of exposed people along with other characteristics of the exposed population (e.g., age, sex).

2. Exposure may be based on measurement of the amount of DNC in various media (air, water) and knowledge of the amount of human intake of these media per unit of time (usually per day) under different conditions of activity.

3. Some individuals may be exposed by contact with several media. It is important to consider total intake from all media in such situations.

4. Because only a limited number of samples of various media can be taken for measurement, the representativeness of measured values of environmental contaminants is always uncertain. If sampling is adequately planned, the degree to which data for a given medium are representative of that medium can usually be known.

5. Sometimes air and water concentrations of pollutants can be estimated by mathematical models. Although some of these models are known to be predictive in many cases, they are not thought to be reliable in all cases.

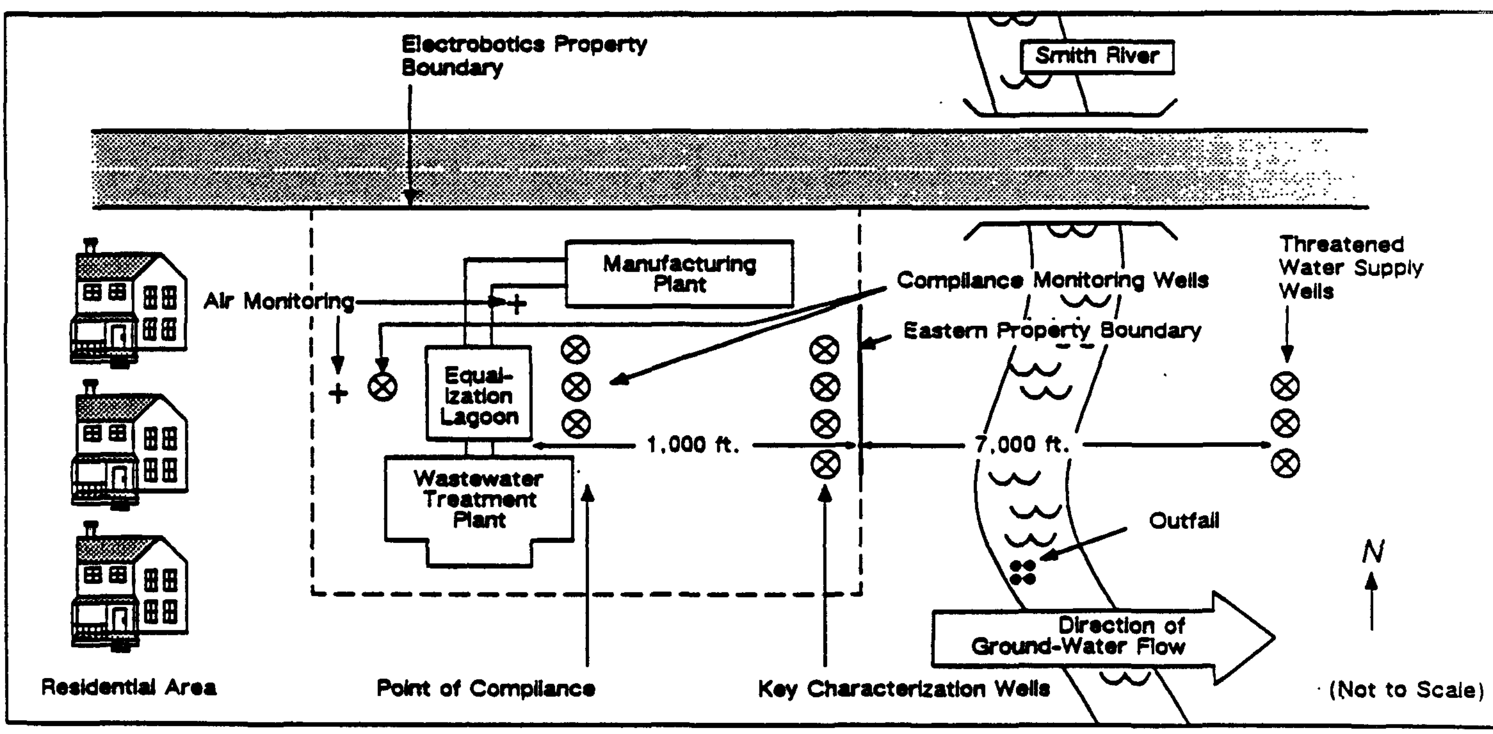
6. Standard average values and ranges for human intake of various media are available and are generally used, unless data on specific agents indicate that such values are inappropriate.

SITE DESCRIPTION

As discussed earlier, the Electrobotics Company, which manufactures parts for Bananachrome® personal computers, operates a production facility. The facility employs 150 workers and includes a wastewater treatment plant and equalization lagoon (surface impoundment). (The site plan is illustrated in Figure 2.) Wastewater from the manufacturing plant operations contains high concentrations of DNC and is periodically discharged to a flow equalization lagoon, which is located within 200 feet of the western facility boundary. There are no other potential sources of DNC releases in the surrounding area. Adjacent to this boundary is a residential area of 20 houses in which 80 individuals reside. Electrobotics has built an 8-foot-high chain-link fence on the property boundary separating the residents from the facility grounds. The area between the Electrobotics facility and the threatened water supply wells to the east is undeveloped and contains few residences. There has been some discussion about building housing on the property, but no definite plans exist at this time. The Smith river is located east of the facility about 1,500 feet from the facility boundary. There are no drinking water intakes along the river, but some recreational fishing and swimming occurs.

Figure 2

Site Plan and Points of Compliance and Exposure



The equalization lagoon maintains a regular flow to an on-site activated sludge wastewater treatment facility. The equalization lagoon is maintained at an average fluid depth of 10 feet and measures 10,000 square feet. The wastewater from the treatment plant is discharged to the river in compliance with the facility's NPDES permit.

The equalization lagoon is underlaid by a compacted natural clay liner with a hydraulic conductivity (a measure of the rate at which it transmits water) of 3×10^{-8} cm/sec, which is designed to provide substantial containment of the wastewater. The uppermost geological formation beneath the site is composed of approximately 75 feet of stratified glacial outwash, which consists of layered sand and gravel with some silt. These unconsolidated sediments form a productive aquifer that is a source of potable water to the surrounding area. A well field is located approximately 1.5 miles to the east (downgradient) of the site and provides approximately 3 million gallons per day (mgd) of potable water to its 50,000 customers. The well field contains 40 separate wells, each pumping 75,000 gallons per day (gpd).

The hydraulic conductivity of the aquifer has been estimated at 40 feet per day, based on field tests in the area. However, there may be thin continuous layers of significantly lower or higher hydraulic conductivity within the glacial outwash. The water table is located about 10 feet below the bottom of the lagoon at the site. The hydraulic gradient (a measure of the slope of the water table), based on the best available potentiometric head measurements, is estimated at 0.005 feet/feet toward the community well field.

The site is located in a humid area. The wind direction is seasonal; however, according to a wind rose from a local meteorological station (which describes wind direction and frequency), the wind blows west across the site toward the 20 homes adjacent to the lagoon approximately 30 percent of the time.

The owners of Electrobotics conducted analysis of the lagoon in preparing their Part B application. The nature of the materials stored in the lagoon and the meteorological and hydrogeological conditions in the vicinity have resulted in some concern by EPA about possible exposure of workers at the facility and residents in the vicinity to DNC via inhalation of air, as well as possible exposure of the community via contamination of drinking water supplies. In an attempt to respond to the regulations and concerns of EPA staff, the owners undertook a program of air, surface-water, and ground-water monitoring.

Measurements of concentrations of DNC on the site are described in the next section. A ground-water monitoring program has been undertaken to comply with regulations promulgated under the Resource Conservation and Recovery Act (RCRA). Electrobotics is monitoring contaminants in ground water at the downgradient limit of the waste management unit, termed the "point of compliance." The point of compliance in this case is at the eastern limit of the berm around the lagoon. Three monitoring wells have been installed at this point, and one well was installed upgradient (see Figure 2). This conforms to the regulatory minimum. No DNC was found in the sample from the upgradient well. The nearest downgradient property boundary is to the east, about 1,000 feet from the lagoon.

Because DNC has been detected at the downgradient compliance-monitoring wells, a ground-water assessment has been initiated, and additional monitoring wells have been constructed at the eastern property boundary to monitor chemical concentrations. Further downgradient, the public well field represents a point of potential human exposure. Three of the 40 wells are located directly downgradient of the lagoon. The relative locations of the point of compliance, eastern regulatory boundary, and actual point of exposure are shown in Figure 2.

AVAILABLE INFORMATION ON DNC CONCENTRATIONS

Measurements of DNC concentrations in air along the western site boundary, outdoors at the facility adjacent to the lagoon, and indoors within the treatment plant have been made during a single air-sampling program. The sampling program was conducted for a period of one week, during which 24-hour average concentrations were measured at the western property boundary, adjacent to the equalization lagoon and within the treatment plant. During the period of measurement, wind was blowing generally west across the lagoon toward the residential area. The mean, standard deviation, and range of measured chemical concentrations in air are shown in Table 4. Air measurements that were made concurrently inside the wastewater treatment plant did not detect measurable concentrations of the solvent. Within the treatment plant, all treatment units are closed and vapor-controlled to limit any fugitive air emissions.

Electrobotics' NPDES permit requires monitoring only for conventional pollutants and indicator parameters, so the effluent from the treatment plant is not monitored for DNC before it is discharged to the Smith river. In preparing its Part B application, however, the owners of Electrobotics collected a limited number of samples from the treatment facility outfall. The results are presented in Table 4, and indicate that no DNC was detected.

Table 4

FIELD MEASUREMENTS OF DNC CONCENTRATIONS

Medium	Location	Detection Level	DNC Mean	DNC Standard Deviation	DNC Range
Air	Inside treatment plant	[$\mu g/m^3$]	ND[1]	-	-
Air	At western boundary of site	[$\mu g/m^3$]	44	16	8-68
Air	On-site	[$\mu g/m^3$]	188	80	120-480
Ground water	Point of compliance	[$\mu g/l$]	332	30	290-350
Ground water	Eastern property boundary	[$\mu g/l$]	BDL[2]		
Ground water	Public well field	[$\mu g/l$]	ND[1]	-	-
Surface water	Treatment plant outfall	[$\mu g/l$]	ND[1]	-	-

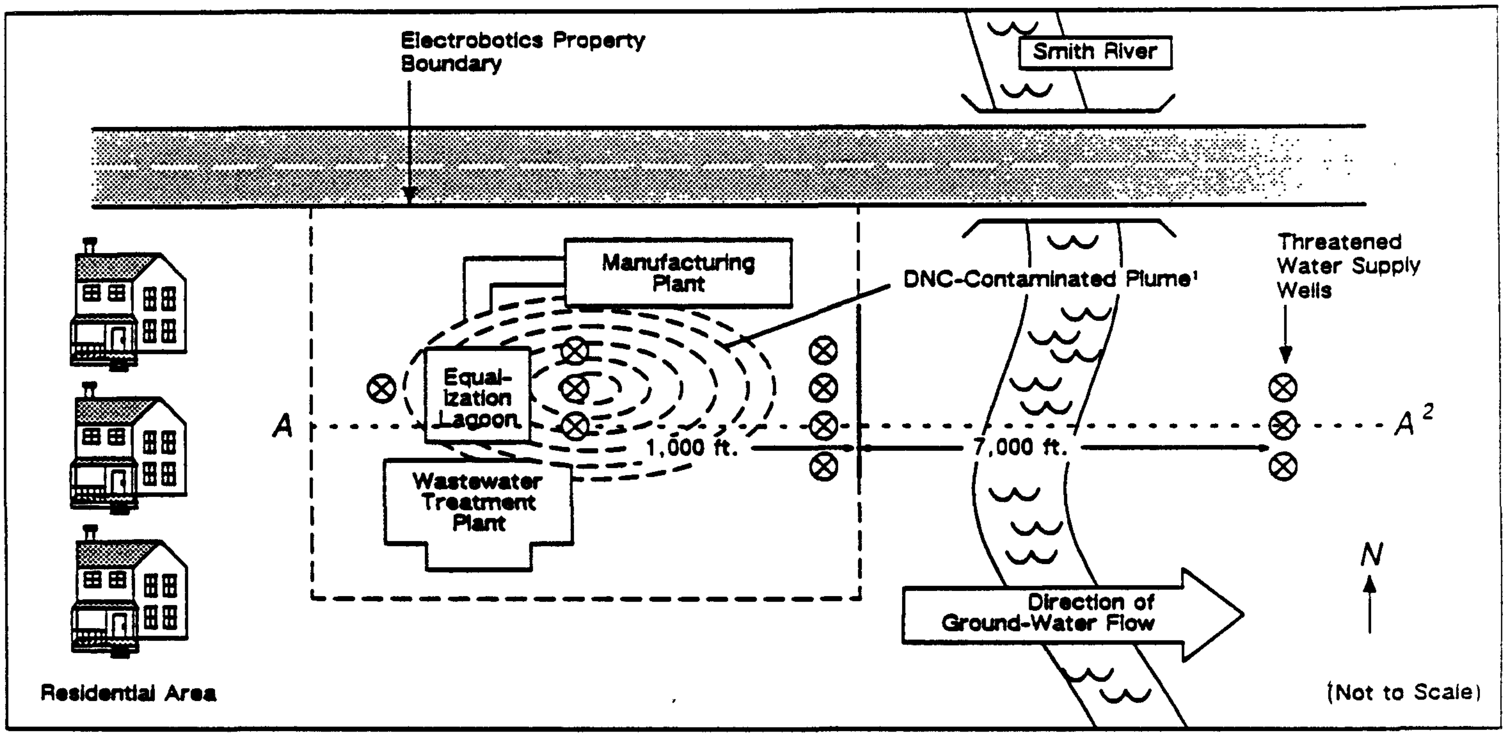
[1]Not detected at 1 $\mu g/m^3$ for air or 1 $\mu g/l$ for water.
[2]Trace concentrations below detection limit of 1 $\mu g/l$.

The ground water has been periodically sampled and tested for DNC both at the point of compliance, the monitoring wells on the eastern boundary, and at the water treatment plant at the community water system, which draws water from the aquifer for the municipal supply. Samples were taken at several depths as well. The concentrations of chemicals in monitoring wells at the point of compliance are indicated in Table 4. The concentrations detected at the compliance point indicate contamination of the aquifer. Trace concentrations of DNC have also been detected at the eastern boundary in the most recent water tests, but at concentrations less than the method-detection limit of 1 $\mu g/l$ (or ppb). The municipal water supply has been tested, and no detectable concentrations of DNC were found. However, the detection limit for DNC offered by available analytical methods for ground water is 1 $\mu g/l$.

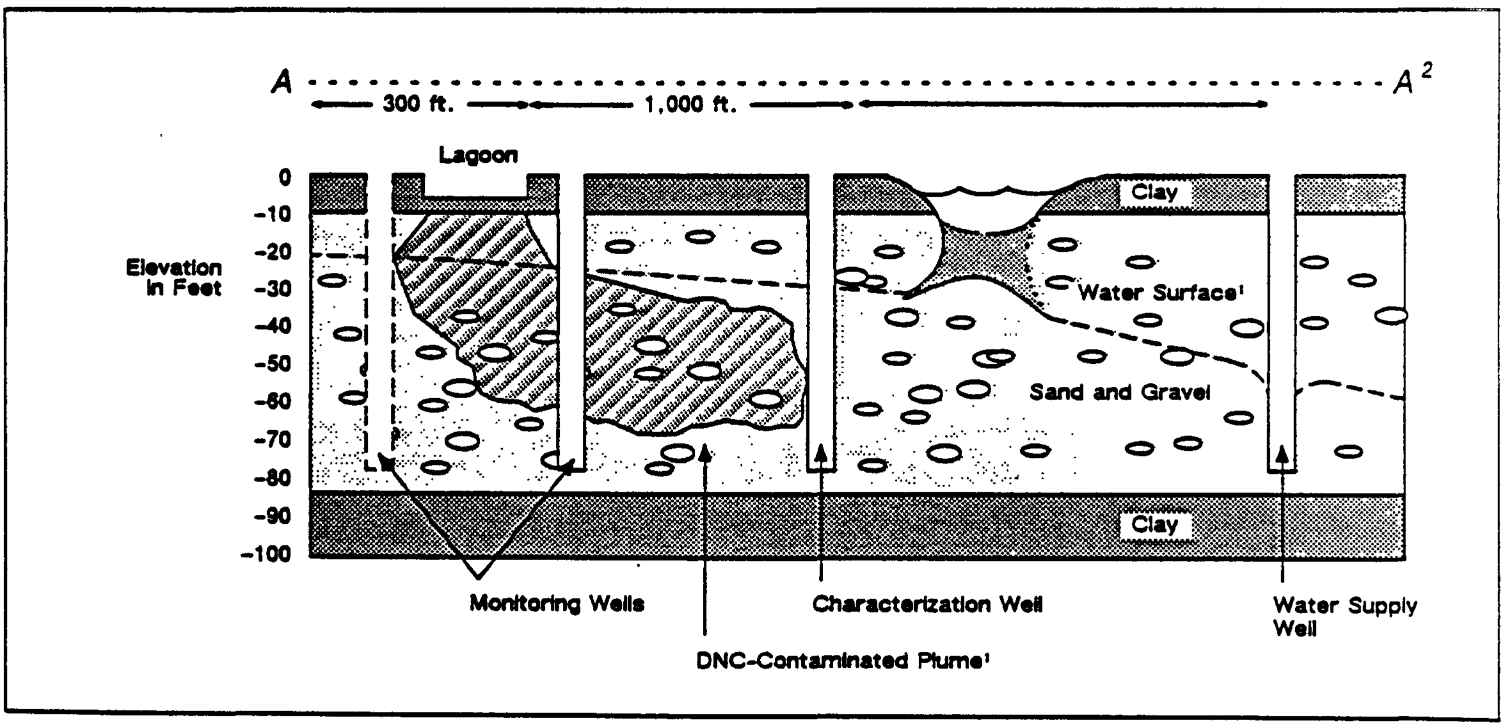
A very simple description of the area's geology and the current status of the DNC-contaminated ground-water plume are presented in Figure 3. Available information suggests that the chemical plume has not yet migrated beyond the eastern property boundary, but without corrective action the concentrations are expected to increase in time in this vicinity, eventually affecting offsite ground water.

Figure 3

Site Plan



Geological Cross Section



[1] The outermost contour line is believed to be the edge of the edge of the DNC-contaminated plume, where the concentration is below the detection limit of 1 ppb.

[2] The water surface has a constant slope of 0.005 feet/feet. The apparent change in slope is an effect of the different horizontal scales.

A mathematical model of the contaminant plume movement in the aquifer has been constructed to estimate future concentrations in the aquifer. A summary of the modeled environmental concentrations in ground water is presented in Table 5. Appendix A contains the calculations and the associated assumptions that were applied in modeling these environmental concentrations.

Table 5

SUMMARY OF MODELED CONCENTRATIONS OF DNC STEADY STATE IN GROUND WATER[1]

Location	DNC (μg/l)
Eastern property boundary	275
Public well-field	5.5

[1]Estimated time for DNC to travel from the lagoon to the property boundary is 1,000 days (about 3 years). The estimated travel time from the lagoon to the public well-field is 8,000 days (about 22 years).

CALCULATIONS OF HUMAN EXPOSURE

The environmental concentrations summarized in Tables 4 and 5 are the starting point for the calculation of estimates of human exposure to DNC.

The medium in which a substance is present will determine the potential route of human exposure. For example, substances present in water may be ingested. Contaminated water may also lead to inhalation exposure when water is used for cooking or showering, although this exposure route is likely to be minor unless the contaminant is present at high concentrations in the water and is highly volatile. Exposure by inhalation of contaminated water or by the dermal route during bathing or showering was considered insignificant in this case because of the low concentrations of these substances in the municipal water supply and the fact that DNC is only moderately volatile. Doses resulting from these exposure routes were therefore not calculated. Substances present in air will be inhaled. Finally, substances present in soil may be ingested, absorbed through the skin, inhaled, or taken up by plants with human exposure resulting if these plants are used as food or if these plants are fed to livestock, the various products of which are used as food.

Human exposure to contaminated soil, however, was considered insignificant at this site because soils potentially contaminated by ground water are located at least 10 feet below the land surface. No concentrations of DNC were found in a limited set of soil samples taken from surface soils around the lagoon. Consequently, doses resulting from potential human exposure to soil were not calculated.

In order to estimate human exposure, or dose of the constituent from each contaminated medium, certain data and assumptions were applied. These data and assumptions relate to the extent and frequency of human contact with these media and the degree of absorption of chemicals for each route of exposure. When the constituent is ingested, a certain fraction will be absorbed through the gastrointestinal wall; when it is inhaled, a certain fraction will be absorbed from the lungs.

The method of dose calculation depends on the route of exposure. Certain standard values have been developed to estimate contact with and intake of certain media. For drinking water, the EPA and other scientific groups generally assume that adults drink 2 liters of water per day. It is also generally assumed that the average adult inhales from 20 to 23 cubic meters (m^3) of air per day. We have assumed an adult inhales 23 m^3/day, although EPA risk assessments are increasingly using 20 m^3/day. It should be noted, however, that the data and assumptions required for estimation of dose from most other routes of exposure are not as readily standardized.

The assumptions and calculations required to estimate DNC dose to the 80 neighboring residents resulting from inhalation of DNC-contaminated air are presented below to illustrate the elements of dose estimation. A complete set of calculations and associated assumptions for the critical pathways is shown in Appendix B.

<u>Inhalation of DNC-Contaminated Air by Neighboring Residents</u>

Assumptions:

- An adult inhales 23 m^3/day of air.
- Based on wind direction analysis, the duration of exposure is 30 percent of the time on an annual average basis.
- The body weight of an adult is 70 kg.
- The inhalation absorption factor for DNC is 0.75.
- The adult lives in the home throughout his lifetime.

Calculations:

$$\frac{0.044 \text{ mg}}{m^3} \text{ (average DNC air concentration at boundary)}$$

$$\times \frac{23 \text{ m}^3}{\text{day}} \times \frac{1}{70 \text{ kg}} \times 0.3 \text{ (percentage of time exposed)}$$

$$\times 0.75 \text{ (inhalation absorption factor)}$$

$$= 3.3 \times 10^{-3} \text{ mg/kg/day}$$

Table 6 presents a summary of all the exposure calculations performed to estimate doses from the contaminated media to the identified exposed population groups.

Table 6

SUMMARY OF RESULTS OF EXPOSURE CALCULATIONS

Medium	DNC (mg/kg/day)	Number of Persons Exposed
Air, neighboring residents[1]	3.3×10^{-3}	80
Air, workers on site (outdoors)[1]	4.7×10^{-3}	150
Ground water, point of compliance[2]	9.5×10^{-3}	0
Ground water, eastern property boundary[3]	7.8×10^{-3}	0
Ground water, public well-field[3]	1.6×10^{-4}	50,000

[1]Estimated exposures from DNC in the air are based on current concentrations in the air.

[2]Estimated exposures at the point of compliance are based on current concentrations of DNC at that point, although no individual is currently exposed to those concentrations.

[3]Estimated exposures at the eastern property boundary will not occur for three years, and no one currently receives their drinking water from that point. Exposure estimates for the public well-field will not occur for about 22 years.

ECOSYSTEM EXPOSURES

The ecosystem in the Smith river has been examined by a biologist employed by the Electrobotics plant. The resulting study characterizes the area upstream and downstream from the facility. No major evidence of ecological damage was found, *although there was some discoloration of the river around the* outfall noted when the plant switched to the use of DNC. This discoloration has persisted.

No threatened or endangered species were found near the Electrobitcs site. However, several threatened or endangered species have been known to inhabit river ecosystems in the vicinity. Fish species include the Snail Darter, Slackwater Darter, Amber Darter, and Spotfin Chub. Terrestrial species include the Eastern Indigo Snake. Furthermore, several of these species are acutely sensitive to compounds similar in structure to DNC. The data available on DNC are not adequate for establishing ambient water quality criteria for aquatic life.

As noted earlier, the effluent discharged to the Smith river from the Electrobotics treatment plant was tested for DNC. No DNC was detected at a detection limit of 1 μg/l.

Remarks on Exposure Data

1. Ground water directly beneath and adjacent to the regulated unit has been routinely sampled and analyzed for the presence of DNC. Concentrations that have been measured have remained relatively constant for the past two years and indicate that DNC has leaked from the storage lagoon into the underlying aquifer. Ground water moves toward a well field that provides drinking water for a community of 50,000 people. DNC has not been detected in the water supply but may be present at concentrations below the current method detection limit, which is 1 μg/l (ppb).

2. DNC is unstable in the environment and will decompose by biodegradation in shallow aquifer systems. The decomposition of the chemical in aquifers has been demonstrated in aquifer restoration programs at other sites, but the rates of decomposition are variable and have only been quantified in laboratory experiments. The rate of decomposition at concentrations less than 10 ppb is uncertain.

3. Trace concentrations (less than 1 μg/l) of DNC have been detected at the eastern facility boundary. A mathematical model has been used to predict future concentrations of DNC in ground water downgradient of the regulated unit. The model prediction indicates that the chemical will migrate in ground water and degrade at a slow rate. On the basis of the model prediction, concentrations are expected to increase at the eastern property boundary if no corrective action is taken. The degradation products are not believed to be carcinogenic.

4. Estimates of future concentrations of DNC in drinking water are based on analytical predictions from a ground-water model. Appropriate adjustments regarding ground-water dilution were made to estimate concentrations at the tap.

5. Estimates of current exposure in air were based on analytical results obtained from measuring the air concentrations in the facility and at the boundary over a single seven-day period in April 1986. Twenty-four-hour composite samples were taken each day over the sampling period. No other air data are available.

6. Estimates of current concentrations of DNC in treatment plant effluent are based on analytical results from samples taken over the same seven-day period in April 1986. Five samples were taken during this period.

Issues to Be Considered

1. Has Electrobotics adequately characterized the ground-water contamination? If not, what additional types of information would you require them to provide and why?

2. The summary exposure data presented in Table 6 include some current exposure estimates and some future exposure estimates. Models are used to predict concentrations of DNC at some point in the future, assuming that releases of the substance from the lagoon occur at the current rate. Should the two types of exposure data (current and future) be treated the same for purposes of characterizing human risk? How should distinctions be reported?

3. Should the ground-water concentration estimates that are based in part on modeling of a degradation process be used at all? How should this be decided? If modeled concentrations are not used, how should the analyses of chemicals that are reported as "below detection limit" or "not detected" in the water supply system be represented in exposure estimates?

4. Are the estimates of DNC in surface water acceptable? What additional information would you want?

5. Is the mean concentration in the various media the appropriate summary statistic to use to characterize human exposure? Should the upper range or statistical upper confidence limit be used as an alternative?

6. Are the various assumptions about human intake and average exposure to various media valid? Should others be substituted or added?

7. Should other routes of exposure to the various contaminated media have been considered?

8. Should the total exposure and risk for the regulated unit be represented by the sum of all incremental risks for each chemical/pathway?

Issues to Be Considered (continued)

9. Was it appropriate to model the exposure based on an adult population? Should other populations-at-risk have been considered?

10. Should exposure and risk to workers at the facility be considered in the same context as residents in the surrounding community?

11. Do you believe DNC is affecting the ecosystem around the Smith River?

Some Possible Conclusions About Human Exposure to DNC

Which of the following conclusions best characterizes the information you have seen?

1. None of the exposure estimates is adequate for use in risk assessment. Given the currently available data, the risk assessment should describe exposure in qualitative terms only. No quantitative risk assessment should be developed until better information is available.

2. The exposure estimates presented in Table 6 for drinking water and air are reliable and can be used for risk assessment. However, no risks should be assessed until more detailed data are obtained from other pathways of exposure, such as showering or ingestion of contaminated soils.

3. The exposure estimates presented in Table 6 and based on field measurements are reliable and can be used for assessing risks. The exposure estimates based on modeling, however, are too uncertain to be used to assess the risks.

4. Although the exposure estimates in Table 6 are based on different data and assumptions, they are all adequate and sufficient for assessing risks. The risk manager should be made aware of the uncertainties in each of the data sets, but a quantitative risk assessment should be developed.

5. In addition to Conclusion 2, it should be noted that all the exposures from various media should be added for those people exposed to all sources of DNC.

6. Other (formulate your own).

IV. DOSE-RESPONSE EVALUATION

Normally, you would not be involved in reviewing dose-response information; the results generally would be provided to you. As discussed before, however, we hope that by having you evaluate this information and address the key issues here, you will be able to better use the dose-response information you will receive.

We have given you the EPA approach to evaluating dose-response relationships. In addition, we have identified alternative approaches so that you develop an understanding of how others may perceive the issue.

DOSE-RESPONSE EVALUATION FOR CARCINOGENICITY: THE GENERAL PROBLEM AND PRINCIPLES GUIDING APPROACHES TO ITS SOLUTION

Because of the relative complexity of dose-response evaluation, the following discussion is substituted for a statement of key principles.

Animal data showing that DNC is carcinogenic were obtained in the high-exposure region of the dose-response curve. Thus, animal exposures were in the 30-to-300-unit range (see Table 1), and these produced measurable risks in the range of 10 to 50 percent (see Table 2). Predictions of human exposure, as discussed in Section III, are at much lower levels. What can be said about risks in the range of human exposure?

At least three general approaches to this problem have been proposed by various experts.

Approach 1

Based on general theories of how carcinogens act to produce cancer (largely derived from experimental studies and epidemiological data), all finite exposure levels will produce a finite risk. The magnitude of the risk will decline as the magnitude of exposure declines (clear even in the animal data).[1]

If the quantitative relationship between exposure and risk were known for all exposures, the risks to rodents exposed at very low levels could be predicted from the measured exposure-risk data. The risks to humans could be predicted at these very low levels if the relationship between rodent and human susceptibilities were known. Although these relationships cannot be known with accuracy, a plausible upper limit on human risk can be predicted with sufficient accuracy to be used as a guide to making risk decisions. Actual human risk is not likely to exceed the upper limit, and it may be less. This is the approach generally adopted by EPA in evaluating the risk associated with low-level exposure to carcinogens.

[1]These two sentences are the proper formulation of the "no-threshold" concept. It does not mean that all finite exposures will cause cancer; rather, it means that all finite exposures will increase the probability (risk) that cancer will occur.

Approach 2

The quantitative relationships between high-exposure and low-exposure risks in rodents and between rodent and human risk are not known with sufficient reliability to be used in risk assessment. Moreover, there is no reliable theory on which one can conclude with assurance that low-level human exposure (i.e., exposure below the range producing detectable risks) poses any risk at all. As with other toxic effects, carcinogenicity will not be initiated within an individual until a minimum threshold of exposure is exceeded. In such circumstances, the only reasonable course is to report the magnitude of the margin-of-exposure (MOE) by which humans are protected. MOE is the maximum amount of exposure producing no measurable tumorigenic response in animals divided by the actual amount of human exposure. MOE gives the risk manager adequate information on which to decide whether exposures must be reduced or eliminated to provide human protection. A relatively large MOE is desirable because it is likely that the threshold for the entire human population is lower than that observed in small groups of experimental animals. This approach is generally applied when evaluating the potential risk of most noncarcinogenic effects.

Approach 3

Although there is adequate theory and some evidence to permit the conclusion that humans are at finite risk at all finite exposure levels, there is insufficient knowledge to allow prediction of the risks in quantitative terms. The risk assessor should simply attempt to describe risks qualitatively, perhaps coupling this description with some information on the potency of the compound and the magnitude of human exposure. This type of presentation is adequate for the risk manager, who should not be concerned with the quantitative magnitude of risk in any case.

* * * * *

Each of these views, and perhaps others as well, has some merit. The first approach is now used by most federal public health and regulatory agencies, including EPA. These agencies emphasize that the predicted numerical risks are not known to be accurate, but because of the nature of the models used to predict them, they are likely to be upper-bound estimates of human risk. An upper-bound estimate is one that is not likely to be lower than the true risk and is likely to exceed the true risk (which could be zero).

For this exercise, we will estimate low-exposure risks using the model currently used by EPA. A model is a mathematical formula that describes the relationships between various measures. Two models are needed to predict low-exposure risks:

- A high to low exposure extrapolation model is needed to predict low-exposure risks to rodents from the measured high-exposure, high-risk data (see Table 2). EPA currently uses a "linearized multistage model" for this purpose. This model is based on general (not chemical-specific), widely held theories on the biological processes underlying carcinogenesis. Application of the model to the rodent exposure risk data produces an estimate of the lifetime risk for each unit of exposure in the low-exposure region. This is called the unit cancer risk. The linearized model is used to ensure that the unit cancer risk is an upper-bound estimate of risk.

- An interspecies extrapolation model is used to extrapolate from rodent unit risks to human unit risks. EPA assumes that rodents and humans are at equal risk at the same exposure measured in milligrams of carcinogen per square meter of body surface area per day. Interspecies extrapolation models are commonly called "scaling factors" because they are used to scale doses between species.

EPA's selection of these models is based on the agency's view that they are the best supported for purposes of deriving an upper-bound estimate of risk. Alternative models are available for both these forms of extrapolation, and several are equally plausible. In most cases, but not always, use of plausible alternative models will yield lower estimates of risk than those predicted by the two described here. Differences can sometimes be very large, but are generally relatively small when the models are limited to those that are linear at low exposures.

Further discussions of various models and their plausibility can be found in the handout "Principles of Risk Assessment: A Nontechnical Review."

APPROACH TAKEN FOR THIS EXERCISE

In this exercise we determine the upper-bound estimate of unit cancer risks predicted for DNC using the models currently preferred by EPA. The effect of using alternative, plausible models is also described, as are the animal data that pertain to the second or third approaches described above for dose-response evaluation (i.e., the MOE or qualitative approaches).

Estimates of Upper-Bound,
Lifetime Slope Factors
Using Current EPA Models

Application of the EPA models for high-to-low-dose and interspecies extrapolation to the measured animal cancer data for DNC (Table 2) yields the results shown in Table 7. The result of such extrapolations is the slope factor. In this exercise, one unit of exposure is equal to one milligram (mg) of the carcinogen per kilogram (kg) body weight of the animal (or human) per day throughout the lifetime of the animal (or human). Thus, if the slope factor for DNC is 0.0897 (8.97×10^{-2}), the risk of developing cancer from 1 mg/kg/day of lifetime exposure to DNC is 8.97×10^{-2} (a probability of about 9 in 100, or 1 in 10).

Table 7

UPPER-BOUND ESTIMATES ON LIFETIME SLOPE FACTORS
PREDICTED BY APPLYING EPA'S PREFERRED MODELS
TO DNC TUMOR DATA

(based on Table 2)

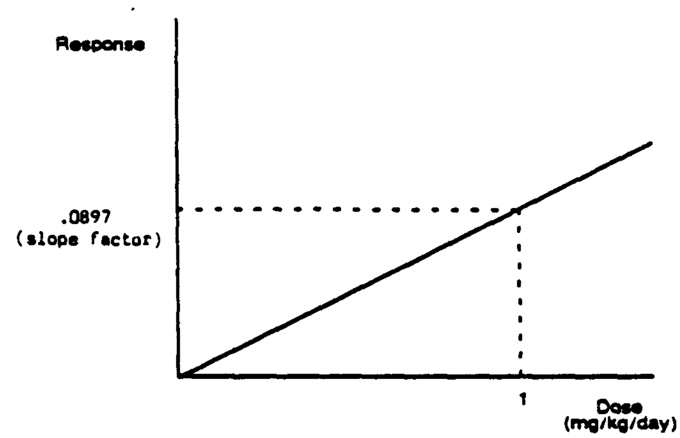
Species, Sex	Route of Exposure	Tumor Site	Slope Factor (potency)
Rat, male	Inhalation	Lung	0.0186 (1.86×10^{-2})
Rat, male	Inhalation	Spleen	0.0126 (1.26×10^{-2})
Rat, male	Inhalation	Liver	0.0168 (1.68×10^{-2})
Rat, male	Gavage	Stomach	0.0054 (5.4×10^{-3})
Rat, female	Gavage	Stomach	0.0054 (5.4×10^{-3})
Rat, male	Gavage	Liver	0.0120 (1.2×10^{-2})
Rat, male	Gavage	Spleen	0.0228 (2.28×10^{-2})
Mouse, male	Gavage	Liver	0.0897 (8.97×10^{-2})
Mouse, male	Gavage	Stomach	0.0096 (9.6×10^{-3})

[1]Risk for an average daily lifetime exposure of one unit. Units are the same as those used earlier for describing the animal exposure (Table 1), such that one unit = one milligram per kilogram body weight per day. Risk is obtained from the slope factor by multiplying the latter by the actual number of units of human exposure. For a given exposure, the higher the slope factor, the higher the risk.

This relationship is presented graphically in Figure 4. The horizontal axis is the dose of DNC measured in mg/kg/day. The vertical axis is the response and is a probability.

Figure 4

Dose-Response Relationship for DNC



To obtain the risk from other levels of exposure, the slope factor is multiplied by the number of units of exposure. The assumption is that at low doses the relationship between dose and response is linear. Thus, if a person were exposed to 0.003 units of DNC throughout his lifetime (0.003 mg/kg/day), the risk would be 0.003 units times 0.0897/unit, or 0.00027 (2.7×10^{-4}), a probability of 2.7 cases arising in 10,000 individuals exposed at this level. The greater the slope of the line the more potent the carcinogen.

Estimates of Lifetime Slope Factors Using Other Models

Application of other models for high-to-low-dose extrapolation yields slope factors equal to or slightly lower than (less than fivefold) those in Table 7, as long as the other models incorporate the concept that risk increases in direct proportion to exposure in the low-exposure region (linear models). Use of the most plausible alternative interspecies extrapolation model (that generally used by FDA) yields slope factors sixfold (for rats) and thirteenfold (for mice) lower than those predicted in Table 7. Thus, alternative models predict slope factors about 30 to 65 times lower than those predicted using the EPA models.

Adoption of certain nonlinear models for high-to-low-dose extrapolation predicts risks about 1,000 to 10,000 times lower than those predicted by use of the EPA model. The nonlinear models are not used by agencies charged with protecting human health, but cannot be rejected on purely scientific grounds.

Carcinogenic Dose-Response Evaluation not Involving Formal Extrapolation

For those who believe formal extrapolation beyond the measurable dose-response data should not be performed, it is important to identify the exposures at which DNC produces tumors and those at which no tumor excess is found (the "no observed adverse effect level" or NOAEL). Table 8 identifies NOAELs from data on DNC in Table 2. This is not the approach generally applied by EPA for carcinogenic substances.

Table 8

CARCINOGENIC NO-OBSERVED ADVERSE EFFECT LEVELS (NOAELs) FOR CHRONIC EXPOSURE TO DNC[1]

(based on Table 2)

Study Group	Sex	Tumor	NOAEL
Rat, inhalation	Male	Lung	30
Rat, inhalation	Male	Spleen	30
Rat, inhalation	Male	Liver	30
Rat, gavage	Male	Stomach	50
Rat, gavage	Female	Stomach	50
Rat, gavage	Male	Liver	50
Rat, gavage	Male	Spleen	None found
Mouse, gavage	Male	Liver	None found
Mouse, gavage	Male	Stomach	60

[1]Units are identical to those in Tables 1 and 2. "None found" means that a measurable excess of tumors was found at both levels of exposure used in the experiment.

Issues to Be Considered

1. If explicit estimates of slope factors are made, should only EPA's currently preferred models be used? Should the results of applying other models also be displayed?

2. Which species/sex/tumor site data from Table 7 should be used for slope factor assessment? All, shown individually as in Table 7? Only the data set yielding the highest slope factor? A sum of all? Other?

3. Should the DNC stomach tumor data set be rejected because there is no exact anatomical counterpart in humans?

4. How should the uncertainties in use of models be described?

5. Are the observed NOAELs true "no-effect" levels? Could they simply reflect the fact that in experiments with relatively small numbers of animals, the failure to observe a statistically significant increase of tumors is an artifact of the experimental design, and not a true absence of biological effect? How should this uncertainty, if it is real, be taken into account?

6. EPA has adopted the first approach, using slope factors, to extrapolate from the high doses used in the animal studies to the low doses at which humans are exposed. How might you respond to someone who argues for one of the other approaches?

Some Possible Conclusions About
Carcinogenic Dose-Response Evaluation

Which of the following conclusions best characterizes the information you have seen?

1. The slope factors listed in Table 7 are true upper-bound estimates. The true slope factor is not likely to exceed those listed, may be lower, and could be zero.

2. The same as the first conclusion, but add: The use of alternative, plausible models yields slope factors about 10 to 100 times lower than those in Table 7.

3. Slope factors should be reported for all plausible models, and the full range of estimates should be reported without bias.

4. There is no justification for calculating and reporting slope factors. What is critical for understanding the public health importance of low-level exposure to DNC is the margin of exposure (MOE). Estimation of the MOE is based on the NOAELs for its carcinogenic effects; these figures are reported in Table 8.

5. Neither slope factors nor NOAELs are reliable indicators of human risk, and neither should be considered for risk assessment. Dose-response relations for the human population are not known for DNC; risk should be described in qualitative terms only.

6. Other (formulate your own conclusion).

DOSE-RESPONSE EVALUATION FOR CHRONIC SYSTEMIC HEALTH EFFECTS: THE GENERAL PROBLEM AND PRINCIPLES GUIDING APPROACHES TO ITS SOLUTION

As discussed earlier, "systemic" effects are toxic effects other than carcinogenicity or mutagenicity, such as liver or kidney damage, induced by a chemical. The EPA's approach to assessing the risks associated with systemic toxicity is different from that for assessing the risks associated with carcinogenicity. This is because different mechanisms of action are thought to be involved in the two cases. In the case of carcinogens, the EPA assumes that a small number of molecular events can evoke changes in a single cell that can lead to uncontrolled cellular proliferation. This is the basis for the no-threshold approach discussed for carcinogenicity in the previous section. The assumption for carcinogens is that there is essentially no level of exposure for such a chemical that does not pose a small, but finite, probability of generating a carcinogenic response. In the case of systemic toxicity, mechanisms must be overcome before the toxic endpoint is manifested. For example, a large number of cells could be performing the same or similar function, and the population must be significantly depleted before the effect is seen.

Generally, based on our understanding of the mechanisms of action, systemic toxicity is treated as if there is an identifiable exposure threshold (both for the individual and for the population), below which effects are not observable. The threshold concept is important in the regulatory context. The individual threshold hypothesis holds that a range of exposures from zero to some finite value can be tolerated by an individual with essentially no chance of expression of the toxic effect.

Reference Doses

To evaluate systemic effects, the EPA has developed the concept of a reference dose (RfD). The RfD is an estimate, with an uncertainty spanning perhaps an order of magnitude or greater, of a daily exposure to the human population (including sensitive subpopulations) that is likely to be without an appreciable risk of deleterious systemic effects during a lifetime.

The RfD is derived from the NOAEL identified during the hazard evaluation stage of the risk assessment. In particular, the NOAEL is reduced by consistent application of uncertainty factors (UFs) that reflect various types of data and a modifying factor (MF) that is based on professional judgment of the entire chemical database. That is:

$$RfD = NOAEL/(UF \times MF)$$

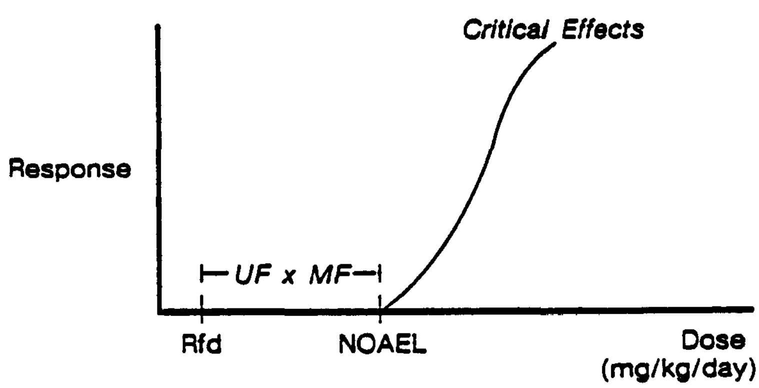
The uncertainty factors account for such considerations as the variation in sensitivity among the members of the human population, the uncertainty in extrapolating animal data to the case of humans, the uncertainty in extrapolating from data obtained in a study that is of less-than-lifetime exposure, and the uncertainty in using data where a NOAEL was not identified. Each level of uncertainty usually adds a factor of ten. Thus, if the RfD for DNC was to be based on the animal study conducted by Dr. Shakespeare, we would have two factors of ten or an uncertainty factor of 10 x 10 = 100. The first factor of ten accounts for sensitivity among the members of the human population, and the second factor of ten is based on the extrapolation from animal data to the case of humans. The Shakespeare study was a chronic study and a NOAEL was identified, hence no other factors apply.

The modifying factor is greater than zero and less than or equal to ten, and reflects qualitative professional judgments about scientific uncertainties not covered under the standard uncertainty factors. These include such considerations as the completeness of the overall database and the number of species and animals tested. The usual modifying factor is one.

The concept of an RfD is presented graphically in Figure 5.

Figure 5

Reference Dose



The RfD is useful as a reference point for gauging the potential effects of various doses. Usually, doses less than the RfD are not likely to be associated with any systemic health risks and are therefore less likely to be of regulatory concern. However, as the frequency of exposure exceeding the RfD increases, and as the size of the excess increases, the probability increases that adverse effects may be observed in a human population. Nonetheless, a clear conclusion cannot be categorically drawn that all doses above the RfD are unacceptable.

An alterantive measure that is sometimes useful is the margin of exposure (MOE) discussed earlier, which is the magnitude by which the NOAEL of the critical toxic effect exceeds the estimated exposure, or:

$$MOE = \frac{\text{NOAEL for Critical Effect}}{\text{Human Dose}}$$

A summary of the reference dose information for DNC is presented in Table 9.

Table 9

REFERENCE DOSE (RfD) FOR ORAL EXPOSURE
SUMMARY TABLE

Critical Effect	Experimental Doses[1]	UF	MF	RfD
Liver and kidney pathology	2 mg/kg/day (NOAEL)	100	1	2×10^{-2} mg/kg/day
Rat oral chronic study	10 mg/kg/day (LOAEL)			
Shakespeare et al. (1978)				

[1]Dose conversion factors and assumptions: none.

Issues to Be Considered
On the Reference Dose for DNC

1. Is the observed NOAEL from the Shakespeare study a true "no-effect" level? Could it simply reflect the fact that in experiments with relatively small numbers of animals, the failure to observe a statistically significant increase of systemic effects is an artifact of the experimental design, and not a true absence of biological effect?

2. Do you think the reference dose approach adequately accounts for the uncertainties associated with NOAELs?

3. Is the information presented in Table 9 an adequate description of the RfD? What, if any, additional information would you like to see?

4. The RfD for DNC is based on oral ingestion of DNC by rats. Is it appropriate to use this RfD when evaluating the potential health risks to residents near the Electrobotics plant who are exposed to DNC through the air?

5. Should systemic health effects from exposure to DNC or carcinogenic effects be of greater concern? Why? Do we have enough information at this time to decide?

6. Are the RfD and unit cancer risks reliable indicators of human risk? Should they be used to conduct quantitative risk assessments, or should risks be described only in qualitative terms?

Some Possible Conclusions About
Systemic Toxicity Evaluation

Which of the following conclusions best characterizes the information you have seen?

1. The RfD listed in Table 9, and the NOAEL from which it is derived, are sufficient to determine the systemic risks associated with exposure to DNC.

2. There is no justification for calculating RfDs. The uncertainty and modifying factors create an artificial sense of precision in an area involving tremendous uncertainty. Risks from systemic toxicants should be described in qualitative terms only.

3. Other (formulate your own conclusion).

V. RISK CHARACTERIZATION

PURPOSE

In the last step of risk assessment, the information collected and analyzed in the first three steps is integrated to characterize the excess risk to humans. In line with the alternative approaches for describing dose-response relationships, at least four approaches to this step can be taken:

1. Provide an explicit numerical estimate of excess lifetime cancer risk for each population group by multiplying the slope factor times the number of units of exposure experienced by each group:

   Excess lifetime risk = (slope factor) x (units of exposure)

   In this equation, excess risk is unitless--it is a probability.

2. Compare the exposure experienced by each group with the RfD.

3. Estimate the margin of exposure (MOE) for each group by dividing the NOAEL from the critical study used to estimate the RfD by the exposure experienced by that group.

4. Describe risks qualitatively for each population group.

Risk characterization would normally include some combination of all four approaches, along with a description of their relative merits.

It is also essential that the statistical and biological uncertainties in estimating the extent of health effects be described in this step.

Tables 10, 11, and 12 present the excess lifetime cancer risks for each population group using data from Tables 6 and 7. These risks are based on the highest slope factor for DNC. If other slope factors from Table 7 had been used, excess cancer risks would be somewhat lower. And if slope factors derived from other dose response models had been used, the excess risks shown in Tables 10, 11, and 12 would be 10 to 100 times lower. The risks in Tables 10, 11, and 12 are thought to be upper-bound lifetime risks.

Tables 10, 11, and 12 also report the RfD and MOE for systemic health effects for each group. The MOE is not an expression of risk, but the ratio of the NOAEL identified in the Shakespeare study to the measured or modeled human exposure.

Table 10

UPPER-BOUND ESTIMATES OF EXCESS LIFETIME HUMAN RISK AND MARGINS OF EXPOSURE FROM EXPOSURE TO DNC BASED ON POTENTIAL CONTAMINATION AT THE PUBLIC WELL-FIELD

	General Population (49,770)	Nearby Residents (80)	Workers (150)
Current excess individual cancer risk from air[1]	-	3×10^{-4}	4×10^{-4}
Potential excess individual cancer risk from water, assuming exposure at the public well-field 22 years hence[1]	1×10^{-5}	1×10^{-5}	1×10^{-5}
Total excess individual cancer risk[2]	1×10^{-5}	3×10^{-4}	4×10^{-4}
Upper-bound estimate of excess cancer cases over a lifetime[3]	0.7	0.02	0.07
Exposure (mg/kg/day)[4]	1.6×10^{-4}	3.5×10^{-3}	4.9×10^{-3}
MOE[5]	12,500	580	410

[1]Excess individual cancer risk obtained by multiplying the highest slope factor from Table 7 (0.0897 for DNC) by the units of exposure from Table 6.
[2]Total excess individual cancer risk obtained by adding excess individual cancer risks from air and water exposures.
[3]Obtained by multiplying total individual excess cancer risk by the estimated number of people exposed.
[4]Exposures for nearby residents and workers are based on current air exposures and estimates of future exposures from drinking water obtained from the public well-field.
[5]MOE for DNC obtained by dividing the NOAEL (2 mg/kg/day) from Table 9 by the appropriate DNC air and water exposures from Table 6. If the MOE is less than 100, the exposure exceeds the RfD. The RfD is 0.002 mg/kg/day.

Table 11

UPPER-BOUND ESTIMATES OF EXCESS LIFETIME HUMAN RISK AND MARGINS OF EXPOSURE FROM EXPOSURE TO DNC BASED ON POTENTIAL CONTAMINATION AT THE EASTERN PROPERTY BOUNDARY

	General Population (49,770)	Nearby Residents (80)	Workers (150)
Current excess individual cancer risk from air[1]	-	3×10^{-4}	4×10^{-4}
Potential excess individual cancer risk from water, assuming all drinking water is obtained at the eastern property boundary[1]	7×10^{-4}	7×10^{-4}	7×10^{-4}
Total excess individual cancer risk[2]	7×10^{-4}	1×10^{-3}	1×10^{-3}
Upper-bound estimate of excess cancer cases over a lifetime[3]	35	0.08	0.2
Exposure (mg/kg/day)[4]	7.8×10^{-3}	1.1×10^{-2}	1.3×10^{-2}
MOE[5]	260	180	160

[1]Excess individual cancer risk obtained by multiplying the highest slope factor from Table 7 (0.0897 for DNC) by the units of exposure from Table 6.
[2]Total excess individual cancer risk obtained by adding excess individual cancer risks from air and water exposures.
[3]Obtained by multiplying total individual excess cancer risk by the estimated number of people exposed.
[4]Exposures for nearby residents and workers are based on current air exposures and estimates of future exposures from drinking water, assuming it is obtained at the eastern property boundary.
[5]MOE for DNC obtained by dividing the NOAEL (2 mg/kg/day) from Table 9 by the appropriate DNC air and water exposures from Table 6. If the MOE is less than 100, the exposure exceeds the RfD.

Table 12

UPPER-BOUND ESTIMATES OF EXCESS LIFETIME HUMAN RISK AND MARGINS OF EXPOSURE FROM EXPOSURE TO DNC BASED ON CONTAMINATION AT THE POINT OF COMPLIANCE

	General Population (49,770)	Nearby Residents (80)	Workers (150)
Current excess individual cancer risk from air[1]	-	3×10^{-4}	4×10^{-4}
Potential excess individual cancer risk from water, assuming all drinking water is obtained at the point of compliance[1]	9×10^{-4}	9×10^{-4}	9×10^{-4}
Total excess individual cancer risk[2]	9×10^{-4}	1×10^{-3}	1×10^{-3}
Upper-bound estimate of excess cancer cases over a lifetime[3]	42	0.09	0.2
Exposure (mg/kg/day)[4]	9.5×10^{-3}	1.3×10^{-2}	1.4×10^{-2}
MOE[5]	210	156	141

[1]Excess individual cancer risk obtained by multiplying the highest slope factor from Table 7 (0.0897 for DNC) by the units of exposure from Table 6.
[2]Total excess individual cancer risk obtained by adding excess individual cancer risks from air and water exposures.
[3]Obtained by multiplying total individual excess cancer risk by the estimated number of people exposed.
[4]Exposures for nearby residents and workers are based on current air exposures and estimates of future exposures from drinking water, assuming it is obtained at the point of compliance.
[5]MOE for DNC obtained by dividing the NOAEL (2 mg/kg/day) from Table 9 by the appropriate DNC air and water exposures from Table 6. If the MOE is less than 100, the exposure exceeds the RfD.

Issues to Be Considered

1. Are the results reported in Tables 10, 11, or 12 an adequate characterization of DNC risks? What else should be added?

2. Risks are presented at three points: the point of compliance, the eastern property boundary, and the public well field. What are the advantages and disadvantages of using each? Which one do you feel best represents the risks?

3. Should risks derived using other slope factors reported in Table 7 and slope factors obtained using alternative models also be discussed? How would you present these uncertainties?

4. The risks, MOE, and number of cases reported in Tables 10, 11, and 12 depend on the assumption that the number of people exposed and their level of exposure will remain constant over a lifetime. Is this a plausible assumption? Can alternative assumptions be used?

5. Is it important to distinguish routes of exposure? Should slope factors obtained from the gavage data be used for population groups exposed by inhalation? Should gavage data be used at all?

6. Is it appropriate to estimate the number of cancer cases by multiplying risk times population size? Which is more important--risk to an individual, or risk to a population?

7. Do you believe that animal data obtained from continuous, lifetime exposure should not be used to characterize the risk of people exposed by certain routes intermittently, for a relatively small fraction of their lifetime?

8. Is the RfD exceeded by any of the exposure levels? How do the risks from cancer compare with the risks from systemic health effects? Are they comparable?

9. How would you characterize the risks to the ecosystem? Would concern about ecosystem damages ever take precedence over concern about risks to human health?

Some Possible Conclusions
About DNC

Which of the following best characterizes the information you have seen?

1. Upper-bound excess cancer risks to humans exposed to DNC are those reported in Tables 10, 11, and 12. Although risks obtained from the use of other models are lower, the risks could be as high as those reported in the table. The risk of systemic health effects are properly represented by the RfD and MOE.

2. Same as Conclusion 1, except restrict estimates of excess risks for inhalation exposure to slope factors estimated from inhalation data, and restrict risks for ingestion to gavage data.

3. The excess cancer risks shown in Tables 10, 11, and 12 as well as those obtained from all other plausible models and all the various tumor site data should be reported, and all estimates should be given equal weight. Such a presentation affords the decision maker a view of the uncertainty in the estimated risks. In addition, a detailed discussion of the RfD should be provided.

4. Upper-bound estimates of excess lifetime cancer risks to humans are those reported in Tables 10, 11, and 12. Use of all other animal data sets and alternative cancer risk models used by some other agencies would result in prediction of lower cancer risks, perhaps up to 65 times lower. These risks are conditional on the assumption that DNC is a probable human carcinogen, based on observations of carcinogenicity in two species of experimental animals. Uncertainties in the exposure and population estimates are those described in the Exposure Assessment section.

5. DNC is a probable human carcinogen, based on observations of carcinogenicity in two animal species. Exposures needed to produce animal carcinogenicity are many times higher than those to which humans are exposed. The margins of exposure by which humans are protected from systemic health effects are shown in Tables 10, 11, and 12.

Some Possible Conclusions
About DNC (continued)

6. DNC is a probable human carcinogen, based on observations of carcinogenicity in two species of experimental animals. Humans are exposed to DNC through air and water. In general, large numbers of people will be exposed continuously to very low levels of DNC in drinking water, and a few groups are exposed to relatively high levels in air, some continuously, others intermittently. The individual cancer risk in the general (larger) population is probably low, and this translates to a very small number of cancer cases. The individual risk to nearby residents is moderate, and this also translates to a small number (<1) of excess cancer cases. The individual risk to workers at the plant is slightly higher than that of nearby residents, although because of the relatively small number of workers, this again translates to less than one excess cancer case expected in this group. In addition, potential exposures to all groups are below the RfD, indicating no significant risks of systemic health effects from DNC exposure.

7. Other? Some combination of the others?

Comparative Risks

An obvious question associated with the quantitative results presented in the risk characterization is, "are these big numbers or small numbers?" To help you think about this question, we have provided a list of some commonplace risks.

Table 2

SOME COMMONPLACE RISKS

(mean values with uncertainty)

Action	Lifetime Risk	Uncertainty
Motor vehicle accident (total)	1.7×10^{-2}	10%
Motor vehicle accident (pedestrian only)	2.9×10^{-3}	10%
Home accidents	7.7×10^{-3}	5%
Electrocution	3.7×10^{-4}	5%
Air pollution, eastern United States	1.4×10^{-2}	Factor of 20 downward only
Cigarette smoking, one pack per day	2.5×10^{-1}	Factor of 3
Sea-level background radiation (except radon)	1.4×10^{-3}	Factor of 3
All cancers	2×10^{-1}	10%
Four tablespoons peanut butter per day	6×10^{-4}	Factor of 3
Drinking water with EPA limit of chloroform	4×10^{-5}	Factor of 10
Drinking water with EPA limit of trichloroethylene	1×10^{-7}	Factor of 10
Alcohol, light drinker	1×10^{-3}	Factor of 10
Police killed in line of duty (total)	1.5×10^{-2}	20%
Police killed in line of duty (by felons)	9.1×10^{-3}	10%
Frequent flying professor	4×10^{-3}	50%
Mountaineering (mountaineers)	4×10^{-2}	50%

Source: Based on annual risks presented by Wilson and Crouch, Science, April 17, 1987.

Which, if any of these, are relevant to the situation at Electrobotics? Why?

GLOSSARY

Acceptable daily intake (ADI). Estimate of the largest amount of chemical to which a person can be exposed daily that is not anticipated to result in adverse effects (usually expressed in mg/kg/day).

Carcinogen. A substance that increases the risk of cancer.

Control animals. Animals that receive identical treatment as test animals, except exposure to DNC, for the purpose of observing the natural or background rate of cancer in that type of animal.

Dose. Measurement of the amount received by the subject, whether human or animal.

Dose-response evaluation. A component of risk assessment that describes the quantitative relationship between the amount of exposure to a substance and the extent of toxic injury or disease.

Dose-response relationship. The quantitative relationship between the amount of exposure to a substance and the extent of toxic injury produced.

Epidemiological study. Study of human populations to identify causes of disease. Such studies often compare the health status of a group of persons who have been exposed to a suspect agent with that of a comparable unexposed group.

Exposure. To be accessible to the influence of a chemical or chemical action.

Extrapolation. The estimation of a value beyond the known range on the basis of certain variables within the known range, from which the estimated value is assumed to follow.

Gavage. Type of exposure in which a substance is administered to an animal through a stomach tube.

Hazard evaluation. A component of risk assessment that involves gathering and evaluating data on the types of health injury or disease (e.g., cancer) that may be produced by a chemical and on the conditions of exposure under which injury or disease is produced.

<u>High-to-low-dose extrapolation</u>. The process of predicting low-exposure risks to rodents from the measured high-exposure, high-risk data.

<u>Human exposure evaluation</u>. A component of risk assessment that involves describing the nature and size of the population exposed to a substance and the magnitude and duration of exposure. The evaluation could concern past exposures, current exposures, or anticipated exposures.

<u>Human health risk</u>. The likelihood (or probability) that a given exposure or series of exposures may have or will damage the health of individuals experiencing the exposures.

<u>Incidence of tumors</u>. Percentage of animals with tumors.

<u>Interspecies extrapolation model</u>. Model used to extrapolate from results observed in laboratory animals to humans.

<u>Linearized multistage model</u>. Derivation of the multistage model, where the data are assumed to be linear at low doses.

<u>Margin of exposure (MOE)</u>. Maximum amount of exposure producing no measurable adverse effect in animals (or studied humans) divided by the actual amount of human exposure in a population. Previously this was called the margin of safety.

<u>Microgram (μg)</u>. One-millionth of a gram (1 μg = 3.5×10^{-8} oz. = 0.000000035 oz.).

<u>Milligram (mg)</u>. One-thousandth of a gram (1 mg = 3.5×10^{-5} oz. = 0.000035 oz.).

<u>Modifying factor</u>. An uncertainty factor, greater than zero and less than or equal to ten inclusive; its magnitude reflects professional judgment regarding aspects of the data used for the assessment; e.g., the number of species tested and the completeness of the overall database.

<u>Multistage model</u>. Mathematical model based on the multistage theory of the carcinogenic process, which yields risk estimates either equal to or less than the one-hit model.

<u>Neoplasm</u>. An abnormal growth of tissue, as a tumor.

<u>No observed adverse effect level (NOAEL)</u>. The highest experimental dose at which there was no statistically or biologically significant increase in a toxicologically significant endpoint.

One-hit model. Mathematical model based on the biological theory that a single "hit" of some minimum critical amount of a carcinogen at a cellular target--namely DNA--can initiate an irreversible series of events, eventually leading to a tumor.

Potency. Amount of material necessary to produce a given level of a deleterious effect.

ppb. Parts per billion.

ppm. Parts per million.

Reference dose (RfD). An estimate (with uncertainty spanning perhaps an order of magnitude or greater) of the daily exposure to the human population (including sensitive subpopulations) that is likely to be without appreciable risk of deleterious effects during a lifetime. The RfD is appropriately expressed in units of mg/kg/day.

Risk. Probability of injury, disease, or death under specific circumstances.

Risk assessment. The scientific activity of evaluating the toxic properties of a chemical and the conditions of human exposure to it both to ascertain the likelihood that exposed humans will be adversely affected, and to characterize the nature of the effects they may experience.

Risk characterization. Final component of risk assessment that involves integration of the data and analysis involved in hazard evaluation, dose-response evaluation, and human exposure evaluation to determine the likelihood that humans will experience any of the various forms of toxicity associated with a substance.

Risk management. Decisions about whether an assessed risk is sufficiently high to present a public health concern and about the appropriate means for control of a risk judged to be significant.

Route of exposure. Method by which the chemical is introduced into the biological organism.

Safe. Condition of exposure under which there is a "practical certainty" that no harm will result in exposed individuals.

Scientifically plausible. An approach or concept having substantial scientific support but without complete empirical verification.

Slope factor. The increased likelihood of an individual developing cancer from exposure to one unit of a substance over a lifetime (exposure measured as mg of the substance per kg of body weight per day--mg/kg/day).

Statistically significant. The difference in tumor incidence between the treated and control animals that is probably not due to chance.

Systemic effects. Effects observed at sites distant from the entry point of a chemical due to its absorption and distribution into the body.

Threshold dose. The dose that has to be exceeded to produce a toxic response.

Total dose. Sum of doses received by all routes of exposure.

Uncertainty factor. Factors used in operationally deriving the RfD from experimental data. These factors are intended to account for (a) the variation in sensitivity among the members of the human population; (b) the uncertainty in extrapolating animal data to the case of humans; (c) the uncertainty in extrapolating from data obtained in a study that is of less-than-lifetime exposure; and (d) the uncertainty in using LOAEL data rather than NOAEL data. Usually these factors are set equal to ten. See Table 1.

Unit cancer risk. The increased likelihood of an individual developing cancer from exposure to one unit of a substance over a lifetime (exposure measured as concentration in a particular media)

Upper-bound estimate. Estimate not likely to be lower than the true risk.

Appendix A

GROUND-WATER MODELING CALCULATIONS AND ASSOCIATED ASSUMPTIONS

<u>Predicted Concentration of DNC in Ground Water at Eastern Property Boundary and Public Well Field</u>

- Concentration in lagoon: 30 ppm (mg/l)
- Concentration measured at compliance point: 332 ppb (µg/l)
- Half-life of DNC in aquifer: 10 years = 3,650 days

  --Degradation rate of DNC = 0.693/half-life
  = 1.9×10^{-4} day^{-1}

  Distance from source to property boundary: 1,000 feet

- Travel time (T) from the source to property boundary:

$$T = \frac{[\text{distance traveled}] \times [\text{effective porosity}]}{[\text{hydraulic conductivity}] \times [\text{hydraulic gradient}]}$$

$$= \frac{1{,}000\text{ft} \times 0.2}{40 \text{ feet/day} \times 0.005} = 1{,}000 \text{ days}$$

- Steady-state concentration at property boundary:

  $[332 \text{ ppb}] \times \exp[(-1.9 \times 10^{-4} \text{ day}^{-1}) \times 1{,}000 \text{ days}]$

  = 275 ppb

- Distance from source to public well field:
  1.5 miles = 8,000 feet

- Travel time from the source to three threatened wells:

$$\frac{8{,}000 \times 0.2}{40 \text{ feet/day} \times 0.005} = 8{,}000 \text{ days}$$

- Steady-state concentration at the three threatened wells:

$$[332 \text{ ppb}] \times \exp[(-1.9 \times 10^{-4} \text{ day}^{-1}) \times 8{,}000 \text{ days}]$$

$$= 73 \text{ ppb}$$

- Steady-state concentration at actual point of exposure (drinking water supply):

  The three threatened wells provide 7.5 percent of total drinking water supply; therefore, the concentration at the actual point of exposure (the drinking water supply):

$$0.075 \times 73 \text{ ppb} = 5.5 \text{ ppb}$$

Appendix B

HUMAN DOSE CALCULATIONS AND ASSOCIATED ASSUMPTIONS

Inhalation of DNC-Contaminated Air by Neighboring Residents

Assumptions:

- An adult inhales 23 m^3/day of air.
- Based on wind direction analysis, the duration of exposure is 30 percent of time on an annual average basis.
- The body weight of an adult is 70 kg.
- The inhalation absorption factor for DNC is 0.75.
- The adult lives in the home throughout his lifetime.

Calculations:

$$\frac{0.044 \text{ mg}}{\text{m}^3} \text{ (average DNC air concentration at boundary)}$$

$$\times \frac{23 \text{ m}^3}{\text{day}} \times \frac{1}{70 \text{ kg}} \times 0.3 \text{ (human intake factor)}$$

$$\times 0.75 \text{ (inhalation absorption factor)}$$

$$= 3.3 \times 10^{-3} \text{ mg/kg/day}$$

Inhalation of DNC-Contaminated Air by Workers

Assumptions:

- An adult inhales 23 m^3/day of air.
- The body weight of an adult is 70 kg.
- The inhalation absorption factor for DNC is 0.75.

- The duration of exposure is 40 hours/week for a 30-year work period, or 10.2 percent of an average lifetime.

Calculations:

$$\frac{0.188 \text{ mg}}{\text{m}^3} \text{ (average DNC air concentration on-site)}$$

$$\times \frac{23 \text{ m}^3}{\text{day}} \times \frac{1}{70 \text{ kg}} \times 0.102 \text{ (human intake factor)}$$

$$\times 0.75 \text{ (inhalation absorption factor)}$$

$$= 4.7 \times 10^{-3} \text{ mg/kg/day}$$

Ingestion of DNC-Contaminated
Drinking Water at Point of Compliance

Calculations:

$$\frac{3.32 \times 10^{-1} \text{ mg}}{\text{liter}}$$ (measured DNC concentration in ground water at point of compliance)

$$\times \frac{2 \text{ liters}}{\text{day}} \times \frac{1}{70 \text{ kg}}$$ (human intake factor)

x 1 (ingestion absorption factor)

$= 9.5 \times 10^{-3}$ mg/kg/day

Ingestion of DNC-Contaminated
Drinking Water at Eastern
Property Boundary

Assumptions:

- An adult consumes 2 liters of water per day.
- The body weight of an adult is 70 kg.
- Absorption is 100 percent.
- The water is consumed throughout the adult's lifetime.

Calculations:

$$\frac{0.275 \text{ mg}}{\text{liter}}$$ (predicted DNC concentration in ground water at eastern property boundary)

$$\times \frac{2 \text{ liters}}{\text{day}} \times \frac{1}{70 \text{ kg}}$$ (human intake factor)

x 1 (ingestion absorption factor)

$= 7.8 \times 10^{-3}$ mg/kg/day

<u>Ingestion of DNC-Contaminated Drinking Water at Public Well Field</u>

Calculations:

$$\frac{5.5 \times 10^{-3}\ \text{mg}}{\text{liter}}$$ (predicted DNC concentration in ground water at public well field)

$$\times \frac{2\ \text{liters}}{\text{day}} \times \frac{1}{70\ \text{kg}}$$ (human intake factor)

$\times$ 1 (ingestion absorption factor)

$= 1.6 \times 10^{-4}$ mg/kg/day

Part II

MANAGING THE RISKS FROM DNC AT THE ELECTROBOTICS SITE

CONTENTS

I. INTRODUCTION

You have just finished analyzing the potential risks from DNC at the Electrobotics facility. Your working group must now decide what actions you will require of Electrobotics' owners to deal with the situation.

Your staff has reviewed several possible approaches to managing the risks. The first option was proposed by the owners of the facility; the other four were developed by your staff. This document briefly summarizes each option, presents its costs and economic impacts, and describes how it alters the risks at the Electrobotics site. In addition, Appendix A describes the hazardous waste treatment technologies available for use at the site.

After reviewing this information, you and your group must choose one of these approaches or develop an alternative of your own. Your choice will be incorporated into a first draft of the permit. Your recommendation is expected at the end of this meeting.

II. REGULATORY BACKGROUND

As discussed earlier, RCRA regulations require that hazardous waste facilities (such as Electrobotics' storage lagoon) be designed and operated in a manner that will prevent the leaking of hazardous waste into ground water. The regulations also require ground-water monitoring and corrective action if a problem is identified.

RCRA's ground-water protection standards require the Regional Administrator to establish in the facility permit a DNC concentration limit, beyond which degradation of ground-water quality is not allowed. The concentration limit determines when corrective action is required and is set at the point of compliance, immediately east of the storage lagoon.

Three possible concentration limits can be used to establish the ground-water protection standard:

- Background level of the hazardous constituent
- Maximum concentration limit (MCL) established by regulation
- Alternate concentration limit (ACL)

The background level and MCL are established in the facility permit unless the facility owner or operator applies for an ACL. In this case, the background level of DNC is zero, and no MCL exists for the solvent. An ACL may be available to Electrobotics' owners if they can demonstrate that the DNC will not pose a substantial present or potential hazard to human health or the environment.

To continue operating the lagoon, the regulations also require that Electrobotics' owners retrofit the lagoon to ensure no DNC leaches into the ground water. The owners of Electrobotics have proposed retrofitting the lagoon, which would require them to:

- Pump out the free liquids from the lagoon
- Excavate the contaminated soil
- Install "minimum technology" to ensure no DNC leaches into the ground water. In this case the owners would install a double liner under the lagoon.

An alternative to retrofitting the lagoon is to close it and install an above-ground storage tank. Existing regulations allow the owners to close the lagoon in one of two ways. They must either remove the hazardous waste and waste residues (clean close) or retain the waste and manage the lagoon as a land disposal unit.

The owners have been advised that, because of existing ground-water contamination, it is probably not possible to meet the standards for clean closure and terminate responsibility for hazardous waste management in the near future. As a result, your staff has developed a closure option based on the owners managing the lagoon as a land disposal unit and installing an above-ground tank. To comply with regulations for this option, the owners must:

- Eliminate the free liquids from the lagoon either by removing them from the impoundment or by solidifying them
- Stabilize the remaining waste and waste residues to support a final cover
- Install a final cover to minimize future infiltration into the lagoon
- Perform post-closure care and ground-water monitoring

You must now decide whether the facility's retrofitting plan is adequate and what actions to require of the owners to clean up both the lagoon and the associated ground-water contamination problem. You will not try to specify the particular concentration limits for the ground-water protection standard. You must only recommend the specific actions required at the site. You may accept the proposal from the owners, pick one of the options presented by your staff, or develop an alternative that you feel is more appropriate. Implicit in your decision, however, is the concentration limit.

III. OPTIONS

OVERVIEW

You must now evaluate five possible approaches to addressing the problem at the Electrobotics plant. The first is the proposal from the owners which involves retrofitting the lagoon. There are four alternative options that have been developed by your staff.

Proposal

The owners of Electrobotics have proposed retrofitting the lagoon. To accomplish this the owners would have to pump out the liquids from the lagoon, excavate any contaminated soil, and install a double liner under the lagoon to stop any leaching of DNC from the lagoon into the ground water. The type of liner to be used has been effective at test sites, although it is generally recognized that there is always the possibility that the liner will fail at some point.

The owners have proposed a limited retrofitting program which does not include any treatment of the current contamination of the ground water. They feel the current contamination of the ground water does not pose a substantial present or potential hazard to human health or the environment.

Alternative Control Options

The four options reviewed by your staff are described below. All four involve closing the lagoon and managing it as a land disposal unit. In addition, all four would require the owners of Electrobotics to install a new above-ground tank. The first involves installing a cap over the lagoon. The second option involves installing the cap and pumping and treating the contaminated ground water. The third option, which is somewhat more expensive, contains the elements of the first two options as well as the construction of a slurry wall around part of the lagoon. The last option requires the owners to excavate the material under and around the lagoon and pump and treat the contaminated ground water.

Option 1: Cap

This option requires the installation of a cap over the lagoon, which directly affects the lagoon but does not deal with the current ground-water contamination.

Scope

- De-water the lagoon and excavate any accumulated sludges, which requires removing any free liquids and managing them as hazardous waste
- Solidify any remaining sludges and refill the lagoon with clean fill
- Install a multimedia cap over the lagoon to prevent infiltration
- Maintain the cap and conduct post-closure monitoring and care

Uncertainties

- Long-term integrity of the cap and its effectiveness in preventing infiltration
- Continued source strength of chemicals, in or near the saturated zone, that are released by ground-water through-flow beneath the cap
- Extent of long-term monitoring and general post-closure care

Option 2: Cap/Pump and Treat

This option includes the cap described in Option 1 plus pumping and treating the contaminated ground-water plume with a carbon adsorption system.

Scope

The scope includes the items described for Option 1. In addition, the owners would have to:

- Conduct an additional hydrogeological study

- Install extraction wells and treat the ground water by carbon adsorption

Uncertainties

The same uncertainties as in Option 1 exist, with two additions:

- Length of time for operating the treatment system

- Effectiveness of ground-water extraction system in removing contaminated ground water

Option 3: Cap with Slurry Wall/Pump and Treat

Scope

This option is similar to Options 1 and 2 in that the lagoon would be capped in the same manner and the ground-water contamination corrected through pumping and a carbon adsorption treatment system. However, Option 3 would also include installation of a soil-bentonite slurry wall at the perimeter of the lagoon to prevent ground-water through-flow and further limit the movement of DNC from the saturated zone beneath the lagoon into the ground water.

Uncertainties

The same uncertainties as in Options 1 and 2 exist, with one addition:

- Long-term integrity of the slurry wall as a method of isolating both the contamination and the potential for future releases of DNC into ground water

Option 4: Excavation/Pump and Treat

Option 4 comes closest to completely eliminating any traces of DNC from the Electrobotics facility and the surrounding area. The current ground-water contamination would be corrected by pumping the ground water and treating it with a carbon adsorption system. In addition, the source of contamination would be controlled by excavating the soil around and under the lagoon.

Scope

- De-water the lagoon and excavate any accumulated sludges and liner material
- Test the underlying soil for chemical contamination and remove soil to the water table if DNC concentrations are above ground-water contamination levels
- Refill the excavation with clean fill and stabilize it with grass or other cover material
- Conduct an additional hydrogeological study
- Install extraction wells and treat ground water by carbon adsorption
- Conduct long-term monitoring and general post-closure care

Uncertainties

- Length of time for operating the treatment system
- Effectiveness of ground-water extraction system in removing contaminated ground-water plume

Issues to Be Considered

1. What are the key components of each option, and how do the options differ?

2. What is the nature of the uncertainties associated with each option? Which ones are most critical?

3. Which aspects of each option do you find most troublesome?

4. Are there other options that you think the Regional Administrator should consider?

ECONOMIC IMPACT OF OPTIONS

Adopting any one of the options discussed above would require cash expenditures by Electrobotics. A summary of the costs for each option is presented in Table 1.

Table 1

COSTS OF CONTROL OPTIONS FOR THE ELECTROBOTICS PLANT

	Present Value of Costs[1]	Annualized Costs[2] (costs per year)
Proposal		
Retrofit	$ 450,000	$ 48,000
Option 1		
Cap and Associated Costs	$ 600,000	$ 64,000
Option 2		
Cap and Associated Costs	$ 600,000	$ 64,000
Pump and Treat System	290,000	31,000
Total	$ 890,000	$ 95,000
Option 3		
Cap and Associated Costs	$ 600,000	$ 64,000
Slurry Wall	500,000	53,000
Pump and Treat System	220,000	24,000
Total	$1,320,000	$141,000
Option 4		
Excavation and Associated Costs	$2,400,000	$255,000
Pump and Treat System	220,000	24,000
Total	$2,620,000	$279,000

[1]Time sequence of costs is discounted at 10 percent.
[2]Present value of costs is annualized at a 10 percent interest rate over 30 years.

Electrobotics has a turbulent history and has been close to bankruptcy several times. Its recent performance, however, has improved, with revenues increasing from $1.5 million in 1980 to $7.5 million in 1986. Even so, the company was only marginally profitable in 1986, with after-tax profits of less than $50,000. We do not have a good forecast of 1987 revenues, although the computer industry as a whole has been performing poorly.

Electrobotics' owners feel they can, with great difficulty, pay the costs of their proposed retrofitting program and costs estimated for Option 1. They are adamant, however, that implementing Options 2, 3, or 4 would force them to declare bankruptcy; these three options would result in annual costs substantially greater than the company's 1986 after-tax profits.

If Electrobotics goes out of business, its 150 employees would have to find new jobs. This would worsen an already difficult situation in the town of Utopia, whose unemployment rate is among the highest in the country. In addition, Electrobotics has paid significant property taxes--about $120,000 in 1986--to the town.

Finally, if the Electrobotics facility were closed because of bankruptcy, it would have to be considered for addition to the National Priority List for cleanup as a Superfund site.

Issues About Economic Impacts to Be Considered

1. How accurate are the cost and economic impact estimates? How does the accuracy of the cost estimates compare with the risk estimates?

2. What additional information would you want? Are any key elements missing?

3. Is it appropriate to consider such factors as costs of the control options and economic impacts in deciding what will be required of Electrobotics' owners? Are any of the impacts large enough to rule out a particular option?

4. If economic considerations are to play a part in the decision making, should the focus be on the dollar costs of each option or on the impact of the option on the continuing viability of Electrobotics and the potential loss of jobs?

CHANGES IN RISK

Adopting the proposal or any of the alternative options identified above would reduce individual exposure to DNC and hence reduce the risk. However, the options do not reduce the risk to the same degree or with the same certainty. In addition, it is difficult to predict the changes in risk by predicting the reduction in concentrations resulting from the adoption of each option. Even so, your staff and the engineers hired by Electrobotics' owners have estimated the reduction in the DNC concentrations in the ground water and air, and the reduction in risk for each option.

A program of retrofitting the lagoon would reduce the risks associated with contaminated ground water. No more DNC would leach into the aquifer (assuming the double liner under the lagoon does not leak). The upper-bound estimates of excess lifetime risks for an individual receiving drinking water from the Eastern property boundary after the retrofitting program are presented in Table 2:

The retrofitting program will not eliminate the air risk associated with the lagoon. As a result, the risks to workers and nearby residents are higher than for the general population. The ground-water risks confronting the general population are estimated using an average concentration of DNC in the ground water over the next 70 years, assuming the retrofitting has been completed.

The upper-bound estimates of excess lifetime human risk for an exposed individual after implementation of one of the alternative control options are also presented in Table 2.

Table 2

UPPER-BOUND ESTIMATES OF EXCESS LIFETIME HUMAN RISK UNDER ALTERNATIVE CONTROL OPTIONS[1]

	Individual Risks[3]	
Proposal (Retrofit)	Eastern Property Boundary	Public Well Field
General Population	1×10^{-5}	2×10^{-7}
Nearby Residents	3×10^{-4}	3×10^{-4}
Workers	4×10^{-4}	4×10^{-4}
Alternative Control Options[2]		
1. Cap	1×10^{-5}	2×10^{-7}
2. Cap/Pump and Treat	1×10^{-6}	2×10^{-8}
3. Cap/Slurry Wall/ Pump and Treat	2×10^{-7}	4×10^{-9}
4. Excavate/Pump and Treat	1×10^{-7}	2×10^{-9}

[1]Risks are obtained by multiplying the highest slope factor estimate from Table 7 of Part I (0.0897 for DNC) by the estimated units of exposure after each option has been implemented.

[2]All four alternative control options eliminate any air risks from the lagoon. The remaining risks are attributable to the risks from DNC remaining in the ground water after completion of the control option. As a result, the risks remaining after implementation of an option are the same for the general population, nearby residents, and workers.

[3]The individual risks at the Eastern property boundary and the public well field are based on estimated average concentrations in the ground water at these points over the next 70 years. Your engineers have estimated that control options will reduce the concentrations of DNC in the ground water, and the associated risks, by 98 percent. Current risks at the Eastern property boundary and the public well field are zero.

The upper-bound estimates of excess cancer cases over a lifetime after implementing the retrofitting program or one of the alternative options are presented in Table 3:

Table 3

UPPER-BOUND ESTIMATES OF EXCESS CANCER CASES OVER A LIFETIME UNDER ALTERNATIVE CLOSURE AND CORRECTIVE ACTION OPTIONS[1]

(Cases based on drinking water consumption at the Eastern property boundary[2])

	Workers (150)	Nearby Residents (80)	General Population (50,000)	Total	Reduction in Upper-Bound Estimates of Excess Cancer Cases
Proposal (Retrofit)	0.06	0.02	0.5	0.6	34.54
Alternative Control Options[3]					
1. Cap	0.0015	0.0008	0.5	0.5	34.62
2. Cap/Pump and Treat	0.0015	0.00008	0.05	0.05	35.07
3. Cap/Slurry Wall/Pump and Treat	0.00003	0.000016	0.01	0.01	35.11
4. Excavate/Pump and Treat	0.000015	0.000008	0.005	0.005	35.12

[1]The estimates of excess cancer cases are obtained by multiplying the excess lifetime risk by the estimated number of people exposed.

[2]The cases are estimated assuming exposure at the Eastern property boundary. Estimated cases assuming exposure at the public well field would be significantly lower.

[3]All four alternative options eliminate any air risks from the lagoon. The estimated excess cancer cases for each option are attributable to the DNC remaining in the ground water after completion of the control option.

Electrobotics' owners are concerned about the air risks after reviewing the material prepared for their Part B application. In response, they have discussed installing a floating synthetic cover over the lagoon to control the air emissions in the short run. This would address some of the risks during the period of negotiation of the permit requirements. The cover would cost $10,000.

Remarks on Risks

1. The proposed approach, retrofitting, would not eliminate the air risks. All four of the alternative options would eliminate the risks from the air route of exposure.

2. Engineers working for Electrobotics' owners have argued that it is technically impossible to completely eliminate DNC from the contaminated ground-water plume. Your staff generally agrees that it is probably not possible to remove all traces of DNC, but feels that the risks could be reduced beyond the most stringent option (Option 4) with an extended pump and treat system. Extended pump and treat would involve increasing the length of time a pump and treat system is operated.

3. It is difficult to forecast the effectiveness of the retrofitting program, or any closure and corrective action option.

4. The four alternative options will eliminate volatilization of DNC from the lagoon. Some members of your staff have speculated that this could potentially increase the concentration of DNC in the wastewater sent to the wastewater treatment plant, which in turn could lead to concentrations of DNC in the treatment plant effluent.

<u>Issues About Changes in Risk</u>

1. Risk to an individual is:

   Excess Lifetime Risk = (slope factor) x (Units of Exposure)

   The allowable units of exposure for a given excess lifetime risk can thus be estimated as follows:

   $$\text{Units of Exposure} = \frac{\text{Excess Lifetime Cancer Risk}}{\text{Slope Factor}}$$

   If the excess lifetime cancer risk at the point of compliance is 1×10^{-6}, what is the associated DNC exposure?

2. What effect would installing the synthetic cover over the lagoon have on the risks from DNC, assuming the cover eliminated the air risks? What percentage of the estimated current excess cancer cases would be eliminated?

3. What are the key uncertainties associated with estimates of risk under each option? What additional information would you want on the effect of each option on the risk?

4. In light of the major uncertainties in the risk estimates, is it valid to compare the different options in terms of risk or reduction in risk?

5. Is it at all appropriate to consider the risk assessment results and the associated estimates of the changes in risk when evaluating possible options? Is a less quantitative and more qualitative approach preferred?

6. Should you balance the increased costs of Options 1, 2, 3, and 4 against the associated benefits (as measured by increased reductions in risk)?

7. What other approaches might be more appropriate?

IV. CONCLUSIONS

At this point, you and your working group should decide what actions you will require of Electrobotics' owners. You have information on a number of options, including the one proposed by the owners. You may accept the owners' proposal, choose one of the alternative options, or develop an alternative you feel is more appropriate. In addition, you may attach any caveats, qualifications, or modifications you wish. At the end of this meeting, you will present your results.

What do you recommend?

APPENDIX A

Overview of Hazardous Waste Treatment Technologies Available for Use at the Electrobotics Site

- Capping
- Installation of a Slurry Wall
- Ground-Water Extraction/Injection
- Carbon Adsorption
- In-situ Biological Treatment

CAPPING

After the lagoon has been dewatered and refilled with clean fill, it must be covered with a secure cap to prevent water infiltration, which could leach DNC from the fixed sludges in the fill. The primary steps in cap construction are layering impermeable material over the landfill, revegetation, and regrading the site.

Impermeable cover material for landfills can be clay, synthetic membranes or liners, or a combination of clay and synthetics. Hazardous waste landfills are usually capped with a sandwich of clay, synthetic liners, and topsoil for vegetation. According to the National Center for Ground Water Research's State-of-the-Art of Aquifer Restoration, synthetic materials (such as bituminous or Portland cement concrete barriers) or synthetic membranes (alone or in conjunction with clay barriers) may be preferable to soil-based systems when protecting high-risk wastes. After the chosen impermeable material has been placed on the site, the area should be covered with topsoil, seeded, and regraded.

Landfill caps, seemingly a good infiltration prevention measure, actually are subject to a number of problems. The problem that often appears first is erosion, which is exacerbated by the cap's impermeability function. (Rain hits the cap and, not being absorbed, carries off the maximum amount of soil.) Regrading techniques, such as terracing the topsoil and creating lined waterways and storage basins, help minimize this problem. Establishing vegetation early will also help control erosion by decreasing rain and wind impact on the cap. Grass should be planted first for a quick cover, and then shrubs and trees should be cultivated.

Other factors that affect clay caps in particular are changes in the fill, such as settling and freeze-thaw/wet-dry cycles, which can cause cracks. In the Midwest, these cracks can reach three to six feet, below commonly practiced cap and cover depths. Plants growing in the cracks can widen them further, as can burrowing animals. In addition, large plant tap roots can increase water infiltration in the cap. Cracks are most likely to form in systems where the clay has been combined with some other agents (e.g., lime, Portland cement, fly ash) to increase impermeability, because the clay and other mixture components do not settle at the same rate.

Synthetic membranes, on the other hand, can be affected by tearing if they are flexible and cracking if they are rigid, especially if differential settlement occurs in the fill. Installation of a smooth sand buffer can reduce the chance of flexible-liner puncture during cap construction. Concrete barriers are subject to both cracking and deterioration, especially in sulfate-rich environments. However, cracks in rigid membranes can be cleaned and sealed (most often with tar) fairly easily, giving rigid membranes an advantage over the flexible variety in the long run.

There is no foolproof method for sealing off a landfill. Therefore, all literature sources stress good initial planning and long-term management as the primary factors in maintaining the integrity of a landfill cap.

INSTALLATION OF A SLURRY WALL

Option 2 calls for the installation of a slurry wall at the lagoon's perimeter to prevent further movement of DNC by restricting ground-water movement under the contaminant source. A slurry wall is a civil engineering technique previously used primarily in construction; its recent use in Superfund sites has made it more popular with hazardous waste landfill operators. By far the most common slurry wall construction method is the trench method.

The first step in building a slurry wall using the trench method is digging a channel in the selected area. (Choosing where to place the wall requires study of the site and ground-water characteristics.) Excavation techniques include the backhoe method, which is good for shallow depths, and the dragline method, which is used for trenches that will be 30 meters or more deep. As the trench is dug, a slurry of 4 to 7 percent bentonite clay is recirculated through to support the channel walls and form a more impermeable soil structure. Bentonite is popular because it swells when wet and so restricts the flow of water through it. Digging usually proceeds a short way into the clay or bedrock underlying the aquifer.

Once the trench has reached the desired depth, it is solidified in one of two ways: backfilling with a mixture of bentonite and the excavated solid (the soil-bentonite, or S-B, method), or letting it solidify by itself by mixing cement with the original slurry (the cement-bentonite, or C-B, method). Choosing a solidification technique requires examination of the pros and cons of each. With the C-B method, there is no worry over availability of quality soil for backfilling, the cement sets quickly, and the trench can be constructed in sections. This method is also better for limited-access areas. The S-B method is cheaper (lower materials costs) and generally less permeable than the C-B, but it is not as strong as the C-B and requires continuous trenching in one direction. S-B trenches are used more often, primarily because of their low cost and low permeability.

Possible problems from slurry walls include inadequate construction and stress/strain forces, which can cause structural damage. Acids and sulfates in ground water can seriously degrade C-B trenches, and the permeability of S-B trenches can increase in the presence of certain organics, calcium, magnesium, heavy metals, and solutions of high ionic strength. Even if the walls do not degrade appreciably, some leakage through slurry walls is inevitable; permeability ranges from less than $1x10^{-8}$ cm/sec for an S-B trench to over $1x10^{-5}$ cm/sec for a C-B trench. A more complete list of the advantages and disadvantages of slurry walls is provided in Table 1.

Table 1

ADVANTAGES/DISADVANTAGES OF SLURRY TRENCHES

Advantages	Disadvantages[1]
1. Construction methods are simple.[1]	1. Shipping bentonite from the West is costly.
2. Adjacent areas are not affected by ground-water drawdown.[1]	2. Some construction procedures are patented and require a license.
3. Bentonite (mineral) will not deteriorate with age.[1]	3. In rocky ground, overexcavation is necessary because of boulders.
4. Leachate-resistant bentonites are available.[1]	4. Bentonite deteriorates when exposed to high-ionic-strength leachates.
5. Maintenance requirements are low.[1]	
6. Risks from pump breakdowns or power failures are eliminated.[2]	
7. Headers and other above-ground obstructions are eliminated.[2]	

[1]Tolman, et al., "Guidance Manual for Minimizing Pollution from Waste Disposal Sites," 1978.
[2]Ryan, "Slurry Cut-off Walls: Methods and Applications," 1980.

Source: National Center for Ground Water Research, State-of-the-Art of Aquifer Restoration, 1984.

GROUND-WATER EXTRACTION/INJECTION

To treat the contaminated ground water, extraction and/or injection wells must be dug. Carbon adsorption requires extraction wells; in-situ biodegradation requires both extraction and injection wells. The same basic sequence of steps is used to install either well type. The first step, drilling the hole, can be accomplished by one of several methods, depending on the site characteristics and economics. Next, casings and liners are installed, annular spaces are grouted and sealed, and well screens and other fittings are put into place. Finally, aboveground facilities (pump houses, etc.) are built.

Some information (e.g., plume size, aquifer characteristics) is necessary before the wells can be constructed. The depth within the aquifer to which each of the wells is drilled is a function of the plume location, which can stretch through the entire aquifer or remain close to the upper boundary. Hydrogeologists can determine plume dimensions as well as plume movement and the hydrogeological characteristics of the aquifer.

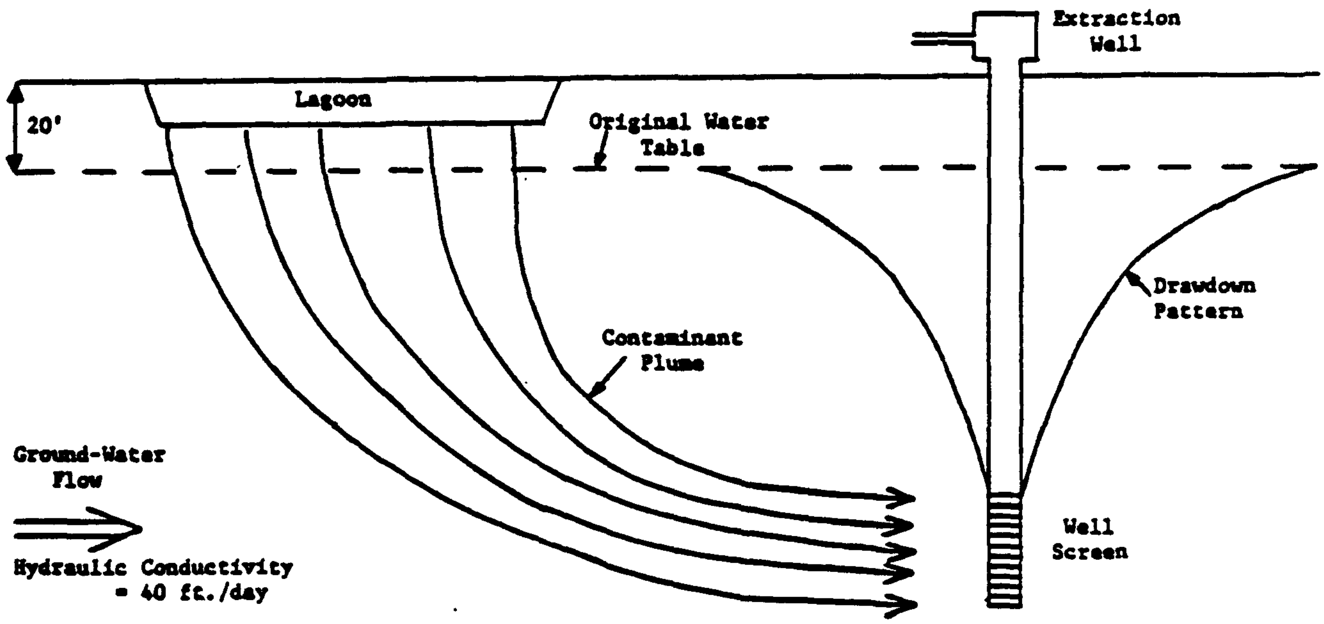
Within the injection and extraction categories, two types of well systems currently are in use. The first, well point systems, consists of a number of closely spaced, shallow wells that are connected to a main pipe, or "header." If water is being extracted, this header leads to a central suction lift pump, which draws the water to the surface. (Injection wells require a different type of pump to force water from the surface to the aquifer.) The main constraint on extraction well point operation is the suction pump, which cannot raise water more than 25 feet. Since the aquifer under Electrobotics is 20 feet below the surface, deeper wells may be needed. The second type of well system, deep well, can be used at greater depths than the well point system. Unlike well point, in which pumping is done for groups of wells, in the deep well system each well is individually pumped.

After the wells are sunk in the path of the plume and pumping starts, a number of things happen in the aquifer. As water is removed from the "zone of influence" around the well, the water level decreases, causing a change in aquifer flow patterns, or "drawdown" (see Figure 1). Wells are designed so that this drawdown intersects the plume. As water is pumped to the surface, plume movement away from the source stops and eventually reverses itself. The rate of extraction must be monitored carefully, as it is fairly easy to pump a well dry if pumping is done too fast. For injection wells, essentially the reverse happens:

water is pumped into the aquifer, and the water table rises, especially around the point of injection. This pushes the plume forward and increases the rate of ground-water flow.

Figure 1

Ground-Water Patterns due to Extraction Wells



Not drawn to scale.

CARBON ADSORPTION

As reported in the March 1986 edition of Pollution Engineering, biological methods are usually the chosen treatment for industrial and municipal waste waters, but "the low concentrations found in ground water . . . make air stripping and carbon adsorption the most widely used ground water treatment methods." The primary constraint on carbon adsorption is the concentration of the hazardous constituents. The concentration must be less than 1 percent for removal to be effective; at this level the ICF RCRA Risk-Cost Analysis Model estimates the efficiency of the process to be 99 percent (i.e., 99 percent of the contaminants in the influent are tied up in the carbon after treatment). Since DNC concentrations in the ground water are well below 1 percent, carbon adsorption should work well in removing the contaminants from the ground water.

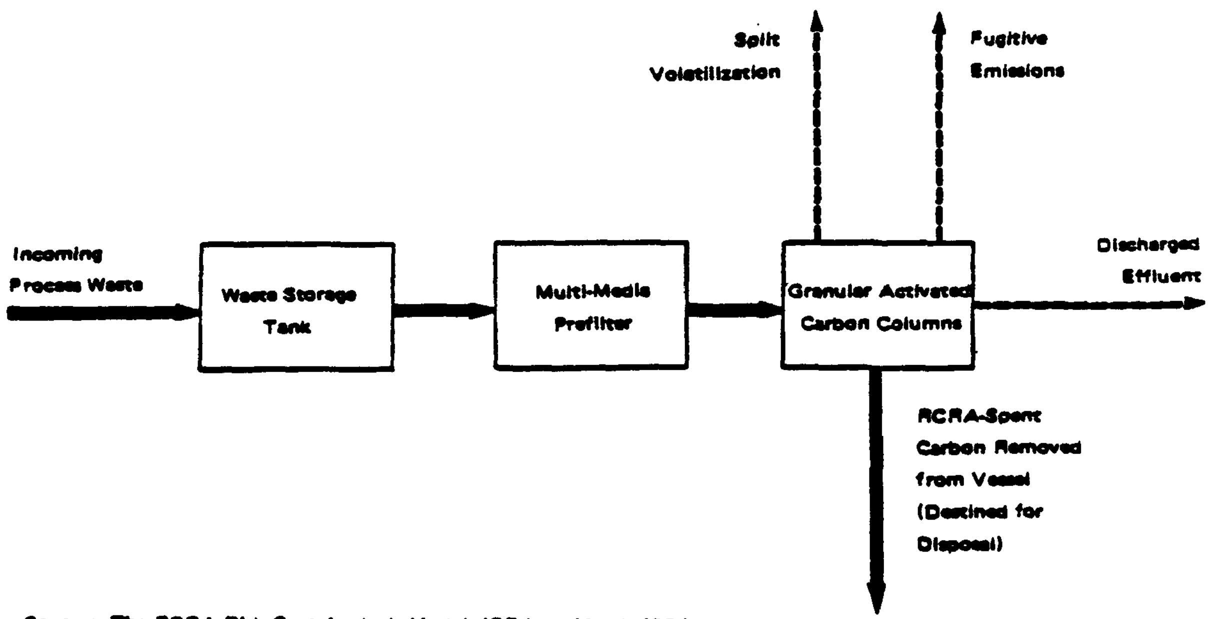
In carbon adsorption, activated carbon granules remove the organic contaminants from the waste water by attracting and holding the constituents onto their surface. Figures 2 and 3 display two slightly different treatment trains for this option. The train selected depends on the amount of carbon used per day: For amounts exceeding 400 pounds per day, it is more economical to recycle the carbon; otherwise, the carbon is placed into containers and disposed of.

The basic treatment steps outlined in Figures 2 and 3 are the same. Contaminated ground water flows from the storage tank into a prefilter. The prefilter removes excess suspended solids, oil, and grease, which can interfere with the adsorption process by clogging the surface of the carbon particles. After this pretreatment, the waste is directed to the activated carbon tank, where the organics are transferred to the carbon granules. The ICF model has determined that the average carbon adsorption capacity is 5 pounds of organics per 100 pounds of carbon; however, this value can vary with the compound being adsorped. (Adsorptivity increases with decreasing solubility.)

As mentioned above, the exhausted carbon is then recycled, or regenerated if over 400 pounds are used per day. (The ICF model estimates that only 90 percent of exhausted carbon can be regenerated; the remaining 10 percent must be made up with fresh carbon.) Regeneration can be performed using heat, steam, or solvents. Thermal regeneration, the most common method, destroys the organics on the carbon but leaves a low-concentration, gaseous emissions stream. Figure 3 depicts the equipment necessary for regeneration (two storage tanks for spent and regenerated carbon and a multiple-hearth furnace). The furnace should destroy most of the organics. (The ICF assumes 99.993 percent; the remaining 0.007 percent will appear in the emissions stream.)

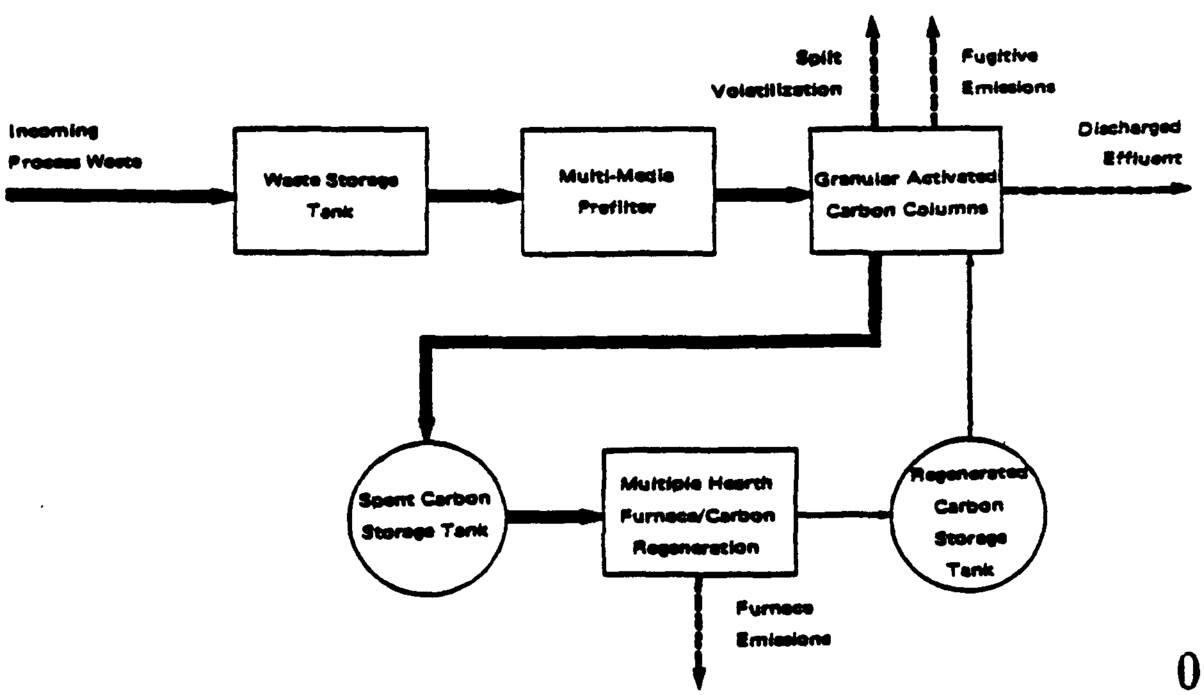
Contaminant releases during the adsorption process can occur through air releases from the furnace as well as from discharge of the treated effluent, which contains approximately 1 percent of the original amount of organics. In addition, contaminants are discharged into the air from vessel failures and/or spills (estimated in the ICF report to occur at a rate of 0.000013 releases per year) and to a lesser degree from pumps, valves, and flanges.

Figure 2
CARBON ADSORPTION FLOW DIAGRAM
(carbon consumption less than 400 pounds per day)



Source: The RCRA Risk-Cost Analysis Model, ICF Inc., March 1984.

Figure 3
CARBON ADSORPTION FLOW DIAGRAM
(carbon consumption greater than 400 pounds per day)



Source: The RCRA Risk-Cost Analysis Model, ICF Inc., March 1984.

IN-SITU BIOLOGICAL TREATMENT

Another method of contaminant treatment advanced by Superfund is in-situ biodegradation, in which the waste is biodegraded in the aquifer by indigenous or added microorganisms to produce carbon dioxide, water, various intermediates, and new cell biomass. The two main techniques used are modifying the environment to enhance microbial activity and altering the microbial population by seeding with microorganisms that have already been acclimated to the pollutants to be degraded. Environmental modification is currently the more popular and more effective technique.

Enhancing the indigenous microbial population involves the addition of nutrients and/or dissolved oxygen. A number of steps are involved. First, the extent of ground-water contamination, site hydrogeology, and other characteristics is examined. Various environmental factors control biodegradation, including pH, temperature, oxidation-reduction potential, salinity, availability of nutrients, dissolved oxygen level, and concentration of contaminants. Next, researchers must determine whether native microorganisms will degrade the spill. If biodegradation is possible, researchers must then find the nutrient/dissolved oxygen levels that will yield maximum cell growth over a set time period at ground-water temperature. Possible nutrient choices are nitrogen, phosphorus, and inorganic salts such as ammonium sulfate, magnesium sulfate, sodium carbonate, ferrous sulfate, and calcium chloride. Nutrients are added at concentrations of 0.005 percent to 0.02 percent by weight; this can result in tons of nutrients being added before treatment is complete.

Once the optimal nutrient/dissolved oxygen levels have been calculated, the well system for injecting the nutrients and oxygen and recirculating them in the aquifer is designed and constructed. Extraction wells are used to draw water for recirculation out of the aquifer, while injection wells are used to force the nutrients, oxygen, and drawn water into the aquifer. Recycling contaminated water for mixing purposes is recommended, as it eliminates problems of waste disposal and permits recirculation of unused nutrients. Wells should be placed at the beginning of the plume so that the nutrients move with the ground water through the contaminated zone.

After the equipment has been set up, the nutrients and oxygen are added. Nutrients can be supplied using either a batch or a continuous process. Generally, the batch process has yielded better results and is more economical. Oxygen is added by forcing air through the wells with diffusers. The advantages and disadvantages of microbial enhancement are listed in Table 2.

Table 2

ADVANTAGES/DISADVANTAGES OF IN-SITU BIODEGRADATION BY MICROBIAL ENHANCEMENT

Advantages	Disadvantages
1. Useful for removing low levels of organic compounds that are difficult to remove by other means.	1. Does not degrade some organics.
2. Environmentally sound (no waste products, uses indigenous microorganisms).	2. Introduction of nutrients could adversely affect nearby surface water.
3. Fast, safe, and generally economical.	3. Residues left in ground water may cause taste and/or odor problems.
4. Treatment moves with the contaminant plume.	4. May be slower than physical recovery methods under certain conditions (e.g., high pollutant concentrations).
5. Good for short-term treatment.	5. Could be expensive if long-term oxygen/nutrient injection is necessary or if equipment maintenance costs are high.
	6. Long-term effects are not known.
	7. Bacteria can plug soil and decrease circulation.

Source: National Center for Ground Water Research, State-of-the-Art of Aquifer Restoration, 1984.

The second technique, adding microorganisms that have been acclimated to the pollutants, is not yet completely successful but has good potential for the future. In this procedure, researchers test a variety of microbes to determine which will best degrade the contaminants. The chosen microbes are used instead of (or in addition to) the indigenous population. It is also possible to genetically alter microorganisms to get strains that will work even better; this, however, is still in the experimental stage.

Since in-situ biodegradation is so new, there is little information on its efficiency. According to the National Center for Ground Water Research's State-of-the-Art of Aquifer Restoration, in-situ biodegradation of organic solvents has been "fairly effective." More research still needs to be done, but this technology has been used with positive results in the past and holds great promise for the future.